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Contributions of Human Enzymes in Carcinogen Metabolism

Slobodan Rendic[1,*] and **F. Peter Guengerich**[2]

[1]University of Zagreb, Zagreb, USA 37232-0146

[2]Department of Biochemistry and Center in Molecular Toxicology, Vanderbilt University School of Medicine, Nashville, Tennessee, USA 37232-0146

Abstract

Considerable support exists for roles of metabolism in modulating the carcinogenic properties of chemicals. In particular, many of these compounds are procarcinogens that require activation to electrophilic forms to exert genotoxic effects. We systematically analyzed the existing literature on metabolism of carcinogens by human enzymes, which has been developed largely in the past 25 years. The metabolism and especially bioactivation of carcinogens are dominated by cytochrome P450 enzymes (66% of bioactivations). Within this group, six P450s—1A1, 1A2, 1B1, 2A6, 2E1, and 3A4—accounted for 77% of the P450 activation reactions. The roles of these P450s can be compared with those estimated for drug metabolism and should be considered in issues involving enzyme induction, chemoprevention, molecular epidemiology, inter-individual variations, and risk assessment.

INTRODUCTION

Knowledge that chemicals can cause cancer goes back to at least 1761 with the report by Hill[1] that the use of tobacco snuff was related to oral cancer in humans. More than 100 years ago, Rehn[2] reported an association of bladder cancer with occupations in the so-called aniline dye factories. Experimental studies in animals showed that chemicals cause cancer, beginning with reports on coal tar in rabbits by Yamagiwa.[3] Classic studies with the polycyclic aromatic hydrocarbon benzo[*a*]pyrene followed.[4] Fieser[5] and others had suggested that metabolism (of carcinogens[1]) plays a role in cancer, and extensive animal studies by James and Elizabeth Miller[6-8] validated the concept (Figure 1). Incorporation of the capability for metabolism led to the success of the bacterial Ames test[9] for mutagenicity and testing for carcinogenic potential.

The roles of individual enzymes in carcinogen metabolism has been studied extensively, and roles of many human P450s in carcinogen activation have been characterized.[10] Much of this work was first done in medium-throughput screens, e.g. bacterial genotoxicity, and then extended with more detailed studies of reaction products and DNA adducts.[10-13] Studies with P450s led the way but similar approaches have been used with other enzymes known to have roles in the metabolism of xenobiotic chemicals.[14,15] Research in this area has been important in several applied disciplines and approaches. These include molecular epidemiology, which is an attempt to relate risk from carcinogens to the enzymes present in an individual.[16-18] Another area of interest is chemoprevention, where a major strategy involves either inhibiting enzymes that activate carcinogens or inducing enzymes that inactive them.[19,20]

[*]Address correspondence to: Slobodan Rendic, Ph. D., Haulikova 6, HR 1000 Zagreb, Croatia, slobodanrendic@yahoo.com.

Several efforts have been made to delineate the levels of expression of individual enzymes, especially P450s, in humans.[21] Another approach is to analyze the fractions of the enzymes involved in reactions. Such analyses have been reported for drugs, for all "xenobiotic-metabolizing enzymes"[22,23] and for P450s.[22-25] The analyses are rather consistent with each other and generally accepted, both with marketed drugs and new chemical entities (drug candidates). Of particular note are the findings that i) ~75% of enzymatic reaction with drugs are catalyzed by P450s,[23] ii) ~90% of the P450 reactions can be accounted for by a set of five P450s: 1A2, 2C9, 2C19, 2D6, and 3A4,[23-25] and iii) the largest fraction of the P450 reactions are catalyzed by P450 3A enzymes, particularly P450 3A4.[23-25]

To our knowledge, there has not been a similar effort to categorize all of the the human enzymes involved in the metabolism of carcinogens. We thought that this would be a useful exercise in the light of continuing scientific interest in chemical carcinogenesis, cancer chemoprevention, and molecular epidemiology of cancer. We report our analysis of the literature in parts—general chemicals (environmental/industrial),Footnote 1 drugs, and natural/physiological compounds—as well as an overall analysis of all literature carcinogens for which information about metabolism is available. The results show a dominant role for P450s, especially the three Family 1 P450 enzymes (1A1, 1A2, 1B1) and P450s 2A6, 2E1, and 3A4 (Figure 2). The aldo-keto reductase (AKR) enzymes are also highly represented.[26]

ASSIGNMENTS OF ROLES OF ENZYMES

Most of the literature on the roles of human enzymes in carcinogen metabolism has been developed in the last 25 years, e.g. a review by one of us in 1988[27] had only a very limited discussion of this aspect. The present literature analysis is a continuation of the work done by one of us (S. Rendic) on literature searches on the metabolism of drugs and other chemicals catalyzed by human P450s, for more than 15 years ending in February 2012. Extensive key-word literature searches were done using the PubMed database, accessing the MEDLINE database of references and abstracts. In the latter stages, the existing literature on metabolism of carcinogens and the original papers was systematically analyzed, extracting those data contributing in a "significant way" to the activation and/or detoxication of general chemicals, drugs, and physiological compounds. (This is a qualitative evaluation, and the reader is referred to a more comprehensive list in Supporting Information Table S1.)

The results are presented in several tables (Tables 1-4), including activation reactions with all chemicals (Table 1) (exclusive of "weak" reactions), followed by the activation of physiological/natural compounds (Table 2) and drugs (Table 3). Detoxication reactions are presented in Table 4. For convenience, PMID numbers of references are included in the tables to facilitate searches and retrievals. In considering the results for all types of metabolism, it is clear that P450s are dominant. The three activation tables (Tables 1-3) contain only data for what are deemed "significant activation". All activation data (potent and weak) are presented as a single table in the Supporting Information (Table S1).

The classification of compounds into Tables 2 and 3 is somewhat arbitrary. Most of the data on activation of carcinogenic chemicals is with "chemicals" and only a limited amount with drugs and physiological compounds/natural products. We selected some compounds found in nature that are known to be carcinogens under some conditions, e.g. estrogens. Natural products are included (although one could also consider the PAHs to be natural, too). The set of drugs is mainly those used to treat cancer by DNA alkylation, topoisomerase poisons,

Footnote 1: For convenience we will use the term "carcinogens" to refer to both carcinogens that act directly (e.g., modifying DNA) and to procarcinogens (i.e., those that require metabolism to be converted to act on biological targets). In the tables the term "chemicals" is used for those chemicals that are not drugs or natural products.

etc. These compounds are often tumorigenic themselves and have been included. The term "chemicals" is used to describe these components that do not fit well into the natural product or drug classification. Even here there is room for change, e.g. many of the nitrosamines can be formed from secondary amines *in vivo*.

Another point that should be made is that we use the term carcinogen broadly, including some compounds that are "cancer suspects" and might have caused cancer at very high doses in experimental animal models. Inclusion in the tables here does not necessarily carry an endorsement as a human carcinogen for any regulatory purposes. Some of the compounds cited here are used effectively as drugs, and some are physiological compounds known to be important in normal homeostasis, e.g. estrogens.

The analysis of greatest interest is the activation of chemical carcinogens, and the results are summarized in Figure 2 as well as in Table 1, the main point of this review. The most striking aspect is the dominant role of the P450 enzymes. Interestingly, beyond these the AKR enzymes have a role that exceeds that of any other enzyme group, driven by their reported roles in PAH activation to quinones.[485]

Of the P450s, six P450s—1A1, 1A2, 1B1, 2A6, 2E1, and 3A4—account for 77% of the reported activations (Figure 2B). The Family 1 enzymes are prominent in the activation of PAHs and heterocyclic aromatic amines, plus arylamines and a variety of other compounds. The values for P450s 2A6 and 2E1 are driven by their roles in the metabolism of *N*-nitrosamines and a variety of low M_r commodity chemicals, including several vinyl monomers.[282]

INTERPRETATIONS OF THE ASSIGNMENT RESULTS

Activation *vs.* Detoxication

We have presented separate tables for activation (Tables 1-3) and detoxication of carcinogens (Table 4). However, distinguishing a role for an enzyme in this regard may be difficult. E.g. there is the classic case of the action of epoxide hydrolase in benzo[*a*]pyrene activation (Figure 3).[486] Another example has a single enzyme forming two different products from the same substrate, the P450 3A4-catalyzed oxidation of AFB_1 to AFQ_1 (3-hydroxylation, detoxication) and AFB_1 8,9-*exo*-epoxide (activation) (Figure 4).[176] The activation of the anticancer drug ellipticine is catalyzed by cyclooxygenases, peroxidases, and P450 enzymes (Tables 1, 2). Hydroxylations at positions C12- and C13, as well as N2-oxidation, are associated to the activation of ellipticine to toxic metabolites. These reactions are catalyzed mainly by the P450 1A1, 1A2, 1B1, and 3A4 enzymes. The same P450 enzymes catalyze detoxication of ellipticine by hydroxylation at the C7- and C9-positions, and the major enzymes considered are P450s 1A1 and 1A2 (Table 4). It has been reported that the balance of activation *vs.* deactivation of this drug is dependent on cytochrome b_5, in that cytochrome b_5 enhances production of 12-hydroxy and 13-hydroxyellipticine and thus changes the product ratio in a favor of increased formation of covalent ellipticine-DNA adducts. The effect of cytochrome b_5 might be even more pronounced *in vivo*, in that it has been reported that ellipticine increases levels of cytochrome b_5 in rat liver.[39,187,189]

Another issue involves tissue selectivity. As a case in point, GSH transferases catalyze the conjugation of bifunctional electrophiles (e.g., ethylene dibromide, Figure 5) with GSH to form half-mustards and then episulfonium ions.[377] These reactive species can react with DNA and are considered to be involved in chemical carcinogenesis. However, if such reactions occur in erythrocytes there is no DNA and this might be considered a detoxication.

Selectivity of activation *vs.* detoxication reactions is observed in the acetylation of *N*-hydroxy heterocyclic and aromatic amines (Table 1 *vs.* Table 4). The vast majority of heterocyclic amines do not undergo detoxication by *N*-acetylation because most heterocyclic amines are poor substrates for NATs. These compounds do undergo bioactivation by NATs via *O*-acetylation, following P450-mediated *N*-oxidation of the exocyclic amine groups. In contrast to heterocyclic amines, many aromatic amines do undergo detoxication by *N*-acetylation with NATs.

As mentioned before, chemical carcinogens are activated by a number of enzymes, of which the major ones are P450, SULT, AKR, and NAT (Figure 2 and Table 2), while the data on activation of natural/physiological compounds show that primarily P450 (92%, of which the major ones are 1A1, 1A2, 1B1, and Subfamily 3A) and SULT (8%) enzymes participate in their activation (Table 3). Similarly to general chemicals, drugs are activated by P450s (76%), SULT (12%), LPO (7%), and COX (5%) enzymes. Major P450 enzymes assigned are 3A4 (20%) and 1A2 (11%), and participation of others is low (Table 2).

When considering activation vs. detoxication reactions for a specific compound and/or reaction, attention should be given to the experimental conditions applied and the properties of the compounds and metabolites formed. For instance, 2-nitroanisole is (under oxidative conditions) detoxicated by C2-, C5-, and C6-hydroxylations catalyzed by P450 2E1, 1A1, and 2B6 enzymes (2E1 being the major one). However, under anaerobic conditions activation by nitroreduction prevails due to catalysis by XOR. In addition, 2-nitroanisole and its metabolite 2-nitrophenol induce P450 1A2 and NQO1 (in rats), thus providing the possibility to influence their own detoxication and/or activation pathways.[423,424]

Our approach here has been to list enzymes under both activation and detoxication in cases that are deemed to be duplicative.

Influence of the Diversities of Different Chemical Classes

In making the assignments shown in Figure 2, the number of compounds available can be considered a contributor to the reported results. For instance, it is known that P450s 1A1 and 1B1 (and AKR enzymes) can oxidize many PAHs.[220,485,486] Many of these are available, given the long-standing interest in individual PAHs,[4] and have been tested with P450s.[41,109,229] Likewise, many arylamines and heterocyclic aromatic amines are known and have been tested with P450 1A2.[12] Further, many *N*-nitrosamines (and vinyl monomers) have been tested with P450s 2A6 and 2E1.[247,282] It is possible that, in the future, the availability of a large number of analogs in another class of carcinogens might lead to more testing and shift the balance of the results in Figure 2.

Another point to be made here is that our classification includes compounds shown to be pro-mutagens, to bind covalently to DNA, etc. We do not have evidence that all of the compounds listed in our tables actually cause tumors in experimental animals or humans, although we believe that there is a likelihood that they do at some dose (readers are referred to the National Toxicology Program, International Agency on Cancer Research, and other sources for *in vivo* cancer results and classifications of human carcinogens).

Types of Reactions

Another analysis involves the type of reactions involved in bioactivation reactions (Figure 6). As seen there, 11 reactions account for 94% of the total, each representing 5-12%. The *O*-acetylation and *O*-sulfonation conjugation collectively account for 18%. Nitroreductions (6%) plus other reductions (0.3%) constitute 6.3%. Most of the other reactions are oxidations, together accounting for ~ 73%. Of these, *N*-hydroxylation (10%) and *C*-hydroxylation (11%) are the most prominent.

The results support the general view that there are many ways to activate procarcinogens (Figures 1, 3-5). As with the classification by enzymes (*vide infra*) there are caveats about representation based on the number of compounds experimentally available.

We have not analyzed the entries in Table 1 in the context of the chemical nature of the substrate, but this is rather obvious from the nature of Figure 6. Epoxidations involve olefins and aryl rings, nitro reductions involve nitro groups, *N*-hydroxylations involve arylamines and heterocyclic amines (*O*-acetylation involves the products), and *O*-sulfonation involves hydroxylarylamines and benzylic allylic alcohols. C^{α}-Hydroxylation is prominent for *N*-nitrosamines. Thus, a single group of chemicals does not dominate.

Weaker Activations

Several enzymes and their reactions have been included in the analyses, although the evidence for significance of their roles in rather weak. There was not a logical reason to delete these from our analysis nor a means of setting a strict benchmark for strong *vs.* weak roles because of the diversity of assays used. Further, “weak activation” (included in Table 1) might become “activation” or “potent activation” either following ingestion of certain enzyme inducers and/or the expression of a more active variant of the enzyme, as exemplified in several animal models.[27]

In this regard, we had reported a major role for P450 2C9 in benzo[*a*]pyrene 3-hydroxylation in human liver.[430] Although this reaction has been studied for many years and is the basis of the classic “AHH” activity,[487] it is generally not considered to be a bioactivation process, especially in liver. P450 enzymes such as those in the P450 2D6 and Subfamily 2C have been tested for several activities and do have low levels of activity (Table 1), but there is little if any evidence that these drug-metabolizing enzymes have major roles in chemical carcinogenesis in humans.

Similar points can also be raised about the activation of AFB_1. Although a number of forms of human P450 have some capability of activating AFB_1 (Table 1),[139] the evidence is very limited that most of these have relevance. The established target of AFB_1 in the liver, and enzymes that are predominantly expressed in other tissues are not very relevant. The existing literature clearly shows roles of primarily two P450s, 3A4 and 1A2.[432,443,488] P450 3A4 forms the highly mutagenic *exo*-8,9-poxide; P450 1A2 forms a roughly equimolar mixture of the dangerous *exo*-plus the *endo*-epoxide, the latter of which is essentially non-genotoxic.[176,432,489] The situation is complicated in that both of these enzymes also catalyze AFB_1 detoxication reactions, 3α-hydroxylation in the case of P450 3A4 (AFQ_1) and 9a-hydroxylation in the case of P450 1A2 (AFM_1).[176]

The information presented in this review is relevant in the context of translational studies. A case in point involves P450 2D6 and lung cancer. The interest began even before the characterization of P450 2D6, with a report that individuals with lung cancer showed a low representation of phenotypically poor metabolizers of debrisoquine, subsequently confirmed as a P450 2D6 prototypic substrate.[490] These results led to the consideration of the hypothesis that P450 2D6 is involved in the bioactivation of a major carcinogen leading to lung cancer. The level of P450 2D6 in lung tissue is low,[491] but it is conceivable that systemic exposure to an entity produced in the liver could be involved. However, attempts to identify a major role of P450 2D6 in the activation of carcinogens have been resoundingly negative.[492,493] Further, studies on the genotoxicity of crude cigarette smoke condensates and liver microsomes showed a role for P450 1A2 but not P450 2D6, based on the use of inhibitors etc.[149]

An alternate hypothesis, given the lack of evidence for a role of P450 2D6 in bioactivation of carcinogens, is that the *CYP2D6* gene is linked to the expression of an oncogene. However, no evidence for this hypothesis exists and the known major genetic defect regulating P450 2D6 is aberrant RNA splicing, which is not likely to involve co-regulation of nearby genes.[494] Additional epidemiology studies have generally not confirmed a major effect of P450 2D6 expression related to any kind of lung cancer.[495,496] In our opinion, resources could be used more effectively if sound experimental studies preceded expensive epidemiological studies with marginal bases of biological causality.

Analysis of Enzymes Involved in Detoxication

Analysis of the data on detoxication is presented in Figure 7. GST and UGT reactions account for > 50% of the reactions, which is not surprising. Two other transferases, NAT and COMT, are also prominent. The fraction attributed to AKR reactions is surprisingly high. Also surprising is the low fraction attributed to epoxide hydrolase, which seem surprising in light of the notoriety of epoxides in toxicology and drug metabolism circles.[497] However, epoxide hydrolase is rather ineffective in hydrolyzing some of the most reactive epoxides[498] and AFB_1 8,9-epoxides.[433] However, the roles of epoxide hydrolase and sulfotransferases in detoxication may be underestimated because of the nature of the reactions that have been reported to date with the human enzymes. We suspect that there is more literature using animal epoxide hydrolases that has not been re-done with the human enzymes, and the overall picture (Figure 7) might be misleading. The results of Figure 7 can be contrasted with those in Figures 2 and 6, when the SULT enzymes figure in many bioactivation reactions. However, judging sulfotransferases to be primary bioactivation enzymes, as opposed to detoxication, may not be a proper conclusion. P450s are involved in ~ 14% of the detoxication reactions with carcinogens (Figure 7), but this estimate may not be accurate. As with all of the enzymes of interest here, the assays for bioactivation (e.g. Ames test, umu assays, covalent binding) are often easier to set up than those that would accurately measure detoxication, and the literature may be misleading as to the relative importance of the detoxication enzymes.

Potential Roles of “Orphan” Enzymes

The analysis of enzymes and P450s (Figure 2) is based on existing knowledge (of the enzymes, as well as the carcinogens), and the pattern might change with time. With the (human) P450s, ~ 1/4 can still be considered “orphans,” in the sense that limited information is available about their catalytic activities and their roles in physiological processes.[499] Further, only limited information is available about roles in carcinogen metabolism. An exception in this regard is P450 2W1, which has been shown (like P450 1B1) to activate several classes of carcinogens.[210] Of interest is the reported expression of P450 2W1 only in tumor tissue.[500] Another orphan P450, P450 4F11, was found not to have appreciable activity towards any carcinogens tested.[501]

The role of P450 2S1 in the activation of carcinogens is controversial, as well as almost all other potential substrates. Following the initial discovery of human P450 2S1,[502] it was reported that the enzyme would oxidize naphthalene.[503] However, this report was not confirmed and no evidence for a role of P450 2S1 in the activation of any carcinogens was seen.[210] Further, the only substrate reported and independently confirmed for P450 2S1 is the drug candidate 1,4-bis{[2-dimethylamino-*N*-oxide)ethyl]amino}-5,8-dihydroxyanthracene-9,10-dione (AQ4N).[504,505] Some carcinogens can be activated by P450 2S1 in the presence of oxygen surrogates (hydroperoxides)[506,507] but the significance of these reactions is unknown, in that P450 2S1 has been demonstrated to be rapidly reduced by NADPH-P450 reductase in the usual manner.[505] Nevertheless, expression of P450 2S1 in

a mammalian cell line did lead to the formation of products of benzo[*a*]pyrene, indicating some mechanism of function.[506,507]

A number of the other P450 orphans have been expressed[508] but apparently roles in carcinogen metabolism have not been investigated. This same statement can be applied to other enzymes under consideration, regarding recently discovered gene products.

We should point out that our analyses are based largely on studies done with the "wild type," or most abundant genetic variants, in the human population. A treatment of all of the implicaitons of variations is beyond the scope of this review and indeed the catalytic efficiencies of only a subset of the variants of these enzymes has been determined with any substrates (e.g., http://www.cypalleles.ki.se/) and few with carcinogens. However, if a racial group exists in which the frequency of a fuctional polymorphism is high, then the balance of enzyme involvement (e.g., Figure 2B) could be shifted.

COMPARISONS OF PATTERNS FOR THE METABOLISM OF DRUGS AND CARCINOGENS

We[25,509-512] and others[22-24] have presented compilations of the roles of P450s and other enzymes involved in the metabolism of drugs. Comprehensive and up-to-date information on the metabolism of chemicals (including drugs and physiological compounds) in humans and animal models is available in a form of Web searchable absorption-distribution-metabolism-excretion (ADME) database (http://jp.fujitsu.com/group/kyushu/en/services/admedatabase/). The generally accepted view is that, for the drugs that undergo metabolism, almost 75% involve P450 reactions.[23-25] Five P450s—1A2, 2C9, 2C19, 2D6, and 3A4—are involved in ~ 90% of these P450 reactions.[23-25] This situation, i.e. a large segment of drug metabolism being controlled by a few enzymes, has been useful in being able to rapidly define metabolism issues in drug development.

In an analysis made previously with a total of 7906 entries (metabolic reactions catalyzed by P450s with different compounds as substrates),[513] 2065 entries are related to P450 Subfamily 3A enzymes, i.e. 26% of the total. Making similar analysis for clinically significant drugs,[513] P450 3A4 and 3A5 enzymes participated in 34% of the total P450-catalyzed metabolic reactions, less than the ~50% presented by others.[23,24] The contribution of the P450 Subfamily 3A enzymes may be overestimated, or the differences may reflect the time period sampled or the possible differences between sets of drugs published in the open literature vs. proprietary drugs and those in development used in the analyses.

The results shown in Figure 2 can be compared to drug metabolism. The first point is that a similar fraction of the total bioactivation (68%) is due to P450 enzymes (Figure 2A). The five P450s involved in drug metabolism are "replaced" with six—1A1, 1A2, 1B1, 2A6, 2E1, and 3A4—that collectively account for 77% of the P450-mediated reactions.

The numbers resulting from the present analysis of updated earlier data[513] on all compounds fit better to the data we report in the activation of the carcinogens by human P450s, and can be used for comparisons. E.g., participation of P450s 1A1, 1A2 and 2E1 in carcinogen activation reactions is 20, 17, and 11%, respectively, and their participation in total metabolic reactions presented here is 7, 10, and 5%, respectively. The participation of P450 1B1 in activation is 11%, and in total metabolism reactions is 3%. However, the participation of P450 3A4 in activation reactions is 10% and its participation in all metabolic reactions is 20%.

The participation of P450 2C9 in activation reactions is ~2% and in total metabolism reactions is 9%; the participation of P450 2C19 in activation reactions is 1% and in total metabolism reactions is 8%. Finally, the apparent participation of P450 2D6 in activation reactons is ~2% and in total metabolism reactions is 10%. We make the general conclusion that the contribution of "toxicologically significant" enzymes (e.g. P450s 1A1, 1A2, 1B1, 2A6, 2E1) is greater in activation reactions and less in considerations of total metabolism. The opposite is the case for generally-detoxicating enzymes, e.g. P450s 2D6, 3A4 (with exceptions), and the 2C Subfamily.

APPLICATIONS

The information presented here is intended to provide a summary to readers who are interested in the literature on human enzymes involved in chemical carcinogenesis reported to date. Further, the analyses (Figure 2) have uses in themselves, despite the stated caveats, in evaluating the individual enzymes.

The analysis provides some guidance in translational applications. For instance, the information presented in Figure 2 can direct the efforts of those in the field of molecular epidemiology of cancer as to which genes and single nucleotide polymorphisms might be most profitable to study. Likewise, some guidance is provided to those in the field of chemoprevention as to which enzymes and reactions might be most useful to inhibit or induce. Such considerations also apply in general issues of risk assessment, in evaluating issues such as inducibility and inter-individual variation.

The analysis (Figure 2) is also useful in basic research. For one thing, it was a matter of curiosity for us—after studying the area for so long[513]—to know which P450s are most prominent in chemical carcinogenesis. Thus, justification is clearly provided for studying the six P450s cited in Figure 2B (1A1, 1A2, 1B1, 2A6, 2E1, 3A4). Of the six, only P450 1A1 has not been reported at the level of a crystal structure. However, none of these P450 structures has been solved with a carcinogen bound. An overall hope is to use our knowledge of structure-activity relationships to predict which new chemicals will be activated and whether products will be toxic or carcinogenic. In addition, there are numerous basic questions regarding how P450s, including those cited here, such as: What is the molecular basis of catalytic selectivity? What factors determine rates of particular P450 reactions? What is the molecular basis of the cooperativity seen in P450s, including some of those described here, e.g. P450 3A4 and also P450 1A2 (with pyrene).[514]

It should be emphasized again that almost all of the work cited here was done in the past 25 years.[27] In dealing with an effort of this scope, we might have overlooked some useful papers in the field and apologize to those authors in advance. An Excel file of an expansion of Table 1 is included for the ease of those readers who wish to search it or use it to develop or update their own databases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

AF	aflatoxin
AGT or MGMT (used in tables)	O^6-alkylguanine DNA-alkyltransferase
AKR	aldo-keto reductase
COX (used in tables) or PTGS	cyclooxygenase (prostaglandin synthase)
P450 or CYP (used in tables)	cytochrome P450
FMO	microsomal flavin-containing monoxygenase
GST	glutathione (GSH) transferase
HAA	heterocyclic arylamine
NAT	*N*-acetyltransferase
NPR or POR (used in tables)	NADPH-P450 reductase
NQO	NADPH-quinone reductase
PAH	polycyclic aromatic hydrocarbon
SULT	sulfotransferase
UGT	UDP glucuronosyl transferase
XOR	xanthine oxidoreductase

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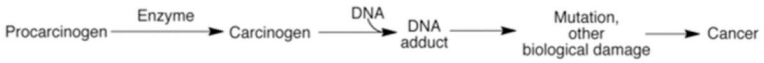

Figure 1.
General paradigm of metabolism of chemical carcinogens.

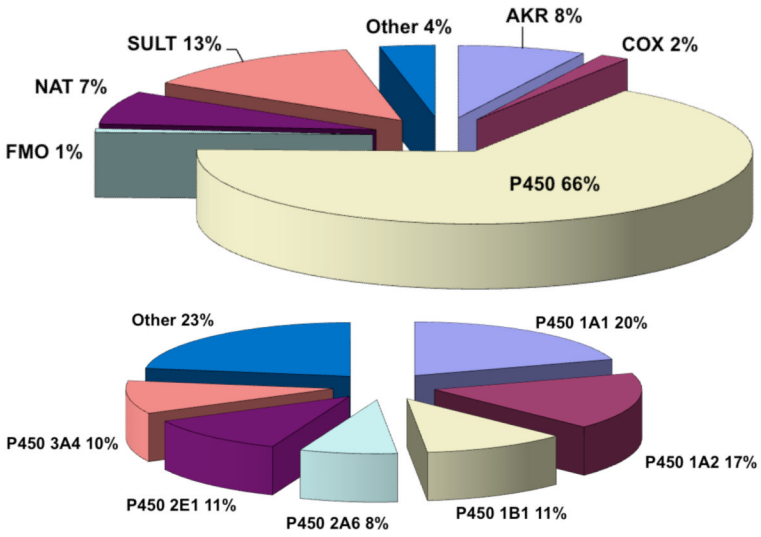

Figure 2.

Enzyme contributions to activation of carcinogens (from Table 1). A: Fractions of activation reactions attributed to groups of enzymes. The analysis is based on 713 reactions. B: Fractions of P450 activation reactions attributed to individual human P450 enzymes (from a total of 473 reactions considered). See text for discussion.

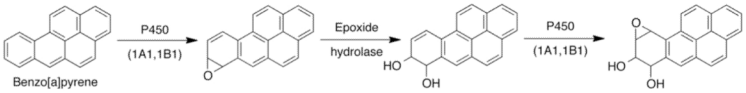

Figure 3.
Diol-epoxide pathway of benzo[*a*]pyrene activation.[486]

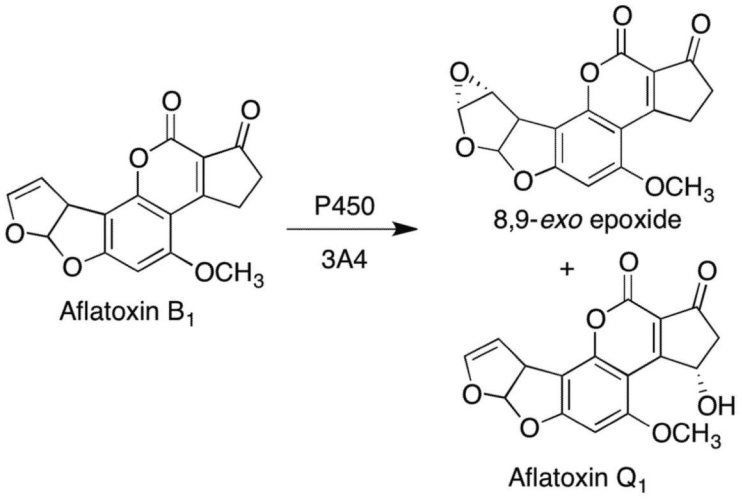

Figure 4.
Oxidation of AFB_1 by P450 3A4.[176]

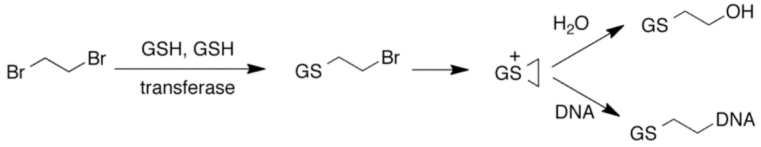

Figure 5.
Conjugation of ethylene dibromide with GSH.[377]

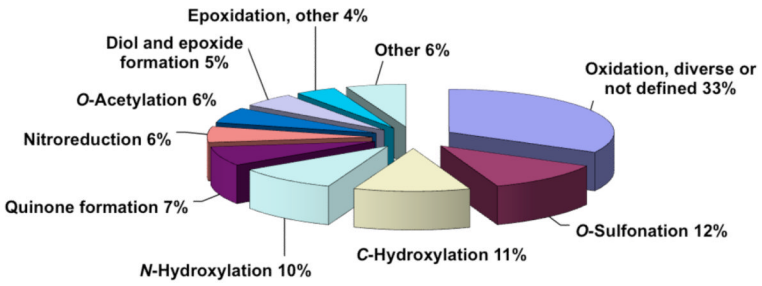

Figure 6.
Analysis of types of activation reactions (data of Table 1, total of 799 reactions). See text for discussion.

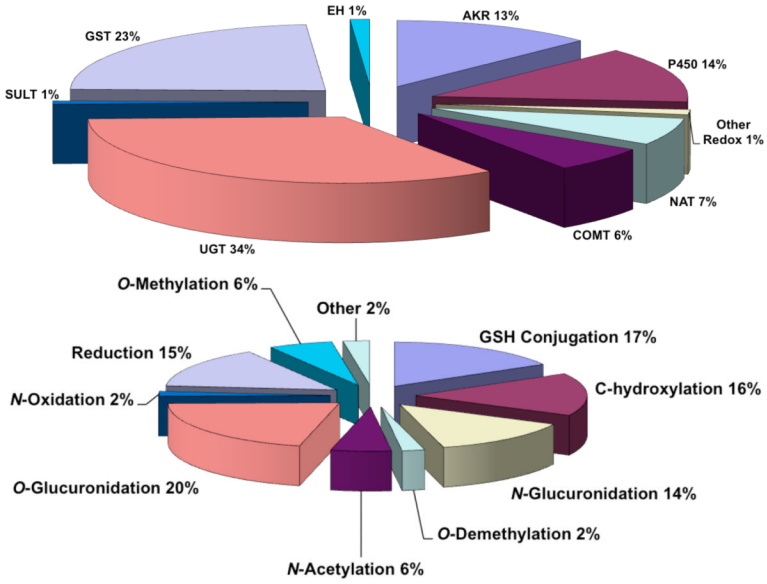

Figure 7.

Analysis of detoxication reactions. A: Enzymes involved in detoxication. B: Reactions involved in detoxication. Data are from Table 4 (total of 281 reactions). See text for discussion.

Table 1

Data on individual enzymes and chemicals, but not including weak bioactivation (see Supporting Information for inclusion of weak activation data)

Note: the term “diol” is used in stead of “dihydrodiol” for convenience with the PAHs.

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
AKR1A1	chemical	PAH, metabolite	(±)-benzo[*a*]pyrene-7,8-dihydrodiol	oxidation, *o*-quinone formation, preferential for (−)-7R,8R-oxidation	activation	26, 28-33	16411658, 11306097, 9973208, 11535067, 15720144, 17295519, 18788756
AKR1A1	chemical	PAH, metabolite	12-methylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	28	11306097
AKR1A1	chemical	PAH, metabolite	5-methylchrysene-1,2-diol	oxidation, *o*-quinone formation (medium K_m, high activity, high efficiency)	activation	28, 30, 34	11306097, 11535067, 16946553
AKR1A1	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone form.	activation	28,30	11306097, 11535067
AKR1A1	chemical	PAH, metabolite	7-methylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation, preferential for (−)3*S*,4*S*-oxidation	activation	28, 30	11306097, 11535067
AKR1A1	chemical	PAH, metabolite	benz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation, preferential for (−)3*R*,4*R*-oxidation	activation	28, 30	11306097, 11535067
AKR1A1	chemical	PAH, metabolite	chrysene-1,2-diol	oxidation, *o*-quinone formation	activation	28	11306097
AKR1B1	chemical	PAH	(+)-benz[*a*]anthracene-3*S*,4*S*-diol	oxidation, *o*-quinoneform, stereospecific for (+)-7*S*-,8*S*	activation	33	18788756
AKR1B1	chemical	PAH, metabolite	(+)-benzo[*a*]pyrene-7*S*,8*S*-diol	oxidation, *o*-quinone formation, stereospecific for (+)-7*S*-,8*S*	activation	33	18788756
AKR1B1	chemical	PAH, metabolite	(+)-*S*,*S*-benzo[*g*]chrysene-11,12-diol	oxidation, *o*-quinone formation, stereospecific for (+)-7*S*-,8*S*	activation	33	18788756
AKR1B10	chemical	PAH, metabolite	(−)-*R*,*R*- and (+)-*S*,*S*-benzo[*g*]chrysene-11,12-diol	oxidation, *o*-quinone formation	activation	33	18788756
AKR1B10	chemical	PAH, metabolite	(+)-benz[*a*]anthracene-3*S*,4*S*-diol	oxidation, *o*-quinone formation, stereospecific for (+)-7*S*-,8*S*	activation	33	18788756

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
AKR1B10	chemical	PAH, metabolite	(+)-benzo[*a*]pyrene-7*S*,8*S*-diol	oxidation, *o*-quinone formation, stereospecific for (+)-7*S*-,8*S*	activation	33	18788756
AKR1B10	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	33	18788756
AKR1C1	chemical	PAH, metabolite	(+,−)- and (−)-benzo[*a*]pyrene-7,8-diol	oxidation, *o*-quinone formation	activation	29, 33, 35, 36	9973208, 18788756, 11978787, 11060293
AKR1C1	chemical	PAH, metabolite	5-methylchrysene-7,8-diol	oxidation, *o*-quinone formation	activation	35, 36	11978787, 11060293
AKR1C1	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation, minor enzyme	activation	35, 36	11978787, 11060293
AKR1C1	chemical	PAH, metabolite	7-methylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation, minor enzyme	activation	35	11978787
AKR1C1	chemical	PAH, metabolite	benz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C1	chemical	aromatic hydrocarbon	benzene diol	oxidation, *o*-quinone formation	activation	36, 37	11060293, 15026176
AKR1C1	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol	oxidation, *o*-quinone formation	activation	35, 36	11978787, 11060293
AKR1C1	chemical	PAH, metabolite	naphthalene 1,2-diol	oxidation, *o*-quinone formation, major enzyme	activation	35, 36	11978787, 11060293
AKR1C2	chemical	PAH, metabolite	(±)- and (−)-benzo[*a*]pyrene-7,8-diol	oxidation, *o*-quinone formation	activation	29, 33, 35	9973208, 18788756, 11978787
AKR1C2	chemical	PAH, metabolite	5-methylchrysene-7,8-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C2	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C2	chemical	PAH, metabolite	7-methylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C2	chemical	PAH, metabolite	benz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C2	chemical	PAH, metabolite	benzene diol	oxidation, *o*-quinone formation	activation	37	15026176

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
AKR1C2	chemical	PAH, metabolite	benzo[*c*]phenanthrene-3,4-diol	oxidation, *o*-quinone form.	activation	35	11978787
AKR1C2	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C2	chemical	PAH, metabolite	chrysene-1,2-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C2	chemical	PAH, metabolite	naphthalene 1,2-diol	oxidation, *o*-quinone formation, major enzyme	activation	35	11978787
AKR1C3	chemical	PAH, metabolite	(+,−)- and (−)-benzo[*a*]pyrene-7,8-dihydrodiol	oxidation, *o*-quinone formation	activation	29, 33, 35	9973208, 18788756, 11978787
AKR1C3	chemical	PAH, metabolite	5-methylchrysene-7,8-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C3	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C3	chemical	PAH, metabolite	7-methylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C3	chemical	PAH, metabolite	benz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C3	chemical	aromatic hydrocarbon, metabolite	benzene diol	oxidation, *o*-quinone formation	activation	37	15026176
AKR1C3	chemical	PAH, metabolite	benzo[*c*]phenanthrene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C3	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C3	chemical	PAH, metabolite	chrysene-1,2-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C3	chemical	PAH, metabolite	naphthalene 1,2-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C4	chemical	PAH, metabolite	(±)- and (−)-benzo[*a*]pyrene-7,8-diol	oxidation, *o*-quinone formation	activation	29, 35	9973208, 11978787
AKR1C4	chemical	PAH, metabolite	(±)-benzo[*a*]pyrene-7,8-diol	oxidation, *o*-quinone formation	activation	33	18788756
AKR1C4	chemical	PAH, metabolite	5-methylchrysene-7,8-diol	oxidation, *o*-quinone formation, major enzyme	activation	35	11978787
AKR1C4	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation, major enzyme	activation	35	11978787

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
AKR1C4	chemical	PAH, metabolite	7-methylbenz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C4	chemical	PAH, metabolite	benz[*a*]anthracene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C4	chemical	aromatic hydrocarbon, metabolite	benzene diol	oxidation, *o*-quinone formation	activation	37	15026176
AKR1C4	chemical	PAH, metabolite	benzo[*c*]phenanthrene-3,4-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C4	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol	oxidation, *o*-quinone formation, major enzyme	activation	35	11978787
AKR1C4	chemical	PAH, metabolite	chrysene-1,2-diol	oxidation, *o*-quinone formation	activation	35	11978787
AKR1C4	chemical	PAH, metabolite	naphthalene 1,2-diol	oxidation, *o*-quinone formation	activation	35	11978787
COX-1	chemical	PAH, metabolite	(±)- and (+)-benzo[*a*]pyrene-7,8-diol	oxidation	activation	38	11159734
COX-1	chemical	heterocyclic amine	2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx)	oxidation	activation	38	11159734
COX-1	chemical	arylamine	4,4′-methylene bis(2-chloroaniline) (MOCA)	oxidation	potent activation	38	11159734
COX-1	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl	oxidation	activation	38	11159734
COX-1	chemical	arylamine	benzidine	oxidation	activation	38	11159734
COX-1	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plant compound, topoisomerase II inhibitor, DNA binding	ellipticine	oxidation	activation	39, 40	16936898, 21753906
COX-2	chemical	PAH, metabolite	(±)- and (+)-benzo[*a*]pyrene-7,8-diol	oxidation	activation	38	11159734
COX-2	chemical	heterocyclic amine	2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx)	oxidation	activation	38	11159734
COX-2	chemical	arylamine	4,4′-methylene bis(2-chloroaniline) (MOCA)	oxidation	potent activation	38	11159734

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
COX-2	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl	oxidation	activation	38	11159734
COX-2	chemical	arylamine	benzidine	oxidation	activation	38	11159734
COX-2	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plant compound, topoisomerase II inhibitor, and DNA binding	ellipticine	oxidation	activation	39, 40	16936898, 21753906
CYP1A1	chemical	PAH, metabolite	(±)-, (−)-, and (+)-benzo[*a*]pyrene-7,8-diol	*trans*-(*anti*)-7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydroformation (*trans*-diol epoxide formation); oxidation	potent activation	13, 31, 32, 34, 41-52	2509067, 8674051, 7955101, 11502724, 11238186, 8043197, 7581497, 11952781, 15720144, 10426814, 8293790, 16946553, 16885195, 17295519, 17525473, 21028851
CYP1A1	chemical	nitroarene	1,8-dinitropyrene	nitroreduction	potent activation	53	11113705
CYP1A1	chemical	arylamine, metabolite of 1-nitropyrene	1-aminopyrene	oxidation	activation	54	11525925
CYP1A1	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-(diallylamino)-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-8)	oxidation	activation	55	18562244
CYP1A1	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-(diethylamino)-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-7)	oxidation	activation	55	18562244
CYP1A1	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-amino-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-4)	oxidation	activation	55	18562244

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A1	chemical	benzotriazole	2-[2-(acetylamino)-4-amino-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-4)	oxidation	activation	56	21786339
CYP1A1	chemical	arylamine, metabolite	2-acetylaminofluorene (2-AAF)	*N*-hydroxylation, oxidation	activation	41, 43, 57	8674051, 11502724, 15279838
CYP1A1	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	*N*-hydroxylation, oxidation	activation	41, 43, 57-61	8674051, 11502724, 15279838, 9111224, 9855011, 21081470, 1377247
CYP1A1	chemical	heterocyclic amine	2-amino-3,4-dimethylimidazo[4,5-*f*]quinoline (MeIQ)	*N*-hydroxylation, oxidation	potent activation	41, 43, 49, 56, 62, 63	8674051, 11502724, 10426814, 21786339, 11473383, 8200084
CYP1A1	chemical	heterocyclic amine	2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (MeIQx)	*N*-hydroxylation, oxidation	activation	41, 43, 49, 58, 62-64	8674051, 11502724, 10426814, 9111224, 11473383, 8200084, 17627018
CYP1A1	chemical	heterocyclic amine	2-amino-3-methylimidazo[4,5-*f*]quinoline (IQ)	*N*-hydroxylation, oxidation	potent activation	41, 43, 49, 58, 61, 65	8674051, 11502724, 10426814, 9111224, 11377247, 9918136
CYP1A1	chemical	heterocyclic amine	2-amino-6-methyldipyrido[1,2-a:3′,2′-d]-imidazole (Glu-P-1)	*N*-hydroxylation, oxidation	activation	41, 43, 61	8674051, 11502724, 11377247
CYP1A1	chemical	arylamine	2-aminoanthracene	*N*-hydroxylation, oxidation (high activity)	potent activation	41, 43, 61, 66	8674051, 11502724, 11377247, 9685642
CYP1A1	chemical	arylamine	2-aminofluorene	*N*-hydroxylation, oxidation	activation	41, 43, 49, 61	8674051, 11502724, 10426814, 11377247
CYP1A1	chemical	nitroarene	2-nitronaphthalene	nitroreduction	activation	67	10521697

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A1	chemical	nitroarene	2-nitropyrene	2-aminopyrene formation (nitroreduction)	activation	41	8674051
CYP1A1	chemical	nitrosamine	3-(*n*-nitrosomethylamino) propionaldehyde	oxidation	activation	68	15725615
CYP1A1	chemical	nitrosamine	3-(*N*-nitrosomethylamino) propionitrile	oxidation (at high concentrations)	activation	68, 69	15725615, 16720019
CYP1A1	chemical	nitroarene	3,6-dinitrobenzo[*e*]pyrene	nitroreduction	activation	70	19393727
CYP1A1	chemical	heterocyclic amine	3-Amino-1,4-dimethyl-5H-pyrido[4,3-*b*]indole (Trp-P-1)	*N*-hydroxylation, oxidation	potent activation	41, 43, 49, 61, 66, 71	8674051, 11502724, 10426814, 11377247, 9685642, 9721189
CYP1A1	chemical	heterocyclic amine	3-amino-1-methyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-2)	*N*-hydroxylation, oxidation	activation	41, 43, 49, 61-63, 66	8674051, 11502724, 10426814, 11377247, 11473383, 8200084, 9685642
CYP1A1	chemical	arylamine, metabolite	3-aminobenzanthrone	*N*-hydroxylation	activation	72, 73	15885895, 16601755
CYP1A1	chemical	azoaromatic amine	3-methoxy-4-aminoazobenzene (3-MeO-AAB)	oxidation	potent activation	41, 43, 49, 66	8674051, 11502724, 10426814, 9685642
CYP1A1	chemical	PAH	3-methylcholanthrene (3MC)	oxidation	activation	74	11360624
CYP1A1	chemical	PAH, metabolite	3-methylcholanthrene-11,12-diol, 3MC-11,12-diol	oxidation	activation	43	11502724
CYP1A1	natural compound	indole, alkylating, pulmonary toxin; in higher concentrations in mammalian digestive tract and coal tar	3-methylindole, skatole	epoxidation (3-methyloxindole formation); dehydrogenation (desaturation, 3-methyleneindolenine formation), low K_m, medium activity, high efficiency	activation	75-78	8558432, 11408359, 12563100, 20795680
CYP1A1	chemical	nitroarene	3-nitrobenzanthrone	nitroreduction	activation	73, 79, 80	16601755, 12740904, 12782579

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A1	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl	*N*-hydroxylation, oxidation	activation	41, 58, 66	8674051, 9111224, 9685642
CYP1A1	chemical	PAH, metabolite	5,6-dimethylchrysene-1,2-diol	oxidation	activation	34, 43, 49, 81	16946553, 11502724, 10426814, 14720319
CYP1A1	chemical	PAH	5-methylchrysene	1,2-dihydrodiol formation (medium K_m, high activity, high efficiency), oxidation	activation	43, 81-83	11502724, 14720319, 8542586, 18992797
CYP1A1	chemical	PAH, metabolite	5-methylchrysene-1,2-diol	oxidation	potent activation	34, 41, 43, 49, 81, 83	16946553, 8674051, 11502724, 10426814, 14720319, 18992797
CYP1A1	chemical	arylamine	6-aminochrysene	oxidation (high activity)	potent activation	41, 43, 66	8674051, 11502724, 9685642
CYP1A1	chemical	arylamine, metabolite	6-aminochrysene-1,2-diol	diol epoxide formation, oxidation	activation	41, 84, 85	8674051, 8118930, 8330339
CYP1A1	chemical	PAH	6-methylchrysene	1,2-dihydrodiol formation	activation	82	8542586
CYP1A1	chemical	nitroarene	6-nitrochrysene	oxidation	activation	43	11502724
CYP1A1	chemical	PAH	7,12-dimethylbenz[*a*]anthracene	oxidation (low K_m, high activity and efficiency)	potent activation	43, 49, 81, 86, 87	11502724, 10426814, 14720319, 12584184, 20507880
CYP1A1	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	3,4-dihydrodiol-1,2-epoxide formation (medium K_m, high activity, high efficiency), oxidation	potent activation	34, 43, 49, 66, 74, 81	16946553, 11502724, 10426814, 9685642, 11360624, 14720319
CYP1A1	chemical	*N*-heterocyclic aromatic hydrocarbon	7*H*-dibenzo[*c,g*]carbazole	oxidation	potent activation	88-91	10984687, 12034315, 15534862, 21809388
CYP1A1	chemical	PAH, aza-aromatic	7-methylbenz[*c*]acridine	3,4-dihydrodiol formation	activation	92	7866988
CYP1A1	chemical	PAH, aza-aromatic	7-methylbenz[*c*]acridine	oxidation	potent activation	92	7866988

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A1	chemical	PAH, metabolite	9-hydroxybenzo[*a*]pyrene	oxidation	activation	43	11502724
CYP1A1	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1	epoxidation 8,9-, oxidation	activation	41, 57, 61, 93, 94	8674051, 15279838, 11377247, 7923587, 8200084
CYP1A1	chemical	heterocyclic amine	aminomethylphenylnorharman	*N*-hydroxylation	activation	95	17067997
CYP1A1	natural compound	phenanthroic acid derivative; nephrotoxin, found in the Aristolochiaceae family of plants	aristolochic acid I	nitroreduction	potent activation	96-99	11511187, 15386410, 16125300, 22086975
CYP1A1	natural compound	phenanthroic acid derivative; nephrotoxin, found in the *Aristolochiaceae* family of plants	aristolochic acid II	nitroreduction	activation	96-99	11511187, 15386410, 16125300, 22086975
CYP1A1	chemical	PAH	benz[*a*]anthracene	oxidation	activation	43, 81, 100	11502724, 14720319
CYP1A1	chemical	PAH, metabolite	benz[*a*]anthracene-1,2-diol	oxidation	activation	34, 43, 74, 101	16946553, 11502724, 11360624, 11377097
CYP1A1	chemical	PAH, metabolite	benz[*a*]anthracene-3,4-diol	oxidation	activation	34, 43, 81	16946553, 11502724, 14720319
CYP1A1	chemical	PAH, metabolite	benz[*a*]anthracene-5,6-diol	oxidation	activation	34, 43	16946553, 11502724
CYP1A1	chemical	diphenylmethanol, metabolite	benzhydrol	oxidation	activation	102	12160905
CYP1A1	chemical	PAH	benzo[a]perylene	oxidation	activation	103	10613181

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A1	chemical	PAH	benzo[*a*]pyrene	*trans*-7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydro- formation (low activity, medium activity, or high activity, high efficiency); 1,6-,3,6-,6,12-dione (quinone formation, low activity); oxidation	activation	41, 43, 50-52, 57, 81, 93, 94, 104-108	8674051, 11502724, 16885195, 17525473, 21028851, 15279838 14720319, 7923587, 8200084, 9806168, 11513247, 8037457, 1486866, 19501186
CYP1A1	chemical	PAH, metabolite	benzo[*b*]fluoroanthene-9,10-diol	oxidation	potent activation	34, 41, 43, 49, 66, 81	16946553, 8674051, 11502724, 10426814, 9685642, 14720319
CYP1A1	chemical	PAH	benzo[*c*]phenanthrene	dihydrodiol 3,4-, 1,2-epoxide formation (major enzyme); oxidation	activation	109	11409939
CYP1A1	chemical	PAH, metabolite	benzo[*c*]phenanthrene-3,4-diol	dihydrodiol 3,4-, 1,2-epoxide formation; oxidation	activation	43, 49	11502724, 10426814
CYP1A1	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol	oxidation	activation	34, 43, 49, 81	16946553, 11502724, 10426814, 14720319
CYP1A1	chemical	aromatic ketone, diphenyl ketone	benzophenone	oxidation	activation	102	12160905
CYP1A1	chemical	PAH, metabolite	chrysene-1,2-diol	oxidation	potent activation	43, 49, 81	11502724, 10426814, 14720319
CYP1A1	chemical	PAH	cyclopenta[*c,d*]pyrene	oxidation	activation	110	7923587
CYP1A1	Drug	imidazole; anticancer, alkylating	dacarbazine	*N*-demethylation (major extrahepatic enzyme)	activation	111	10473105
CYP1A1	chemical	PAH, metabolite, aza-aromatic	dibenz[*a,h*]acridine	10,11-diol formation	potent activation	112	15144224
CYP1A1	chemical	PAH	dibenz[*a,h*]anthracene	oxidation	activation	43	11502724
CYP1A1	chemical	PAH, aza-aromatic	dibenz[*a,j*]acridine	3,4-dihydrodiol formation	activation	92	7866988
CYP1A1	chemical	PAH	dibenzo[*a,e*]fluoranthene	oxidation	activation	103	10613181

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A1	chemical	PAH	dibenzo[*a,e*]pyrene	oxidation	activation	103	10613181
CYP1A1	chemical	PAH	dibenzo[*a,f*]fluoranthene	oxidation	activation	103	10613181
CYP1A1	chemical	PAH	dibenzo[*a,h*]pyrene	oxidation	activation	103	10613181
CYP1A1	chemical	PAH	dibenzo[*a,k*]fluoranthene	oxidation	activation	103	10613181
CYP1A1	chemical	PAH	dibenzo[*a,l*]pyrene	(−)-*syn*- and (−)-*anti*-11,12-dihydrodiol-13,14-epoxide formation (medium K_m, high activity, high efficiency); oxidation	potent activation	43, 81, 103, 113-119	11502724, 14720319, 10613181, 9625737, 10207125, 10493514, 10506751, 8968059, 16581046, 17509623
CYP1A1	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	11,12-dihydrodiol-13,14-epoxide formation (medium K_m, high activity, high efficiency); oxidation	potent activation	34, 43, 49, 71, 81, 113-115, 118-120	16946553, 11502724, 10426814, 9721189, 14720319, 9625737, 10207125, 10493514, 16581046, 17509623, 16485905
CYP1A1	chemical	PAH	dibenzo[*b,k*]fluoranthene	oxidation	activation	103	10613181
CYP1A1	physiologi-cal compound	estrogen	17β−estradiol	C2-hydroxylation (major reaction, medium K_m, high activity, high efficiency), major metabolite and major extrahepatic enzyme; C4-hydroxylation (minor reaction, medium K_m, medium efficiency, low activity), oxidation, 3,4-quinone formation (lower activity); oxidation, 2,3-quinone formation; C16α-hydroxylation (high K_m, low activity)	potent activation	71, 106, 121-130	9721189, 8037457, 7826886, 9625734, 9054608, 9667077, 8930523, 11555828, 12865317, 15784278, 16112414, 17570247
CYP1A1	physiologi cal compound	estrogen	estrone	C2-hydroxylation (major reaction, medium K_m, low activity), oxidation, 2,3-quinone formation; C4-hydroxylation (medium K_m, low activity, or	activation	49, 127, 130, 131	10426814, 12865317, 17570247, 15805301

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
				medium activity); C16α-hydroxylation (minor reaction, very low activity)			
CYP1A1	chemical	PAH, metabolite	fluoranthene-2,3-diol	oxidation	activation	34, 43	16946553, 11502724
CYP1A1	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	oxidation (at high concentrations)	activation	87	20507880
CYP1A1	chemical	PAH	naphtho[1,2-*k*]fluoranthene	oxidation	activation	103	10613181
CYP1A1	chemical	PAH	naphtho[2,1-*a*]pyrene	oxidation	activation	103	10613181
CYP1A1	chemical	PAH	naphtho[2,3-*a*]pyrene	oxidation	activation	103	10613181
CYP1A1	chemical	*N*-heterocyclic aromatic hydrocarbon, dibenzocarbazole	*N*-methyldibenzo[*c,g*]carbazole	oxidation	potent activation	88-91	10984687, 12034315, 15534862, 21809388
CYP1A1	chemical	tobacco-specific nitrosamine	*N*′-nitrosoanabasine	oxidation	activation	132, 133	11774366, 12214673
CYP1A1	chemical	nitrosamine	*N*-nitrosodibutylamine (*N, N*-dibutylnitrosamine)	oxidation	activation	134	11600130
CYP1A1	chemical	nitrosamine	*N*-nitrosodiethylamine (*N, N*-diethylnitrosamine)	oxidation	activation	132-134	11774366, 12214673, 11600130
CYP1A1	chemical	nitrosamine	*N*-nitrosodi-*n*-propylamine (*N*-nitrosodipropylamine)	oxidation	activation	134	11600130
CYP1A1	chemical	nitrosamine	*N*-nitrosoethylbutylamine	oxidation (major enzyme)	activation	134	11600130
CYP1A1	chemical	nitrosamine	*N*-nitrosomethylbutylamine	oxidation	activation	134	11600130
CYP1A1	chemical	nitrosamine	*N*-nitrosomethylethylamine	oxidation	activation	134	11600130
CYP1A1	chemical	nitrosamine	*N*-nitrosomethylpropylamine	oxidation	activation	69, 134	16720019, 11600130
CYP1A1	chemical	nitrosamine	*N*-nitrosomorpholine	oxidation	activation	132, 133	11774366, 12214673
CYP1A1	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	oxidation	activation	132, 133	11774366, 12214673
CYP1A1	chemical	nitrosamine	*N*-nitrosopyrrolidine	Cα-hydroxylation (2-OH-tetrahydrofuran formation); oxidation	activation	132, 133	11774366, 12214673
CYP1A1	chemical	azoarylamine	*o*-aminoazotoluene	oxidation	activation	41, 66	8674051, 9685642

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A1	chemical	diphenylketone, metabolite	*p*-benzoylphenol,4-hydroxybenzophenone	oxidation	activation	102	12160905
CYP1A1	chemical	PAH	phenanthrene	oxidation to 1,2- (major reaction), 9,10-, and 3,4-dihydrodiols (minor reactions) and phenols, at high concentration	activation	46, 135	7581497, 19766613
CYP1A1	chemical	aza-aromatic	Sudan I	oxidation, major enzyme	activation	136, 137	12384524, 17159775
CYP1A2	chemical	PAH, metabolite	(±)-, (−)-, and (+)-benzo[*a*]pyrene-7,8-dihydrodiol	*trans*-(*anti*)-7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydro-formation; oxidation	activation	13, 34, 41-43, 120, 138, 139	2509067, 16946553, 8674051, 7955101, 1502724, 16485905, 9014198, 2803520
CYP1A2	chemical	triazole	1-aminobenzotriazole (1-ABT)	oxidation	activation	140	17584015
CYP1A2	chemical	arylamine, metabolite of 1-nitropyrene	1-aminopyrene	oxidation	activation	54, 141-144	11525925, 15728263, 15843388, 17158518, 9860501
CYP1A2	chemical	PAH, aza-aromatic	1-azabenzo[*a*]pyrene	oxidation	potent activation	145	14729370
CYP1A2	chemical	arylamine, metabolite	2-acetylaminofluorene (2-AAF)	*N*-hydroxylation (major enzyme), oxidation	potent activation	12, 41, 57, 107, 139, 146, 147	2655891, 8674051, 15279838, 1486866, 2803520, 11375903, 15450435

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A2	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	*N*-hydroxylation, oxidation (high activity, major enzyme, major reaction)	potent activation	57-61, 63, 107, 146, 148-156, 157	15279838, 9111224, 9855011, 21081470, 11377247, 8200083, 1486866, 11375903, 8082563, 1913651, 9705755, 11013410, 10503887, 12351158, 14744142, 14725854, 15073045, 16167840
CYP1A2	chemical	heterocyclic amine	2-amino-3,4,8-trimethylimidazo[4,5-]quinoxaline (DiMeIQx)	*N*-hydroxylation	potent activation	107	1486866
CYP1A2	chemical	heterocyclic amine	2-amino-3,4-dimethylimidazo[4,5-*f*]quinolone (MeIQ)	*N*-hydroxylation; oxidation (major enzyme)	potent activation	12, 41, 56, 61-63, 71, 94, 107, 120, 150, 151, 154, 155, 158	2655891, 8674051, 21786339, 11377247, 11473383, 8200083, 9721189, 8200084, 1486866, 16485905, 9705755, 11013410, 14744142, 14725854, 10861951
CYP1A2	chemical	heterocyclic amine	2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (MeIQx)	*N*-hydroxylation (major enzyme, high activity)	potent activation	12, 41, 58, 61-63, 94, 107, 151-155	2655891, 8674051, 9111224, 11377247, 11473383, 8200083, 8200084, 1486866, 11013410, 10503887, 12351158, 14744142, 14725854

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A2	chemical	arylamine, heterocyclic	2-amino-3-methyl-9*H*-pyrido[2,3-*b*]indole (MeAαC)	*N*-hydroxylation, oxidation	potent activation	159	14729582
CYP1A2	chemical	heterocyclic amine	2-amino-3-methylimidazo[4,5-*f*]quinolone (IQ)	*N*-hydroxylation, oxidation (high activity, major enzyme)	potent activation	12, 41, 58, 61, 65, 71, 141-144, 151, 154, 155, 160-163	2655891, 8674051, 9111224, 11377247, 9918136, 9721189, 15728263, 15843388, 17158518, 9860501, 11013410, 14744142, 14725854, 1486866, 2813353, 9675256, 10023085, 15089095
CYP1A2	chemical	heterocyclic amine	2-amino-6-methyldipyrido[1,2-a:3′,2′-d]-imidazole (Glu-P-1)	*N*-hydroxylation, oxidation (high activity, major enzyme)	potent activation	12, 41, 61, 107, 139, 154, 155, 160	2655891, 8674051, 11377247, 1486866, 2803520, 14744142, 14725854, 2813353
CYP1A2	chemical	heterocyclic amine	2-amino-α-carboline	oxidation	activation	149, 164	1913651, 8801053
CYP1A2	chemical	arylamine	2-aminoanthracene	*N*-hydroxylation, oxidation (major enzyme)	potent activation	12, 41, 61, 107, 139, 141-144, 162, 165	2655891, 8674051, 11377247, 1486866, 2803520, 15728263, 15843388, 17158518, 9860501, 10023085, 9477228
CYP1A2	chemical	heterocyclic amine	2-aminodipyrido[1,2-*a*:3,2′-*d*]-imidazole (Glu-P-2)	oxidation	activation	12, 107, 139	2655891, 1486866, 2803520

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A2	chemical	arylamine	2-aminofluorene (2-AF)	*N*-hydroxylation, oxidation (major enzyme, high activity)	potent activation	12, 41, 61, 107, 139, 166-168	2655891, 8674051, 11377247, 1486866, 2803520, 15840428, 16372832, 10727902
CYP1A2	chemical	arylamine	2-naphthylamine (β-naphthylamine)	*N*-hydroxylation, oxidation	activation	12, 61, 107, 147, 160	2655891, 11377247, 1486866, 15450435, 2813353
CYP1A2	chemical	nitroarene	2-nitrofluoranthene	nitroreduction	activation	53	11113705
CYP1A2	chemical	nitrosamine	3-(*N*-nitrosomethylamino) propionaldehyde	oxidation	activation	68	15725615
CYP1A2	chemical	nitroarene	3,6-dinitrobenzo[*e*]pyrene	nitroreduction	activation	70	19393727
CYP1A2	chemical	nitroarene	3-acetylaminobenzanthrone	*N*-hydroxylation (concentration dependent)	activation	79	12740904
CYP1A2	chemical	heterocyclic amine	3-amino-1,4-dimethyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-1)	*N*-hydroxylation; oxidation (major enzyme)	activation	12, 41, 61, 139, 151	2655891, 8674051, 11377247, 2803520, 11013410
CYP1A2	chemical	heterocyclic amine	3-amino-1-methyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-2)	*N*-hydroxylation, oxidation (major enzyme)	activation	12, 41, 61, 62, 94, 107, 151, 160	2655891, 8674051, 11377247, 11473383, 8200084, 1486866, 11013410, 2813353
CYP1A2	chemical	arylamine, metabolite	3-aminobenzanthrone	*N*-hydroxylation (major enzyme, concentration dependent)	activation	72, 73	15885895, 16601755
CYP1A2	chemical	azoaromatic amine	3-methoxy-4-aminoazobenzene	oxidation	activation	41	8674051
CYP1A2	chemical	arylamine	3′-methyl-4-dimethylaminazobenzene	oxidation	potent activation	169	10720750
CYP1A2	chemical	nitroarene	3-nitrobenzanthrone	nitroreduction	activation	73, 79, 80	16601755, 12740904, 12782579
CYP1A2	chemical	nitroarene	3-nitrofluoranthene	nitroreduction	activation	53	11113705

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A2	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl	*N*-hydroxylation, oxidation	activation	12, 41, 58, 107, 147, 160, 170, 171	2655891, 8674051, 9111224, 1486866, 15450435, 2813353, 9163700, 16988941
CYP1A2	natural compound	furanoterpene produced by sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	oxidation (major enzyme)	activation	172, 173	1651809, 15892579
CYP1A2	chemical	nitroarene	4-nitropyrene	4-aminopyrene formation (nitroreduction)	activation	174	10197616
CYP1A2	chemical	PAH, metabolite	5,6-dimethylchrysene-1,2-diol	oxidation	activation	34, 43, 81	16946553, 11502724, 14720319
CYP1A2	chemical	*N*-heterocyclic aromatic hydrocarbon,	5,9-dimethyldibenzo[*c,g*]carbazole	oxidation	activation	88-91	10984687, 12034315, 15534862, 21809388
CYP1A2	chemical	PAH, metabolite	5-methylchrysene-1,2-diol	oxidation	activation	31, 34, 43, 81	16946553, 8674051, 11502724, 14720319
CYP1A2	chemical	arylamine	6-aminochrysene	oxidation	activation	41, 66, 84, 85, 141-144	8674051, 9685642, 8118930, 8330339, 15728263, 15843388, 17158518, 9860501
CYP1A2	chemical	arylamine, metabolite	6-aminochrysene-1,2-diol	diol epoxide formation; oxidation	activation	41, 84, 85	8674051, 8118930, 8330339
CYP1A2	chemical	PAH	7,12-dimethylbenz[*a*]anthracene	oxidation	activation	43, 81, 86	11502724, 14720319, 12584184
CYP1A2	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	oxidation	activation	34, 43, 81	16946553, 11502724, 14720319

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A2	chemical	*N*-heterocyclic aromatic hydrocarbon	7*H*-dibenzo[*c*,*g*]carbazole	oxidation	activation	88-90	10984687, 12034315, 15534862
CYP1A2	chemical	PAH, aza-aromatic	7-methylbenz[*c*]acridine	3,4-dihydrodiol formation	activation	92	7866988
CYP1A2	chemical	PAH, aza-aromatic	7-methylbenz[*c*]acridine	oxidation	activation	92	7866988
CYP1A2	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation (both *exo*-8,9- and *endo*-8,9-), oxidation	activation	11, 12, 41, 42, 57, 61, 93, 94, 162, 175-182	2492107, 2509067, 8674051, 7955101, 15279838, 11377247, 7923587, 8200084, 10023085, 2162057, 766804, 8261428, 12079611, 1902334, 11782366, 16385575, 16608170
CYP1A2	chemical	heterocyclic amine	aminomethylphenylnorharman	*N*-hydroxylation	activation	95	17067997
CYP1A2	chemical	arylamine, heterocyclic	aminophenylharman	*N*-hydroxylation	activation	95	17067997
CYP1A2	chemical	arylamine, heterocyclic	aminophenylnorharman	*N*-hydroxylation	activation	95	17067997
CYP1A2	natural compound	phenanthroic acid derivative; nephrotoxin, found in the *Aristolochiaceae* family of plants	aristolochic acid I	nitroreduction	potent activation	96-99	11511187, 15386410, 16125300, 22086975
CYP1A2	natural compound	phenanthroic acid derivative; nephrotoxin, found in the *Aristolochiaceae* family of plants	aristolochic acid II	nitroreduction	potent activation	96-99	11511187, 15386410, 16125300, 22086975
CYP1A2	chemical	PAH, metabolite	benz[*a*]anthracene-3,4-diol	oxidation	activation	34, 43, 81	16946553, 11502724, 14720319
CYP1A2	chemical	diphenylmethanol, metabolite	benzhydrol	oxidation	activation	102	12160905

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A2	chemical	PAH, metabolite	benzo[*b*]fluoroanthene-9,10-diol	oxidation	activation	34, 41, 43, 81	16946553, 8674051, 11502724, 14720319
CYP1A2	chemical	PAH, metabolite	benzo[*c*]phenanthrene-3,4-diol	oxidation	activation	43	11502724
CYP1A2	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol	oxidation	activation	34, 43, 81	16946553, 11502724, 14720319
CYP1A2	chemical	aromatic ketone, diphenyl ketone	benzophenone	oxidation	activation	102	12160905
CYP1A2	chemical	PAH, metabolite	chrysene-1,2-diol	oxidation	activation	34, 41, 81	16946553, 11502724, 14720319
CYP1A2	drug	imidazole; anticancer, alkylating	dacarbazine	*N*-demethylation (major enzyme)	potent activation	111	10473105
CYP1A2	natural compound	bicyclic monoterpene	Δ^3-carene	epoxidation (high K_m, medium activity)	activation	183	16379671
CYP1A2	chemical	PAH	dibenz[*a,h*]anthracene	3,4-dihydrodiol formation	activation	184	8638931
CYP1A2	chemical	PAH, aza-aromatic	dibenz[*a,j*]acridine	3,4-dihydrodiol formation	activation	92	7866988
CYP1A2	chemical	PAH	dibenzo[*a,l*]pyrene	(−)-*anti*-11,12-dihydrodiol-13,14-epoxide formation, oxidation	activation	81	14720319
CYP1A2	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	oxidation	activation	34, 71, 81	16946553, 9721189, 14720319
CYP1A2	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plant compound, topoisomerase II inhibitor and DNA binding	ellipticine	hydroxylation, C12- and C13- (low activity)	activation	39, 40, 185-189	16936898, 21753906, 11755121, 12123750, 15548707, 17197724, 21683692

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A2	physiological compound	estrogen	17β-estradiol	C2-hydroxylation (major reaction, medium K_m, medium activity, medium efficiency), major metabolite and major enzyme in liver; C4-hydroxylation (minor reaction); C16α-hydroxylation (major enzyme, high K_m, no activity, or low activity)	activation	71, 106, 122-124, 126-129, 190-194	9721189, 8037457, 9625734, 9054608, 9667077, 11555828, 12865317, 15784278, 16112414, 1449532, 9635876, 11454902, 11741520, 14703066
CYP1A2	natural compound	alkenylbenzene; occurs in a variety of foods including essential oils of tarragon, sweet basil, sweet fennel, anis	estragole	C1′-hydroxylation (major enzyme, medium K_m, low activity)	potent activation	195-197	17407329, 15914212, 21459083
CYP1A2	physiological compound	estrogen	estrone	C2-hydroxylation (medium K_m, high activity, major metabolite); C4-hydroxylation (medium K_m, medium activity, very low activity); C16α-hydroxylation (minor reaction, very low activity)	activation	49, 122, 123, 127, 128, 191, 192, 198	10426814, 9625734, 9054608, 12865317, 15784278, 9635876, 11454902, 16537715
CYP1A2	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	oxidation (at high concentration)	activation	87	20507880
CYP1A2	natural compound	phenylpropene; from *Rhizoma acorigraminei*	methyleugenol	C1′-hydroxylation (medium K_m, major enzyme)	activation	196, 199	15914212, 16411663
CYP1A2	chemical	arylamine, metabolite	*N*-acetyl-*N*-hydroxy-3-aminobenzanthrone	oxidation, at higher concentrations	activation	79	12740904
CYP1A2	chemical	PAH	naphthalene	oxidation	activation	200	11356140
CYP1A2	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-3-aminobenzanthrone	reduction to amine	activation	79	12740904
CYP1A2	chemical	*N*-heterocyclic aromatic hydrocarbon	*N*-methyldibenzo[*c,g*]carbazole	oxidation	activation	88-91	10984687, 12034315, 15534862, 21809388
CYP1A2	chemical	nitrosamine	*N*-nitrosoethylbutylamine	oxidation	activation	134	11600130

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A2	chemical	nitrosamine	*N*-nitrosomethylbutylamine	oxidation	activation	134	11600130
CYP1A2	chemical	nitrosamine	*N*-nitrosomethylethylamine	oxidation	activation	134	11600130
CYP1A2	chemical	nitrosamine	*N*-nitrosomethylpropylamine	oxidation	activation	69, 134	16720019, 11600130
CYP1A2	chemical	nitrosamine	*N*-nitrosopyrrolidine	Cα-hydroxylation (2-OHtetrahydrofuran formation)	activation	132, 133	11774366, 12214673
CYP1A2	chemical	azoarylamine	*o*-aminoazotoluene	oxidation	activation	41, 66	8674051, 9685642
CYP1A2	chemical	*o*-methoxyaniline	*o*-anisidine (2-methoxyaniline)	*N*-hydroxylation (major enzyme with recombinant model), oxidation	activation	147, 201	15450435, 15828049
CYP1A2	chemical	diphenylketone, metabolite	*p*-benzoylphenol (4-hydroxybenzophenone)	oxidation	activation	102	12160905
CYP1A2	chemical	PAH	phenanthrene	oxidation to 1,2- (major reaction), 3,4-, and 9,10-dihydrodiols and phenols	activation	46, 135	7581497, 19766613
CYP1A2	natural compound	furanoxanthone; mycotoxin, produced by *Aspergillus* species	sterigmatocystin	oxidation	activation	41	8674051
CYP1A2	chemical	aromatic hydrocarbon, alkyl benzene	styrene (vinyl benzene)	oxidation, 7,8-oxide formation	activation	202-207	9253143, 7696548, 11407535, 12616646, 12834847, 18266326
CYP1B1	chemical	PAH, metabolite	(±)-, (−)-, and (+)-benzo[*a*]pyrene-7,8-dihydrodiol	*trans*-(*anti*)-7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydro-formation, *trans*-diol epoxide form (low K_m, high activity, high efficiency); oxidation	potent activation	26, 31, 32, 34, 41, 43, 49, 52, 120, 208-210	16411658, 15720144, 17295519, 16946553, 8674051, 11502724, 10426814, 21028851, 16485905, 12628515, 12807732, 16551781
CYP1B1	chemical	nitroarene	1,8-dinitropyrene	nitroreduction	potent activation	53	11113705
CYP1B1	chemical	arylamine, metabolite of 1-nitropyrene	1-aminopyrene	oxidation	potent activation	54	11525925
CYP1B1	chemical	PAH	2,3-dihydroxy-2,3-dihydrofluoranthene	oxidation	activation	66	9685642

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1B1	chemical	heterocyclic amine	2-amino-3,4-dimethylimidazo[4,5-*f*]quinolone (MeIQ)	*N*-hydroxylation, oxidation	activation	41, 49, 61, 100, 210, 211	8674051, 10426814, 11377247, 11502724, 16551781, 11719446
CYP1B1	chemical	heterocyclic amine	2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (MeIQx)	*N*-hydroxylation, oxidation	activation	41, 49, 61	8674051 10426814, 11377247
CYP1B1	chemical	heterocyclic amine	2-amino-3-methylimidazo[4,5-*f*]quinolone (IQ)	*N*-hydroxylation, oxidation	activation	41, 49, 61, 65, 100	8674051, 10426814, 11377247, 9918136, 11502724
CYP1B1	chemical	arylamine	2-aminoanthracene	*N*-hydroxylation, oxidation (high activity)	potent activation	41, 61, 100, 210	8674051, 11377247, 11502724, 16551781
CYP1B1	chemical	arylamine	2-aminofluorene (2-AF)	*N*-hydroxylation, oxidation	potent activation	41, 49, 61, 100, 210	8674051, 10426814, 11377247, 11502724, 16551781
CYP1B1	chemical	nitroarene	2-nitrofluoranthene	nitroreduction	potent activation	53	11113705
CYP1B1	chemical	nitroarene	2-nitropyrene	2-aminopyrene formation (nitroreduction)	potent activation	41, 100	8674051, 11502724
CYP1B1	chemical	nitrosamine	3-(*N*-nitrosomethylamino) propionaldehyde	oxidation	activation	68	15725615
CYP1B1	chemical	heterocyclic amine	3-amino-1,4-dimethyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-1)	*N*-hydroxylation; oxidation	potent activation	41, 49, 61, 66, 71, 100, 210	8674051, 10426814, 11377247, 9685642, 9721189, 11502724, 16551781
CYP1B1	chemical	heterocyclic amine	3-amino-1-methyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-2)	*N*-hydroxylation; oxidation	activation	41, 49, 61, 62, 66, 71, 100	8674051, 10426814, 11377247, 11473383, 9685642, 11502724
CYP1B1	chemical	arylamine, metabolite	3-aminobenzanthrone	*N*-hydroxylation	activation	212	15310241

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1B1	chemical	azoaromatic amine	3-methoxy-4-aminoazobenzene	oxidation	potent activation	41, 49, 66, 100, 210	8674051, 10426814, 9685642, 11502724, 16551781
CYP1B1	chemical	nitroarene	3-nitrofluoranthene	nitroreduction	activation	53	11113705
CYP1B1	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	oxidation	activation	132, 133, 213-217	11774366, 12214673, 1312898, 7595636, 8806763, 10803680, 9106248
CYP1B1	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl	*N*-hydroxylation; oxidation	activation	41, 218	8674051, 19274671
CYP1B1	chemical	PAH, metabolite	5,6-dimethylchrysene-1,2-diol	oxidation	activation	34, 41, 43, 49, 66, 81, 210	16946553, 8674051, 11502724, 10426814, 9685642, 14720319, 16551781
CYP1B1	chemical	PAH	5-methylchrysene	oxidation	activation	83, 210	18992797 16551781
CYP1B1	chemical	PAH, metabolite	5-methylchrysene-1,2-diol	oxidation (medium K_m, high activity, high efficiency)	potent activation	34, 41, 43, 49, 66, 81, 83, 120, 210	16946553, 8674051, 11502724, 10426814, 9685642, 14720319, 18992797, 16485905, 16551781
CYP1B1	chemical	arylamine	6-aminochrysene	oxidation	potent activation	41, 43	8674051, 11502724
CYP1B1	chemical	arylamine, metabolite	6-aminochrysene-1,2-diol	diolepoxide formation, oxidation	potent activation	41, 84, 85	8674051, 8118930, 8330339
CYP1B1	chemical	nitroarene	6-nitrochrysene	nitroreduction; 5,6-quinone formation	activation	41, 43, 219	8674051, 11502724, 8481905
CYP1B1	chemical	PAH	7,12-dimethylbenz[*a*]anthracene	oxidation (low K_m, high activity and efficiency)	activation	43, 49, 81, 86, 210	11502724, 10426814, 14720319, 12584184, 16551781

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1B1	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	3,4-dihydrodiol-1,2-epoxide formation (medium K_m, high activity, high efficiency); oxidation	potent activation	34, 41, 43, 49, 66, 81	16946553, 8674051, 11502724, 10426814, 9685642, 14720319
CYP1B1	chemical	PAH, metabolite	9-hydroxybenzo[*a*]pyrene	oxidation	activation	43	11502724
CYP1B1	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	oxidation	activation	61, 210, 217	11377247, 16551781, 9106248
CYP1B1	chemical	diphenylmethanol, metabolite	benzhydrol	oxidation	activation	102	12160905
CYP1B1	chemical	PAH	benzo[*a*]pyrene	*trans*-7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydro- formation (medium K_m, high activity, high efficiency); 1,6-,3,6-dione (quinone form., low activity); oxidation (major enzyme)	activation	34, 41, 43, 49, 52, 61, 81, 104, 208, 210, 220-222	16946553, 8674051, 11502724, 10426814, 21028851, 11377247, 14720319, 9806168, 12628515, 16551781, 10409402, 11465393, 15958554
CYP1B1	chemical	PAH, metabolite	benzo[*b*]fluoroanthene-9,10-diol	oxidation	activation	34, 43, 49, 50, 81	16946553, 8674051, 11502724, 10426814, 14720319
CYP1B1	chemical	PAH	benzo[*c*]phenanthrene	dihydrodiol 3,4-, 1,2-epoxide formation (major enzyme); oxidation	activation	43, 81, 109, 217, 223	11502724, 14720319, 11409939, 9168260, 21781864
CYP1B1	chemical	PAH, metabolite	benzo[*c*]phenanthrene-3,4-diol	dihydrodiol 3,4-, 1,2-epoxide formation	activation	43, 49	11502724, 10426814
CYP1B1	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol	oxidation	potent activation	34, 41, 43, 49, 66, 81	16946553, 8674051, 11502724, 10426814, 9685642, 14720319
CYP1B1	chemical	aromatic ketone, diphenyl ketone	benzophenone	oxidation	activation	102	12160905

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1B1	chemical	PAH, metabolite	chrysene-1,2-diol	oxidation	potent activation	34, 41, 43, 49, 66, 81, 210	16946553, 8674051, 11502724, 10426814, 9685642, 14720319, 16551781
CYP1B1	chemical	PAH	cyclopenta[*c,d*]pyrene	oxidation	activation	217	9106248
CYP1B1	chemical	PAH, aza-aromatic	dibenz[*a,h*]acridine	10,11-diol formation	activation	111	15144224
CYP1B1	chemical	PAH	dibenzo[*a,l*]pyrene	(−)-anti-11,12-dihydrodiol-13,14-epoxide formation (medium K_m, high activity, high efficiency); oxidation	potent activation	43, 81, 113-119, 208, 210, 224	11502724, 14720319, 9625737, 10207125, 10493514, 10506751, 8968059, 16581046, 17509623, 12628515, 16551781, 17623886
CYP1B1	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	11,12-dihydrodiol-13,14-epoxide formation (medium K_m, high activity, high efficiency)	potent activation	34, 41, 43, 49, 71, 81, 113-115, 118, 120, 208, 210	16946553, 8674051, 11502724, 10426814, 9721189, 14720319, 9625737, 10207125, 10493514, 16581046, 17509623, 16485905, 12628515, 16551781
CYP1B1	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plant compound, topoisomerase II inhibitor and DNA binding	ellipticine	oxidation	activation	39, 185-188	16936898, 11755121, 12123750, 15548707, 17197724

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1B1	physiological compound	estrogen	17β-estradiol	C4-hydroxylation (major enzyme, medium K_m, medium activity, medium and low efficiency), oxidation, 3,4-quinone formation; C2-hydroxylation (low activity, minor reaction), oxidation, 2,3-quinone formation; C16α-hydroxylation (minor enzyme, medium and high K_m, low activity)	potent activation	49, 71, 121-130, 194, 211, 221, 225-228	10426814, 9721189, 7826886, 9625734, 9054608, 9667077, 8930523, 11555828, 12865317, 15784278, 16112414, 17570247, 14703066, 11719446, 11465393, 8790407, 7568105, 10862525, 10910054
CYP1B1	physiological compound	estrogen	estrone	C4-hydroxylation (low K_m, major reaction); C2-hydroxylation (low activity, minor reaction), oxidation, 2,3-quinone formation;	potent activation	49, 127, 128, 130, 198	10426814, 12865317, 15784278, 17570247, 16537715
CYP1B1	chemical	nitrosamine	*N*-nitrosodiethylamine (*N,N*-diethylnitrosamine)	oxidation	activation	132-134	11774366, 12214673, 11600130
CYP1B1	chemical	nitrosamine	*N*-nitrosoethylbutylamine	oxidation	activation	134	11600130
CYP1B1	chemical	nitrosamine	*N*-nitrosomethylbutylamine	oxidation	activation	134	11600130
CYP1B1	chemical	nitrosamine	*N*-nitrosomethylpropylamine	oxidation	activation	69, 134	16720019, 11600130
CYP1B1	chemical	nitrosamine	*N*-nitrosomorpholine	oxidation	activation	132, 133	11774366, 12214673
CYP1B1	chemical	nitrosamine	*N*-nitrosopyrrolidine	Cα-hydroxylation (2-OHtetrahydrofuran formation), oxidation	activation	132, 133	11774366, 12214673
CYP1B1	chemical	diphenylketone, metabolite	*p*-benzoylphenol,4-hydroxybenzophenone	oxidation	activation	102	12160905
CYP1B1	chemical	PAH	phenanthrene	oxidation to 9,10- (major reaction), and 1,2- and 3,4- (minor reaction) dihydrodiols and phenols	activation	135	19766613
CYP1B1	chemical	nitroarene	1-nitropyrene	1-aminopyrene form. (nitroreduction), at low concentrations, epoxidation C4,5-, at high	potent activation	53, 54, 229	11113705, 11525925, 15310239

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
				concentration			
CYP2A6	chemical	haloalkane	1, 2-dibromoethane (ethylene dibromide)	oxidation to 2-bromoacetaldehyde	activation	230	8870687
CYP2A6	chemical	diene	1,3-butadiene	butadiene monoxide (epoxybutene) formation (high activity)	activation	231-233	7586124, 8901879, 9016811
CYP2A6	chemical	nitrile, herbicide	2,6-dichlorobenzonitrile (dichlobenil)	epoxidation, C2,3-	activation	234, 235	8649351, 8863822
CYP2A6	chemical	arylamine	2,6-dimethylaniline	*N*-hydroxylation (at higher concentrations), major enzyme	activation	236	11409937
CYP2A6	chemical	nitrosamine	3-(*N*-nitrosomethylamino) propionaldehyde	oxidation	activation	68	15725615
CYP2A6	chemical	nitrosamine	3-(*N*-nitrosomethylamino) propionitrile	oxidation (at high concentrations, major enzyme)	potent activation	68, 69	15725615, 16720019
CYP2A6	chemical	arylamine, metabolite	3-aminobenzanthrone	*N*-hydroxylation	activation	212	15310241
CYP2A6	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	Cα-hydroxylationmethylene (lactol/acid formation or Cα-methyl (diol/acid formation)	activation	170, 237, 238	9163700, 12975327, 21473878
CYP2A6	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	Cα-hydroxylationmethylene (keto aldehyde and keto alcohol formation), high K_m, low activity, oxidation	activation	66, 132-134, 141-143, 213-216, 238-246	9685642, 11774366, 12214673, 11600130, 15728263, 15843388, 17158518, 1312898, 7595636, 8806763, 10803680, 11016631, 15333516, 17671098, 21473878, 10837014, 11080669, 12920169, 1423839
CYP2A6	chemical	arylamine	4,4′-methylene bis(2-chloroaniline) (MOCA)	oxidation, *N*-hydroxylation	activation	65, 106, 248, 249	9685642, 1486866, 1944238, 1740010

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2A6	chemical	arylamine	6-aminochrysene	oxidation	activation	248	1944238
CYP2A6	chemical	diphenylmethanol, metabolite	benzhydrol	oxidation (major enzyme)	activation	102	12160905
CYP2A6	chemical	aromatic ketone, diphenyl ketone	benzophenone	oxidation (major enzyme)	activation	102	12160905
CYP2A6	chemical	aliphatic epoxide, metabolite	butadiene monoxide (1,2-epoxy-3-butene)	diepoxybutane meso- (major) and (±)- formation (at high concentrations)	activation	231-233	7586124, 8901879, 9016811
CYP2A6	chemical	haloalkane	chloroform (trichloromethane)	dehalogenation, reductive (at high concentrations); oxidation (major enzyme at high concentrations)	activation	250	12584152
CYP2A6	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation (minor enzyme, high K_m); oxidation	activation	101, 108, 251-254	11377097, 19501186, 8242617, 9010702, 10348794, 10692561
CYP2A6	natural compound	alkenylbenzene; occurs in a variety of foods including essential oils of tarragon, sweet basil, sweet fennel, anis	estragole	C1′-hydroxylation (major enzyme, medium K_m, medium activity)	potent activation	195, 197	17407329, 21459083
CYP2A6	chemical	phosphoramide	hexamethylphosphoramide	oxidation, formaldehyde production	activation	235, 255	8863822, 9007030
CYP2A6	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation (minor reaction, high K_m), oxidation (at high concentration)	activation	87, 247, 253	20507880, 8242617, 10348794
CYP2A6	natural compound	furanocoumarin; anti-psoriatic, photosensitizer, found in several species of plants	methoxalen (8-methoxypsoralen, xanthotoxin)	epoxidation (furanoepoxide formation) and hydrolysis	activation	140	17584015
CYP2A6	chemical	tobacco-specific nitrosamine	*N*′-nitrosoanabasine	oxidation	activation	132, 133	11774366, 12214673
CYP2A6	chemical	tobacco-specific nitrosamine	*N*′-nitrosoanatabine	oxidation	activation	132, 133	11774366, 12214673
CYP2A6	chemical	nitrosamine	*N*-nitrosodibutylamine (*N, N*-dibutylnitrosamine)	oxidation	activation	244, 134	10837014, 11600130

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2A6	chemical	nitrosamine	*N*-nitrosodiethylamine (*N*,*N*-diethylnitrosamine)	oxidation	potent activation	106, 132-134, 141-144, 245-247	1486866, 11774366, 12214673, 11600130, 15728263, 15843388, 17158518, 9860501, 10837014, 11080669, 1423839
CYP2A6	chemical	nitrosamine	*N*-nitrosodi-*n*-propylamine (*N*-nitrosodipropylamine)	oxidation	potent activation	134, 141-143, 244	11600130, 15728263, 15843388, 17158518, 10837014
CYP2A6	chemical	nitrosamine	*N*-nitrosoethylbutylamine	oxidation (major enzyme)	potent activation	134, 244	11600130, 10837014
CYP2A6	chemical	nitrosamine	*N*-nitrosomethylbutylamine	oxidation (major enzyme)	potent activation	134, 244	11600130, 10837014
CYP2A6	chemical	nitrosamine	*N*-nitrosomethylethylamine	oxidation	potent activation	134, 243	11600130, 10837014
CYP2A6	chemical	nitrosamine	*N*-nitrosomethylphenylamine	oxidation	activation	134, 243, 245	11600130, 10837014, 11080669
CYP2A6	chemical	nitrosamine	*N*-nitrosomethylpropylamine	oxidation	activation	68, 134, 244	16720019, 11600130, 10837014
CYP2A6	chemical	nitrosamine	*N*-nitrosomorpholine	oxidation (major enzyme)	activation	132, 133	11774366, 12214673
CYP2A6	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	pyridine, N-oxidation C5′- (lactol formation, medium K_m, high to medium activity), oxidation (major enzyme)	activation	132-134, 244, 256-258	11774366, 12214673, 11600130, 15651850, 10837014, 9276639, 7646564
CYP2A6	chemical	nitrosamine	*N*-nitrosopiperidine	Cα-hydroxylation (2-OH-tetrahydropyran and 2-OH-5-methyltetrahydropyran formation), major enzyme; oxidation	activation	132, 133, 258	11774366, 12214673, 15651850

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2A6	chemical	nitrosamine	*N*-nitrosopyrrolidine,	Cα-hydroxylation (2-OH-tetrahydrofuran formation); oxidation (major enzyme)	activation	132-134, 244, 258	11774366, 12214673, 11600130, 15651850, 10837014
CYP2A6	chemical	diphenylketone, metabolite	*p*-benzoylphenol (4-hydroxybenzophenone)	oxidation (major enzyme)	activation	102	12160905
CYP2A6	natural compound	Methylenedioxypheny l (benzodioxole)	safrole	C1′-hydroxylation (major enzyme at low concentrations), medium K_m, medium activity	activation	195, 196, 259, 260	17407329, 15914212, 15377158, 15310247
CYP2A13	chemical	nitrosamine	3-(*N*-nitrosomethylamino) propiona ldehyde	oxidation (major enzyme)	potent activation	68	15725615
CYP2A13	natural compound	indole, alkylating, pulmonary toxin; in higher concentrations in mammalian digestive tract and coal tar	3-methylindole (skatole)	dehydrogenation (desaturation, 3-methyleneindolenine form., low K_m, medium activity, high efficiency), epoxidation (3-methyloxindole formation)	potent activation	77, 261	20795680, 19608696
CYP2A13	chemical	nitrosamine	3-*N*-nitrosoguvacoline	oxidation (major enzyme)	activation	68, 69	15725615, 16720019
CYP2A13	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	Cα-hydroxylation-methyl (keto alcohol formation), major enzyme, medium K_m, medium activity, or high activity	potent activation	237-240, 262-266	11016631, 12975327, 15333516, 15528319, 15962925, 12130698, 16917071, 17671098, 19074523, 21473878
CYP2A13	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl	*N*-hydroxylation; oxidation	activation	58, 171	9111224, 16988941
CYP2A13	chemical	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation 8,9-, oxidation	potent activation	181, 265	16385575, 16917071
CYP2A13	natural compound	furanocoumarin; anti-psoriatic, photosensitizer, found in bergamot essential oil, in other citrus essential oils, and in	bergapten, 5-methoxypsoralen	epoxidation and	activation	267	20798279

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
		grapefruit juice		hydrolysis to dihydrodiol			
CYP2A13	chemical	nitrosamine	*N*-nitrosomethylpropylamine	oxidation	potent activation	69, 134	16720019, 11600130
CYP2A13	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	hydroxylation C5′- (lactol formation, medium K_m, high activity) and C2′- (keto alcohol formation, medium K_m, low activity)	activation	258, 266	19074523, 15651850
CYP2A13	chemical	nitrosamine	*N*-nitrosopiperidine	Cα-hydroxylation (2-OH-tetrahydropyran and 2-OH-5-methyl tetrahydrofuran formation)	activation	258	15651850
CYP2A13	chemical	nitrosamine	*N*-nitrosopyrrolidine	Cα-hydroxylation (2-OH-tetrahydrofuran formation)	activation	258	15651850
CYP2A13	chemical	aromatic hydrocarbon, alkyl benzene	styrene (vinyl benzene)	oxidation, 7,8-oxide formation	activation	207	18266326
CYP2B6	chemical	haloalkane	1, 2-dibromoethane (ethylene dibromide)	oxidation to 2-bromoacetaldehyde	activation	230	8870687
CYP2B6	chemical	haloalkane	2, 2-dichloro-1,1,1-trifluoroethane (HCFC-123)	oxidation	activation	268, 269	11684364, 11684365
CYP2B6	chemical	arylamine, metabolite	3-aminobenzanthrone	*N*-hydroxylation	activation	212	15310241
CYP2B6	chemical	azoaromatic amine	3-methoxy-4-aminoazobenzene	oxidation	activation	270	7905383
CYP2B6	chemical	nitroarene	3-nitrobenzanthrone	nitroreduction	potent activation	80	12782579
CYP2B6	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	hydroxylation, alphamethyl (keto alcohol form.), major reaction and Cα-methylene (keto aldehyde form.), minor reaction	activation	74, 213-216, 252, 271, 272	11360624, 1312898, 7595636, 8806763, 10803680, 12920169, 9280407, 16174803
CYP2B6	chemical	unsaturated	4-vinyl-1-cyclohexene (*S*)- and (*R*)-	epoxidation 7,8- (major reaction, stereoselective for (*R*)-); epoxidation 1,2-	activation	100, 273	11502734, 11159809
CYP2B6	chemical	arylamine	6-aminochrysene	oxidation	activation	85, 270	8330339, 7905383
CYP2B6	chemical	herbicide, chloroacetamide	alachlor	oxidation	activation	274	11133395

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2B6	chemical	herbicide, chloroacetamide	butachlor	oxidation	activation	274	11133395
CYP2B6	chemical	haloalkane	chloroform (trichloromethane)	oxidation (at high conc.)	activation	250	12584152
CYP2B6	drug	azaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation (major enzyme, major reaction, high K_m, high activity); oxidation	potent activation	74, 101, 108, 251-254, 271, 275	11360624, 11377097, 19501186, 8242617, 9010702, 10348794, 10692561, 9280407, 15919850
CYP2B6	chemical	polycyclic aromatic hydrocarbon (PAH)	dibenz[*a,h*]anthracene	3,4-dihydrodiol form.	activation	184	8638931
CYP2B6	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation stereoselective for (*S*)- (high K_m, major enzyme), oxidation (at high concentrations)	activation	87, 259, 261, 262, 275-278	20507880, 8242617, 10348794, 10692561, 15919850, 10534317, 15821045, 16854777
CYP2B6	chemical	herbicide, chloroacetamide	metolachlor	oxidation	activation	274	11133395
CYP2B6	chemical	aziridine	*N, N*', *N*'-triethylene thiophosphoramide (thioTEPA)	desulfuration, TEPA formation (major enzyme)	activation	140, 279	17584015, 12107550,
CYP2B6	chemical	nitrosamine	*N*-nitrosomorpholine	oxidation	activation	74	11360624
CYP2B6	chemical	*o*-methoxyaniline	*o*-anisidine (2-methoxyaniline)	*N*-hydroxylation	activation	201	15828049
CYP2B6	chemical	aromatic hydrocarbon, alkyl benzene	styrene (vinyl benzene)	oxidation (major enzyme in liver microsomes at high concentration)	activation	202-205, 2780	9253143, 7696548, 11407535, 12616646, 16125881
CYP2C8	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	oxidation	activation	132, 133	11774366, 12214673
CYP2C8	chemical	haloalkane	chloroform (trichloromethane)	dehalogenation reductive (at high concentrations)	activation	258	12584152
CYP2C8	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation (minor enzyme, high K_m), oxidation (at high concentrations)	activation	87, 259, 261	20507880, 8242617, 10348794

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2C8	chemical	nitrosamine	*N*-nitrosomethylbutylamine	oxidation	activation	134	11600130
CYP2C8	chemical	nitrosamine	*N*-nitrosomethylpropylamine	oxidation	activation	134	11600130
CYP2C8	chemical	nitrosamine	*N*-nitrosopyrrolidine	Cα-hydroxylation (2-OH-tetrahydrofuran formation); oxidation	activation	132, 133	11774366, 12214673
CYP2C8	chemical	aromatic hydrocarbons, alkyl benzene	styrene (vinyl benzene)	oxidation (major enzyme in liver microsomes at high concentrations)	activation	202-205, 280	9253143, 7696548, 11407535, 12616646, 16125881
CYP2C9	chemical	diene	1,3-butadiene	butadiene monoxide (epoxybutene) formation (high activity)	activation	231-233	7586124, 8901879, 9016811
CYP2C9	chemical	triazole	1-aminobenzotriazole (1-ABT)	oxidation	activation	140	17584015
CYP2C9	chemical	PAH	7,12-dimethylbenz[*a*]anthracene	oxidation	activation	43, 81, 87	11502724, 14720319, 20507880
CYP2C9	chemical	PAH	benzo[*c*]phenanthrene	oxidation	activation	81	14720319
CYP2C9	chemical	aliphatic epoxide, metabolite	butadiene monoxide (1, 2-epoxy-3-butene)	diepoxybutane *meso*- and (±)- formation	activation	231-233	7586124, 8901879, 9016811
CYP2C9	chemical	haloalkane	chloroform (trichloromethane)	dehalogenation reductive (at high concentrations)	activation	250	12584152
CYP2C9	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation (low K_m, low activity, major enzyme at low concentrations); oxidation	activation	101, 108, 251-254	11377097, 19501186, 8242617, 9010702, 10348794, 10692561
CYP2C9	chemical	PAH	dibenz[*a,h*]anthracene	3,4-dihydrodiol formation	activation	184	8638931
CYP2C9	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation (low K_m), oxidation (at high concentration)	activation	87, 259	20507880, 8242617
CYP2C9	natural compound	phenylpropene, from *Rhizoma acorigraminei*	methyleugenol	C1′-hydroxylation (medium activity, high K_m), at high concentration	activation	196, 199	15914212, 16411663
CYP2C19	chemical	triazole	1-aminobenzotriazole (1-ABT)	oxidation	activation	140	17584015
CYP2C19	natural compound	furanoterpene produced in sweet	4-ipomeanol	oxidation (major enzyme)	activation	173	15892579

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
		potatoes infected with Fusarium solani; pulmonary toxin, alkylating					
CYP2C19	chemical	haloalkane	chloroform (trichloromethane)	dehalogenation reductive (at high concentration); oxidation (at high concentration)	activation	250	12584152
CYP2C19	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation (low K_m, low activity); oxidation	activation	108, 251-254	19501186, 8242617, 9010702, 10348794, 10692561
CYP2C19	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation stereoselective for (*S*)- (minor reaction, high K_m), oxidation (at high concentration)	activation	87, 259, 253, 276	20507880, 8242617, 10348794, 10534317
CYP2C19	chemical	nitrosamine	*N*-nitrosomethylbutylamine	oxidation	activation	134	11600130
CYP2C19	chemical	nitrosamine	*N*-nitrosomethylethylamine	oxidation	activation	134	11600130
CYP2C19	chemical	nitrosamine	*N*-nitrosopyrrolidine	Cα-hydroxylation (2-OH-tetrahydrofuran formation)	activation	132, 133	11774366, 12214673
CYP2D6	chemical	triazole	1-aminobenzotriazole (1-ABT)	oxidation	activation	140	17584015
CYP2D6	chemical	nitrosamine	3-(*N*-nitrosomethylamino) propionaldehyde	oxidation	activation	68	15725615
CYP2D6	chemical	nitroarene	3-nitrobenzanthrone	nitroreduction	potent activation	80	12782579
CYP2D6	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	Cα-hydroxylation,methylene	activation	170	9163700
CYP2D6	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	Cα-hydroxylation, methyl (keto alcohol formation), high K_m, medium activity, or high activity, major reaction and Cα-methylene (keto aldehyde formation), high K_m, low activity, minor reaction	activation	170, 213-216, 281	9163700, 1312898, 7595636, 8806763, 10803680, 8485585
CYP2D6	natural compound	furanoterpene produced in sweet potatoes infected with Fusarium solani;	4-ipomeanol	oxidation	activation	173	15892579

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
		pulmonary toxin, alkylating					
CYP2D6	chemical	PAH	7,12-dimethylbenz[*a*]anthracene	oxidation	activation	87	20507880
CYP2D6	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	oxidation	activation	61	11377247
CYP2D6	chemical	haloalkane	chloroform (trichloromethane)	dehalogenation, reductive (at high concentration)	activation	250	12584152
CYP2D6	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plant compound, topoisomerase II inhibitor and DNA binding	ellipticine	oxidation N^2-; hydroxylation, C13- (low activity)	activation	39, 40, 187, 188	16936898, 21753906, 15548707, 17197724
CYP2D6	drug	oxazaphosporine; anticancer, nitrogen mustard	alkylating ifosfamide	oxidation (at high concentration)	activation	87	20507880
CYP2E1	chemical	haloalkane	1, 2-dibromoethane (ethylene dibromide)	oxidation to 2-bromoacetaldehyde	activation	107, 230, 180	1486866, 8870687, 1664256
CYP2E1	chemical	haloalkane	1, 2-dichloroethane (ethylene dichloride)	oxidation	activation	107, 282	1486866, 1664256
CYP2E1	chemical	haloalkane	1, 2-dichloropropane (propylene dichloride)	oxidation	activation	107, 282	1486866, 1664256
CYP2E1	chemical	hydrazine	1, 2-dimethylhydrazine	oxidation	activation	283	15576447
CYP2E1	chemical	haloalkane	1,1,2-trichloroethane	oxidation	activation	284	8671747
CYP2E1	chemical	haloalkene	1,1,3-trichloropropene	oxidation	activation	284	8671747
CYP2E1	chemical	haloalkene	1,1-dichloroethylene (vinylidene chloride)	epoxidation	activation	285	15319346
CYP2E1	chemical	diene	1,3-butadiene	butadiene monoxide (epoxybutene) (*S*)- and (*R*)- formation (high activity, major enzyme)	potent activation	231-233, 286	7586124, 8901879, 9016811, 9635416
CYP2E1	chemical	halobenzene	1,4-dichlorobenzene	oxidation	activation	287	9817075
CYP2E1	chemical	triazole	1-aminobenzotriazole (1-ABT)	oxidation	activation	140	17584015

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2E1	chemical	haloalkane	2, 2-dichloro-1,1,1-trifluoroethane (HCFC-123)	oxidation	activation	268, 269, 288, 289	11684364, 11684365, 7975716, 8199305
CYP2E1	chemical	halobenzene	2,3-dichlorobutane	oxidation	activation	284	8671747
CYP2E1	chemical	nitrile, herbicide	2,6-dichlorobenzonitrile (dichlobenil)	epoxidation, C2,3-	activation	234,235	8649351, 8863822
CYP2E1	chemical	arylamine	2,6-dimethylaniline	*N*-hydroxylation (at higher concentration)	activation	236	11409937
CYP2E1	chemical	arylamine	2-aminoanthracene	*N*-hydroxylation	activation	61	11377247
CYP2E1	chemical	arylamine	2-aminofluorene (2-AF)	*N*-hydroxylation	activation	61	11377247
CYP2E1	natural compound	furanoterpene produced in sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	oxidation	activation	173	15892579
CYP2E1	chemical	unsaturated	4-vinyl-1-cyclohexene, (*S*)- and (*R*)-	epoxidation 7,8-, stereoselective for (*S*)-; epoxidation 1,2-, stereoselective for (*R*)-	activation	100, 273	11502734, 11159809
CYP2E1	chemical	acrylic amide	acrylamide	epoxidation to glycidamide	activation	290, 291	19190172, 20209648
CYP2E1	chemical	aliphatic nitrile	acrylonitrile (vinyl cyanide, cyanoethylene)	oxidation (2-cyanoethylene oxide formation)	activation	107, 282, 290	1486866, 1664256, 8117926
CYP2E1	chemical	oxidoazanium	azoxymethane	oxidation	activation	283	15576447
CYP2E1	chemical	aromatic hydrocarbon	benzene	hydroxylation, aromatic (via benzene oxide, muconic acid, and benzoquinone formation, major enzyme at low concentrations)	activation	107, 110, 282, 293-295	1486866, 7923572, 1664256, 10207612, 11083083, 15122651
CYP2E1	chemical	aliphatic epoxide, metabolite	butadiene monoxide (1, 2-epoxy-3-butene)	diepoxybutane *meso*- (major) and (±)- formation, high activity, major enzyme	potent activation	231-233, 296	7586124, 8901879, 9016811, 17298833
CYP2E1	chemical	haloalkane	carbon tetrachloride	dechlorination reductive (at low concentrations), oxidative stress induction	potent activation	106, 297-300	1486866, 8571359, 10731522, 8471158, 12235922

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2E1	chemical	haloalkane	chloroform (trichloromethane)	dehalogenation reductive (at high concentration, major enzyme); oxidation (major enzyme at low concentration)	potent activation	66, 107, 252, 282, 299, 301	9685642, 1486866, 12584152, 1664256, 8471158, 15129551
CYP2E1	chemical	haloalkene	chloroprene	epoxidation	activation	302	11397396
CYP2E1	drug	platinum-containing; anticancer	cisplatin	oxidation	activation	303, 304	16251482, 17761302
CYP2E1	drug	imidazole; anticancer, alkylating	dacarbazine	*N*-demethylation	activation	111	10473105
CYP2E1	chemical	haloalkene dichloromethane (methylene chloride)	dehalogenation	oxidative	activation	107, 282, 284, 297	1486866, 1664256, 8671747, 8571359
CYP2E1	chemical	organic solvents, alcohol	ethanol	oxidation, reactive oxygen species production	activation	305-309	7687464, 16052683, 16878272, 16356668, 21146245
CYP2E1	natural compound	carbamic acid derivative; fermentation by-product	ethyl carbamate (urethane)	oxidation to vinyl carbamate epoxide	activation	107, 282, 310-312	1486866, 1664256, 9344892, 9150748, 11181492
CYP2E1	chemical	furan	furan	oxidation, *cis*-2-butene-1,4-dial formation	activation	313	16006568
CYP2E1	chemical	organic solvents, alkylformamide	*N, N*-dimethylformamide(DMF)	*N*-demethylation (high activity)	activation	314, 315	8477011, 11684354
CYP2E1	chemical	organic solvents, alkylformamide	*N*-methylformamide	oxidation (methylisocyanate formation)	activation	316	1538706
CYP2E1	chemical	nitrosamine	*N*-nitrosodiethanolamine	oxidation	activation	317	18616954
CYP2E1	chemical	nitrosamine	*N*-nitrosodiethylamine (*N,N*-diethylnitrosamine,)	oxidation (major enzyme)	potent activation	107, 132-134, 141-144, 244, 318, 319	1486866, 11774366, 12214673, 11600130, 15728263, 15843388, 17158518, 9860501, 10837014, 11733072, 14669323

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2E1	chemical	nitrosamine	*N*-nitrosodimethylamine (*N*,*N*-dimethylnitrosamine, DMN)	oxidation (major enzyme)	activation	107, 134, 170, 244, 246, 317, 318, 320, 321, 322	1486866, 11600130, 9163700, 10837014, 1423839, 18616954, 11733072, 8692217, 10366544, 15668106
CYP2E1	chemical	nitrosamine	*N*-nitrosodi-*n*-propylamine (*N*-nitrosodipropylamine)	Cα-hydroxylation and *N*-depropylation (major enzyme); oxidation	activation	134, 141-143, 244, 318, 323-325	11600130, 15728263, 15843388, 17158518, 10837014, 11733072, 9247615, 8824531, 10910959
CYP2E1	chemical	nitrosamine	*N*-nitrosoethylbutylamine	oxidation	activation	134, 244	11600130, 10837014
CYP2E1	chemical	nitrosamine	*N*-nitrosomethylbutylamine	oxidation	potent activation	107, 134, 244	1486866, 11600130, 10837014,
CYP2E1	chemical	nitrosamine	*N*-nitrosomethylethylamine	oxidation	potent activation	134, 244	11600130, 10837014
CYP2E1	chemical	nitrosamine	*N*-nitrosomethylpropylamine	oxidation	potent activation	134, 244	11600130, 10837014
CYP2E1	chemical	nitrosamine	*N*-nitrosomorpholine	oxidation	activation	132, 133, 326	11774366, 12214673, 10461547
CYP2E1	chemical	nitrosamine	*N*-nitroso-*N*-methylbenzylamine	oxidation	activation	107	1486866
CYP2E1	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	hydroxylation C5′- (lactol formation, low activity)	activation	134, 244, 247, 256, 257	11600130, 10837014, 1423839, 9276639, 7646564
CYP2E1	chemical	nitrosamine	*N*-nitrosopyrrolidine	Cα-hydroxylation (2-OH-tetrahydrofuran formation); oxidation	activation	132-134, 244, 327	11774366, 12214673, 11600130, 10837014, 17457417
CYP2E1	chemical	*o*-methoxyaniline	*o*-anisidine (2-methoxyaniline)	*N*-hydroxylation (major enzyme in microsomal model)	potent activation	201, 328	15828049, 21217841

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2E1	chemical	aromatic hydrocarbons, alkyl benzene	styrene (vinyl benzene)	oxidation, medium K_m, major enzyme in liver at low concentration, stereoselective	activation	66, 107, 202-205, 280, 282, 329	9685642, 1486866, 9253143, 7696548, 11407535, 12616646, 16125881, 1664256, 16872732
CYP2E1	chemical	haloalkene	tetrachloroethylene	oxidation	activation	284	8671747
CYP2E1	chemical	haloalkene	trichloroethylene (TCE)	oxidation to trichloroethylene oxide and chloral hydrate form ation (major enzyme)	activation	107, 282, 330-333	1486866, 1664256, 9070354, 10807551, 11304134, 15987776
CYP2E1	chemical	vinyl halide	vinyl bromide (bromoethylene)	oxidation	activation	66, 107, 282	9685642, 1486866, 1664256
CYP2E1	chemical	carbamic acid derivative, metabolite	vinyl carbamate	epoxide formation	activation	66, 107, 282, 312	9685642, 1486866, 1664256, 11181492
CYP2E1	chemical	vinyl halide	vinyl chloride (chloroethylene)	oxidation	potent activation	66, 107, 282, 299	9685642, 1486866, 1664256, 8471158
CYP2E1	chemical	cyclohexane derivative	vinylcyclohexane	oxidation (epoxidation)	activation	329	16872732
CYP2F1	natural compound	indole, alkylating, pulmonary toxin; present in higher concentrations in mammalian digestive tract and coal tar	3-methylindole, skatole	dehydrogenation (desaturation, 3-methyleneindolenine form., low K_m, medium activity, high efficiency), major enzyme	potent activation	75-78, 334, 335	8558432, 11408359, 12563100, 20795680, 10383923, 17962375
CYP2F1	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	hydroxylation, α-methyl (keto alcohol formation)	activation	213-216	1312898, 7595636, 8806763, 10803680
CYP2F1	natural compound	furanoterpene produced in sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	oxidation	activation	172	1651809
CYP2F1	chemical	PAH	naphthalene	oxidation	activation	334	10383923

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2F1	chemical	aromatic hydrocarbon, alkyl benzene	styrene (vinyl benzene)	oxidation (major enzyme in lung microsomes)	activation	202-205, 278	9253143, 7696548, 11407535, 12616646, 16125881
CYP2W1	chemical	PAH, metabolite	(±)-benzo[*a*]pyrene-7,8-diol	oxidation	activation	210	16551781
CYP2W1	chemical	arylamine	2-aminoanthracene	oxidation	activation	210	16551781
CYP2W1	chemical	arylamine	2-aminofluorene (2-AF)	oxidation	activation	210	16551781
CYP2W1	chemical	heterocyclic amine	3-amino-1,4-dimethyl-5H-pyrido[4,3-*b*]indole (Trp-P-1)	oxidation	activation	210	16551781
CYP2W1	chemical	azoaromatic amine	3-methoxy-4-aminoazobenzene	oxidation	activation	210	16551781
CYP2W1	chemical	PAH, metabolite	5-methylchrysene-1,2-diol	oxidation	activation	210	16551781
CYP2W1	Natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	oxidation	activation	210	16551781
CYP2W1	chemical	PAH, metabolite	chrysene-1,2-diol	oxidation	activation	210	16551781
CYP2W1	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	oxidation	activation	210	16551781
CYP2W1	natural compound	furanoxanthone; mycotoxin, produced by *Aspergillus* species	sterigmatocystin	oxidation	activation	210	16551781
CYP3A4	chemical	nitroarene	1, 2-dihydro-1,2-dihydroxy-6-nitrochrysene	oxidation	activation	219	8481905
CYP3A4	chemical	nitroarene	6-nitrochrysene	oxidation	activation	12	2655891
CYP3A4	chemical	nitroarene	1,6-dinitropyrene	nitroreduction	activation	174	10197616
CYP3A4	chemical	triazole	1-aminobenzotriazole (1-ABT)	oxidation	activation	140	17584015
CYP3A4	chemical	arylamine, metabolite of 1-nitropyrene	1-aminopyrene	oxidation	activation	54	11525925
CYP3A4	chemical	nitroarene	1-nitropyrene	epoxidation C4,5-, minor reaction	activation	54, 107, 174	11525925, 1486866, 10197616
CYP3A4	chemical	arylamine	2-aminofluorene	oxidation	activation	61, 336	9328287, 11377247
CYP3A4	chemical	nitroarene	3,6-dinitrobenzo[*e*]pyrene	niroreduction and O-acetylation	activation	70	19393727

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP3A4	chemical	heterocyclic amine	3-amino-1,4-dimethyl-5H-pyrido[4,3-*b*]indole (Trp-P-1)	*N*-hydroxylation	potent activation	12, 61	2655891, 11377247
CYP3A4	chemical	heterocyclic amine	3-amino-1-methyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-2)	*N*-hydroxylation	potent activation	61	11377247
CYP3A4	chemical	azoaromatic amine	3-methoxy-4-aminoazobenzene	oxidation	activation	336	9328287
CYP3A4	chemical	arylamine	4,4′-methylene bis(2-chloroaniline) (MOCA)	oxidation, *N*- (major enzyme)	activation	66, 107, 249	9685642, 1486866, 1740010
CYP3A4	Natural compound	furanoterpene produced in sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	epoxidation; oxidation, minor enzyme	activation	140, 172, 173	17584015, 1651809, 15892579
CYP3A4	chemical	nitroarene	4-nitropyrene	4-aminopyrene formation (nitroreduction), major enzyme	activation	174	10197616
CYP3A4	chemical	*N*-heterocyclic aromatic hydrocarbon, dibenzocarbazole	5,9-dimethyldibenzo[*c,g*]carbazole	oxidation	activation	337	21798277
CYP3A4	chemical	arylamine	6-aminochrysene	oxidation (high activity)	potent activation	12, 84, 85, 107, 336, 338	2655891, 8118930, 8330339, 1486866, 9328287, 9493761
CYP3A4	chemical	arylamine, metabolite	6-aminochrysene-1,2-diol	Diol epoxide formation; oxidation	activation	84, 85	8118930, 8330339
CYP3A4	chemical	*N*-heterocyclic aromatic hydrocarbon, dibenzocarbazole	7*H*-dibenzo[*c,g*]carbazole	oxidation	activation	337	21798277
CYP3A4	chemical	PAH, aza-aromatic	7-methylbenz[*c*]acridine	oxidation.	potent activation	92	7866988
CYP3A4	chemical	PAH, metabolite	benzo[*a*]pyrene 7,8-diol	oxidation	activation	12	2655891

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP3A4	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation exo-C8,9- (major activating enzyme), oxidation	activation	11, 12, 42, 57, 61, 175-180, 182, 336, 339-341	2492107, 2655891, 7955101, 15279838, 11377247, 2162057, 7766804, 8261428, 12079611, 1902334, 11782366, 16608170, 9328287, 1643250, 7545582, 7850790
CYP3A4	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin G_1 (AFG_1)	oxidation	activation	11, 12, 107, 148, 341-343	2492107, 2655891, 1486866, 8082563, 7850790, 352361, 12849689
CYP3A4	chemical	herbicide, chloroacetamide	alachlor	oxidation	activation	274	11133395
CYP3A4	chemical	herbicide, chloroacetamide	butachlor	oxidation	activation	274	11133395
CYP3A4	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation; oxidation	activation	108, 251-254, 275, 344	19501186, 8242617, 9010702, 10348794, 10692561, 9923542, 15919850
CYP3A4	chemical	PAH), aza-aromatic	dibenz[*a,f*]acridine	3,4-dihydrodiol formation	potent activation	92	7866988
CYP3A4	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	ellipticine	hydroxylation, C13- (major enzyme) and C12- (minor reaction); oxidation N2- (major enzyme	potent activation	39, 40, 287-290, 345	16936898, 21753906, 11755121, 12123750, 15548707, 17197724, 20576524

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP3A4	physiological compound	estrogen	17β-estradiol	C2-hydroxylation (major reaction, major enzyme, medium K_m, medium efficiency, high activity), major metabolite and major enzyme in liver; oxidation, 2,3-quinone formation (lower activity); C4-hydroxylation (minor reaction, major enzyme, medium K_m, medium activity, medium efficiency); oxidation, 3,4-quinone formation; C16α-hydroxylation (high K_m, low activity)	activation	107, 122-124, 126-130, 190-193, 346, 347	1486866, 9625734, 9054608, 9667077, 11555828, 12865317, 15784278, 16112414, 17570247, 1449532, 9635876, 11454902, 11741520, 10821664, 12124305
CYP3A4	physiological compound	estrogen	estrone	C2-hydroxylation (high K_m, major metabolite, low activity); oxidation, 2,3-quinone formation; C4-hydroxylation (high K_m, low activity, major enzyme); C16α-hydroxylation (high K_m, low activity, major enzyme)	activation	48, 122-124, 127, 128, 130, 191, 192	10426814, 9625734, 9054608, 9667077, 12865317, 15784278, 17570247, 9635876, 11454902
CYP3A4	drug	estradiol derivative; estrogen, contraceptive	17α-ethynylestradiol (ethinylestradiol 17α-)	oxygenation (2-hydroxylation, 17α-inactivation)	activation	140, 348	17584015, 17251390
CYP3A4	drug	antimitotic, epipodophyllotoxin, topoisomerase II inhibitor	etoposide (VP-16)	*O*-demethylation (catechol formation), high K_m, high activity, major enzyme	activation	349-351	8114683, 9456308, 17168690
CYP3A4	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation stereoselective for (*R*)- (high K_m, high activity), oxidation at high concentrations	potent activation	87, 251, 254, 275-277, 344, 352-355	20507880, 8242617, 10692561, 15919850, 10534317, 15821045, 9923542, 8161344, 10101149, 10348794, 16854777
CYP3A4	chemical	herbicide, chloroacetamide	metolachlor	oxidation	activation	274	11133395

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP3A4	natural compound	alkaloid, pyrrolizidine, genotoxic	monocrotaline	dehydrogenation	activation	356	15649625
CYP3A4	chemical	aziridine	*N, N*′, *N*″-triethylene thiophosphoramide (thioTEPA)	desulfuration, TEPA formation (minor enzyme)	activation	279	12107550
CYP3A4	chemical	tobacco-specific nitrosamine	*N*′-nitrosoanabasine	oxidation (major enzyme)	activation	132, 133	11774366, 12214673
CYP3A4	chemical	nitrosamine	*N*-nitrosodibutylamine (*N,N*-dibutylnitrosamine)	oxidation	activation	134	11600130
CYP3A4	chemical	nitrosamine	*N*-nitrosodiethylamine (*N,N*-diethylnitrosamine)	oxidation	activation	134, 255	11600130, 1423839
CYP3A4	chemical	nitrosamine	*N*-nitrosoethylbutylamine	oxidation	activation	134	11600130
CYP3A4	chemical	nitrosamine	*N*-nitrosomethylbutylamine	oxidation	activation	134	11600130
CYP3A4	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	hydroxylation C2′- (keto alcohol formation); oxidation	activation	132, 133, 264, 265	11774366, 12214673, 9276639, 7646564
CYP3A4	chemical	nitrosamine	*N*-nitrosopiperidine	Cα-hydroxylation (2-OH-tetrahydropyran and 2-OH-5-methyltetrahydrofuran formation); oxidation	activation	132, 133	11774366, 12214673
CYP3A4	chemical	nitrosamine	*N*-nitrosopyrrolidine	Cα-hydroxylation (2-OH-tetrahydrofuran formation); oxidation	activation	132, 133	11774366, 12214673
CYP3A4	natural compound	pyrrolizidine alkaloid from *Senecio retrorsus*	retrorsine	dehydrogenation	activation	356	15649625
CYP3A4	natural compound	pyrrolizidine alkaloid, food contaminant (meat, milk, and honey)	riddelline	dehydrogenation	activation	356	15649625
CYP3A4	natural compound	pyrrolizidine alkaloid, genotoxic	senecionine	dehydrogenation	activation	107, 357	1486866, 2009596
CYP3A4	natural compound	furanoxanthone; mycotoxin, produced by *Aspergillus* species	sterigmatocystin	oxidation	activation	11, 12, 66, 107, 336, 341	2492107, 2655891, 9685642, 1486866, 9328287, 7850790

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP3A4	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator	tamoxifen	Cα-hydroxylation (major enzyme), catechol formation, oxidation, at high concentrations	activation	87, 354, 358-364	20507880, 10348797, 12018981, 12971802, 14678348, 15159443, 16533026, 12124303, 12419838
CYP3A4	chemical	organophosphate	tris(2,3-dibromopropyl)phosphate	oxidation	activation	12, 107	2655891, 1486866
CYP3A5	chemical	PAH, aza-aromatic	7-methylbenz[*c*]acridine	oxidation	potent activation	92	7866988
CYP3A5	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation *exo*-8,9- (major reaction); oxidation	activation	182, 365	16608170, 7893152
CYP3A5	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation (very low activity) activation to cytotoxic metabolites	activation	253	10348794
CYP3A5	chemical	PAH, aza-aromatic	dibenz[*a,j*]acridine	3,4-dihydrodiol formation	activation	92	7866988
CYP3A5	physiological compound	estrogen	17β-estradiol	C2-hydroxylation; C4-hydroxylation (major reaction); C16α-hydroxylation (low activity)	activation	127, 128, 191, 192, 347	12865317, 15784278, 9635876, 11454902, 12124305
CYP3A5	drug	estradiol derivative; estrogen, contraceptive	17α-ethynylestradiol (ethinylestradiol, 17α-)	oxygenation (2-hydroxylation, 17α-mechanism-based inactivation)	activation	140, 348	17584015, 17251390
CYP3A5	drug	antimitotic, epipodophyllotoxin, topoisomerase II inhibitor	etoposide (VP-16)	*O*-demethylation (catechol formation), medium K_m, high activity, minor enzyme	activation	349	8114683
CYP3A5	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation, stereoselective for (*R*)-	activation	253, 276, 277, 353, 355	10348794, 10534317, 15821045, 10101149, 16854777
CYP3A5	chemical	tobacco-specific nitrosamine	*N*'-nitrosoanabasine	oxidation	activation	132, 133	11774366, 12214673
CYP3A5	natural compound	nitrosamine, tobacco-specific	*N*'-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	oxidation	activation	132, 133	11774366, 12214673
CYP3A7	chemical	arylamine	2-aminofluorene (2-AF)	oxidation	activation	336	9328287

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP3A7	chemical	azoaromatic amine	3-methoxy-4-aminoazobenzene	oxidation	activation	336	9328287
CYP3A7	chemical	arylamine	6-aminochrysene	oxidation	activation	336, 338	9328287, 9493761
CYP3A7	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation *exo*-C8,9-; oxidation	activation	107, 182, 336, 338, 341, 366	1486866, 16608170, 9328287, 9493761, 7850790, 9044840
CYP3A7	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin G_1 (AFG_1)	oxidation	activation	341	7850790
CYP3A7	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation	activation	253, 275	10348794, 15919850
CYP3A7	physiological compound	estrogen	17β-estradiol	C2-hydroxylation (medium K_m, low activity, major reaction); C4-hydroxylation (low activity, high K_m); C16α-hydroxylation (very low activity, high K_m)	activation	127, 128, 347	12865317, 15784278, 12124305,
CYP3A7	physiological compound	estrogen	estrone	C2-hydroxylation (medium K_m, medium activity); C4-hydroxylation (low activity, medium K_m); C16α-hydroxylation (medium K_m, medium activity)	activation	127, 128	12865317, 15784278
CYP3A7	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation stereoselective for (*R*)- (high K_m, medium (*S*-) and high (*R*-) activity, minor enzyme and reaction)	activation	253, 273	10348794, 15919850
CYP3A7	natural compound	furanoxanthone; mycotoxin, produced by *Aspergillus* species	sterigmatocystin	oxidation	activation	336, 338, 341	9328287, 9493761, 7850790
CYP4B1	chemical	arylamine	2-aminofluorene (2-AF)	*N*-hydroxylation; oxidation	activation	367, 368	11396967, 11062028
CYP4B1	natural compound	furanoterpene produced in sweet	4-ipomeanol	oxidation	activation	172	1651809

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
		potatoes infected with Fusarium solani; pulmonary toxin, alkylating					
CYP4B1	chemical	aromatic hydrocarbon	benzene	oxidation (at high conc., minor reaction)	activation	294	11083083
CYP19A1 (aromatase)	physiological compound	estrogen	17β-estradiol	C2-hydroxylation (medium K_m)	activation	125, 369	8930523, 8476762
CYP19A1 (aromatase)	physiological compound	estrogen	estrone	C2-hydroxylation (medium K_m)	activation	125, 369	8930523, 8476762
Epoxide hydrolase, EH	chemical	PAH, metabolite	benzo[*a*]pyrene-7,8-oxide	hydrolysis to benzo[*a*]pyrene -7,8-diol	activation	51, 220	21028851, 10409402
FMO1	chemical	thiocarbamide	thiourea	*S*-oxidation (medium K_m, high activity)	activation	370, 371	10901713, 14976351
FMO2	chemical	thiocarbamide	1-phenylthiourea	*S*-oxidation	activation	372	15144220
FMO2	chemical	thiocarbamide	α-naphthylthiourea	*S*-oxidation	activation	372	15144220
FMO2	chemical	thiocarbamide	ethylenethiourea	*S*-oxidation	activation	372	15144220
FMO2	chemical	thiocarbamide	thiourea	*S*-oxidation (medium K_m, high activity)	activation	372, 373	15144220, 11744609
FMO3	chemical	thiocarbamide	thiourea	*S*-oxidation (medium K_m, high activity)	activation	374	12093470
GST	chemical	haloalkane	1, 2-dibromoethane (ethylene dibromide)	GSH conjugation	activation	375-378	8330352, 16948056, 12542971, 15554237
GST	chemical	haloalkane	1, 2-dichloroethane, ethylene dichloride	GSH conjugation	activation	375, 378	8330352, 15554237
GST	chemical	haloalkene	chlorotrifluoroethene	GSH conjugation	activation	378	15554237
GST	chemical	haloalkane	dichloromethane, methylene chloride	GSH conjugation	activation	284, 377, 378	8671747, 12542971, 15554237
GST	chemical	haloalkene	hexachlorobutadiene	GSH conjugation	activation	378	15554237
GST	chemical	haloalkene	tetrafluoroethene	GSH conjugation	activation	378	15554237
GST	chemical	haloalkene	trichloroethene	GSH conjugation	activation	378	15554237
GST T1-1	chemical	haloalkane	1, 2-dibromoethane (ethylene dibromide)	GSH conjugation	activation	378	8565128

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
GST T1-1	chemical	haloalkane	dibromomethane (methylene dibromide)	GSH conjugation	activation	378	8565128
GST T1-1	chemical	haloalkane	diepoxybutane (butadiene diepoxide)	GSH conjugation	activation	379, 380	8565128, 222181695
GST A1-1	chemical	haloalkane	diepoxybutane, butadiene diepoxide	GSH conjugation	activation	380	222181695
GST A3-3	chemical	haloalkane	diepoxybutane (butadiene diepoxide)	GSH conjugation	activation	380	222181695
GST M1-1	chemical	haloalkane	diepoxybutane (butadiene diepoxide)	GSH conjugation	activation	380	222181695
GST P1-1	chemical	haloalkane	diepoxybutane (butadiene diepoxide)	GSH conjugation	activation	380	222181695
Lactoperoxidase (LPO)	chemical	arylamine, metabolite	3-aminobenzanthrone	*N*-oxidation	activation	72, 73	15885895, 16601755
Lactoperoxidase (LPO)	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	Ellipticine	oxidation	activation	39, 40	16936898, 21753906
Myeloperoxidase (MPO)	chemical	arylamine, metabolite	3-aminobenzanthrone	*N*-oxidation	activation	72, 73	15885895, 16601755
Myeloperoxidase (MPO)	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	ellipticine	oxidation	activation	39, 40	16936898, 21753906
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	1,2-dibromoethane (ethylene dibromide)	conjugation	activation	381, 382	12151404, 15257623
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	dibromomethane (methylene dibromide)	conjugation	activation	382, 383	15257623, 15206895

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	bromomethyl acetate	conjugation	activation	383	15206895
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	dichloromethane (methylene dichloride)	conjugation	activation	382	15257623
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	bromochloromethane	conjugation	activation	382	15257623
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	1,2-diiodoethane (ethylene diiodide)	conjugation	activation	382	15257623
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	1,2-bromochloroethane	conjugation	activation	382	15257623
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	1,3-dibromopropane	conjugation	activation	382	15257623
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	1,4-dibromobutane	conjugation	activation	382	15257623
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	1,3-diiodopropane	conjugation	activation	382	15257623
***O*^{6}-alkylguanine DNA alkyl transferase (MGMT)**	chemical	bifunctional electrophile	diepoxybutane (butadiene diepoxide)	conjugation	activation	382	15257623

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
NADPH-cytochrome P450 reductase (POR)	chemical	nitroarene	1,8-dinitropyrene	nitroreduction	activation	53, 384	11113705, 15606153
NADPH-cytochrome P450 reductase (POR)	chemical	nitroarene	1-nitro-6-nitrosopyrene	reduction	activation	384	15606153
NADPH-cytochrome P450 reductase (POR)	chemical	nitroarene	1-nitro-8-nitrosopyrene	reduction	activation	384	15606153
NADPH-cytochrome P450 reductase (POR)	chemical	nitroarene	3,6-dinitrobenzo[*e*]pyrene	niroreduction and *O*-acetylation	activation	70	19393727
NADPH-cytochrome P450 reductase (POR)	chemical	nitroarene	3-nitrobenzanthrone	nitroreduction	activation	80	12782579
NADPH-cytochrome P450 reductase (POR)	chemical	quinone	anthraquinone	reduction	activation	385	11697035
NADPH-cytochrome P450 reductase (POR)	drug	dihydroxyanthraquinone; laxative	danthron	reduction	activation	383	11697035
Xanthine oxidoreductase (XOR)	chemical	nitroarene	2-nitroanisole	nitroreduction to hydroxylamine	activation	328	21217841
Xanthine oxidoreductase (XOR)	chemical	nitroarene	3-nitrobenzanthrone	nitroreduction to hydroxylamine	activation	79	12740904
NAT1	chemical	nitroarene	1,8-dinitropyrene	*O*-acetylaton after nitroreduction	activation	386	10357791

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
NAT1	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-(diallylamino)-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-8)	*O*-acetylation	activation	55	18562244
NAT1	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-(diethylamino)-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-7)	*O*-acetylation	activation	55	18562244
NAT1	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-[bis(2-hydroxyethyl)amino]-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-6)	*O*-acetylation	activation	55	18562244
NAT1	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-amino-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-4)	*O*-acetylation	activation	55	18562244
NAT1	chemical	arylamine, metabolite	2-acetylaminofluorene (2-AAF)	*O*-acetylation after *N*-hydroxylation	potent activation	147	15450435
NAT1	chemical	heterocyclic amine	2-amino-6-methyldipyrido[1,2-*a*:3′,2′-*d*]-imidazole (Glu-P-1)	*O*-acetylation after *N*-hydroxylation	activation	386	10357791
NAT1	chemical	arylamine	2-aminofluorene (2-AF)	*O*-acetylaton after *N*-hydroxylation	activation	386, 387	10357791, 1617672
NAT1	chemical	arylamine	2-naphthylamine	*O*-acetylation after *N*-hydroxylation	activation	147	15450435
NAT1	chemical	nitroaromatic	2-nitrofluorene	*O*-acetylaton after nitroreduction	activation	386	10357791
NAT1	chemical	nitroarene	3-acetylaminobenzanthrone	*O*-acetylation after *N*-hydroxylation, at higher conc.	potent activation	79	12740904
NAT1	chemical	arylamine, metabolite	3-aminobenzanthrone	*O*-acetylation after *N*-hydroxylation, at higher conccentrations	potent activation	79	12740904
NAT1	chemical	nitroarene	3-nitrobenzanthrone	*O*-acetylation after nitro-reduction to hydroxylamine, at higher concentrations	potent activation	73, 79, 388	16601755, 12740904, 12419844
NAT1	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl (4-ABP)	*O*-acetylation after *N*-hydroxylation	potent activation	147, 389	15450435, 8353847
NAT1	chemical	arylamine, heterocyclic	aminophenylnorharman	*O*-acetylation after *N*-hydroxylation	activation	95	17067997

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
NAT1	chemical	arylamine	benzidine	*O*-acetylation after *N*-hydroxylation	activation	147, 387	15450435, 1617672
NAT1	chemical	arylamine, metabolite	*N*-acetyl-*N*-hydroxy-3-aminobenzanthrone	*O*-acetylation at higher concentrations	potent activation	79, 387	12740904, 12419844
NAT1	chemical	arylamine, tobacco smoke compound, metabolite	*N*-hydroxy-4-aminobiphenyl (*N*-OH-4-ABP)	*O*-acetylation	activation	389	8353847
NAT1	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-2-aminofluorene (*N*-OH-2-AF)	*O*-acetylation	activation	389	8353847
NAT1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-aminomethylphenylnorharman	*O*-acetylation	activation	95	17067997
NAT1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-aminophenylnorharman	*O*-acetylation	activation	95	17067997
NAT1	chemical	nitroarene	nitrofen	*O*-acetylation after nitroreduction	activation	390	14754874
NAT1	chemical	*o*-methoxyaniline	*o*-anisidine, 2-methoxyaniline	*O*-acetylation after *N*-hydroxylation	activation	147	15450435
NAT2	chemical	nitroarene	1,8-dinitropyrene	*O*-acetylaton after nitroreduction	potent activation	386	10357791
NAT2	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-(diallylamino)-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2Hbenzotriazole (PBTA-8)	oxidation	activation	55	18562244
NAT2	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-(diethylamino)-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2Hbenzotriazole (PBTA-7)	oxidation	activation	55	18562244
NAT2	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-[bis(2-hydroxyethyl)amino]-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-6)	oxidation	activation	55	18562244
NAT2	chemical	2-phenylbenzotriazole	2-[2-(acetylamino)-4-amino-5-methoxyphenyl]-5-amino-7-bromo-4-chloro-2*H*-benzotriazole (PBTA-4)	oxidation	activation	55	18562244
NAT2	chemical	hydroxylamine, heterocyclic amine, metabolite	2-amino-3,4-dimethylimidazo[4,5-*f*]quinolone (MeIQ)	*O*-acetylation after *N*-hydroxylation	activation	386, 387	10357791, 1617672

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
NAT2	chemical	heterocyclic amine	2-amino-6-methyldipyrido[1,2-*a*:3′,2′-*d*]-imidazole (Glu-P-1)	*O*-acetylation after *N*-hydroxylation	activation	386	10357791
NAT2	chemical	nitroarene	2-nitrobenzanthrone	*O*-acetylation after reduction to hydroxylamine	activation	391	17483118
NAT2	chemical	nitroarene	3-acetylaminobenzanthrone	*O*-acetylation after Nhydroxylation, at higher concentration	potent activation	79	12740904
NAT2	chemical	arylamine, metabolite	3-aminobenzanthrone	*O*-acetylation after Nhydroxylation, at higher concentration	potent activation	79	12740904
NAT2	chemical	nitroarene	3-nitrobenzanthrone	*O*-acetylation after nitro-reduction to hydroxylamine, at higher concentration	potent activation	73, 79, 388, 391	16601755, 12740904, 12419844, 17483118
NAT2	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl (4-ABP)	*O*-acetylation after *N*-hydroxylation	activation	147, 389	15450435, 8353847
NAT2	chemical	arylamine	6-aminochrysene	*O*-acetylation after *N*-hydroxylation	activation	386	10357791
NAT2	chemical	arylamine, heterocyclic	aminomethylphenylnorharman	*O*-acetylation after *N*-hydroxylation	activation	95	17067997
NAT2	chemical	arylamine, heterocyclic	aminophenylharman	*O*-acetylation after *N*-hydroxylation	activation	95	17067997
NAT2	chemical	arylamine, heterocyclic	aminophenylnorharman	*O*-acetylation after *N*-hydroxylation	activation	95	17067997
NAT2	chemical	arylamine, metabolite	*N*-acetyl-*N*-hydroxy-3-aminobenzanthrone	*O*-acetylation at higher conc.	potent activation	79, 388	12740904, 12419844
NAT2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methylimidazo[4,5-*f*]quinolone (*N*-hydroxyisoIQ)	*O*-acetylation	activation	392	7697826
NAT2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-3,4-dimethylimidazo[4,5-*f*]quinolone (*N*-hydroxy-MeIQ)	*O*-acetylation	activation	392	7697826
NAT2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (*N*-hydroxy-MeIQx)	*O*-acetylation	activation	392	7697826
NAT2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-3-methylimidazo[4,5-*f*]quinolone (*N*-hydroxy-IQ)	*O*-acetylation	potent activation	392, 393	7697826, 12067565

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
NAT2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-6-methyldipyrido[1,2-*a*:3′,2′-*d*]-imidazole (*N*-hydroxy-Glu-P-1)	*O*-acetylation	activation	392	7697826
NAT2	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-2-aminobenzanthrone	*O*-acetylation	activation	391	17483118
NAT2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-aminodipyrido[1,2-*a*:3,2′-*d*]-imidazole (*N*-hydroxy-Glu-P-2)	*O*-acetylation	ativation	392	7697826
NAT2	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-3-aminobenzanthrone	*O*-acetylation	activation	391	17483118
NAT2	chemical	arylamine, tobacco smoke compound, metabolite	*N*-hydroxy-4-aminobiphenyl (*N*-OH-4-ABP)	*O*-acetylation	activation	389	8353847
NAT2	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxyaminofluorene (*N*-OH-2-AF)	*O*-acetylation	activation	389	8353847
NAT2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxyaminomethylphenylnorharman	*O*-acetylation	activation	95	17067997
NAT2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxyaminophenylnorharman	*O*-acetylation	activation	95	17067997
NAT2	chemical	*o*-methoxyaniline	*o*-anisidine, 2-methoxyaniline	*O*-acetylation after *N*-hydroxylation	activation	147	15450435
Prostaglandin H synthase (PHS, COX)	chemical	arylamine, metabolite	3-aminobenzanthrone	*N*-oxidation	activation	72, 73	15885895, 16601755
Quinone oxidoreductase (NQO1)	chemical	nitroarene	3-nitrobenzanthrone	nitroreduction (major enzyme)	potent activation	73, 80	16601755, 12782579
SULT1A1	chemical	PAH, metabolite	(−)-1-hydroxyethylpyrene	*O*-sulfonation	activation	169, 394	10720750, 11535246
SULT1A1	chemical	PAH, metabolite	1-(1-pyrenyl)ethanol	*O*-sulfonation	activation	395	9141497
SULT1A1	chemical	PAH, metabolite	1-hydroxymethylpyrene	*O*-sulfonation	potent activation	169, 390, 396, 397	10720750, 14754874, 10657971, 17936463
SULT1A1	natural compound	1-methoxy-3-indolylmethyl	1-methoxy-3-indolylmethyl-alcohol	*O*-sulfonation	activation	398	20846518

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
		glucosinolate breakdown product, in many *Brassica* vegetables					
SULT1A1	chemical	benzylic alcohol, nitroatromatic	2,4-dinitrobenzylalcohol	*O*-sulfonation	activation	169, 394, 399	10720750, 11535246, 11154739
SULT1A1	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	*O*-sulfonation after oxidation	activation	400	22006426
SULT1A1	chemical	heterocyclic amine	2-amino-6-methyldipyrido[1,2-*a*:3′,2′-*d*]-imidazole (Glu-P-1)	*O*-sulfonation after *N*-hydroxylation	potent activation	401	22072630
SULT1A1	chemical	benzylic alcohol	2-aminobenzylalcohol	*O*-sulfonation	activation	3979	11154739
SULT1A1	chemical	arylamine, heterocyclic	2-hydroxylamino-3-methyl-9H-pyrido[2,3-*b*]indole (*N*-OH-MeAαC)	*O*-sulfonation	potent activation	160	14729582
SULT1A1	chemical	hydroxylamine, heterocyclic	2-hydroxylamino-5-phenylpyridine	*O*-sulfonation	activation	394	11535246
SULT1A1	chemical	nitroarene	2-nitrobenzanthrone	*O*-sulfonation after reduction to hydroxylamine	activation	391	17483118
SULT1A1	chemical	nitroarene	3,9-dinitrofluoranthene	*O*-sulfonation	potent activation	401	22072630
SULT1A1	chemical	nitroarene	3-acetylaminobenzanthrone	*O*-sulfonation after *N*-hydroxylation, at higher concentrations	potent activation	79	12740904
SULT1A1	chemical	arylamine, metabolite	3-aminobenzanthrone	*O*-sulfonation after *N*-hydroxylation, at higher concentrations	potent activation	79	12740904
SULT1A1	chemical	azoaromatic amine	3-methoxy-4-aminoazobenzene	*O*-sulfonation	potent activation	401	22072630
SULT1A1	chemical	nitroarene	3-nitrobenzanthrone	*O*-sulfonation after nitroreduction to hydroxylamine	potent activation	73, 79, 364, 391, 401	16601755, 12740904, 12419844, 17483118, 22072630
SULT1A1	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-sulfonation	activation	402, 403	12034366, 21537383

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
SULT1A1	chemical	furaldehyde derivative	5-hydroxymethylfurfural	*O*-sulfonation	activation	322, 397, 400	15668106, 17936463, 22006426
SULT1A1	chemical	nitroaromatic	5-nitroacenaphthene	*O*-sulfonation	potent activation	401	22072630
SULT1A1	chemical	PAH, metabolite	7-hydroxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene	*O*-sulfonation	activation	395	9141497
SULT1A1	natural compound	nephrotoxin, *Aristolochia fangchi* compound, nitroarene	aristolochic acids I and II	*O*-sulfonation after nitroreduction to hydroxylamine	potent activation	404	16161050
SULT1A1	chemical	furan	furan	*O*-sulfonation after oxidation	activation	322	15668106
SULT1A1	chemical	furan derivative	furfuryl alcohol	*O*-sulfonation	activation	405	21729924
SULT1A1	chemical	arylamine, metabolite	*N*-acetyl-*N*-hydroxy-3-aminobenzanthrone	*O*-sulfonation, at higher concentrations	potent activation	79, 364	12740904, 12419844
SULT1A1	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylamino-3-methyl-5-phenylpyridine	*O*-sulfonation	activation	399	11154739
SULT1A1	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*O*-sulfonation	activation	169, 406	10720750, 11535243
SULT1A1	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminol-5-phenylpyridine	*O*-sulfonation	activation	399	11154739
SULT1A1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-hydroxy-PhIP)	*O*-sulfonation	potent activation	393, 399	12067565, 11154739
SULT1A1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-3-methylimidazo[4,5-*f*]quinolone (*N*-hydroxy-IQ)	*O*-sulfonation	potent activation	407	16708048
SULT1A1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-6-methyldipyrido[1,2-*a*:3′,2′-*d*]-imidazole (*N*-hydroxy-Glu-P-1)	*O*-sulfonation	activation	408	7834621
SULT1A1	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-2-aminobenzanthrone	*O*-sulfonation	activation	401	17483118
SULT1A1	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-3-aminobenzanthrone	*O*-sulfonation	activation	391	17483118
SULT1A1	chemical	arylamine, tobacco smoke compound, metabolite	*N*-hydroxy-4-aminobiphenyl (*N*-OH-4-ABP)	*O*-sulfonation	activation	409	7859374

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
SULT1A1	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-2-aminofluorene (*N*-OH-4-AF)	*O*-sulfonation	activation	408	7834621
SULT1A1	chemical	nitroarene	nitrofen	*O*-sulfonation after nitroreduction to hydroxylamine	potent activation	322, 390	15668106, 14754874
SULT1A1	chemical	nitrosamine	*N*-nitrosodimethylamine (*N*, *N*-dimethylnitrosamine, DMN)	*O*-sulfonation after oxidation	activation	322	15668106
SULT1A1	chemical	heterocyclic amine	*N*-OH-4,4′-methylenebis(2-chloroaniline) (*N*-OHMOCA)	*O*-sulfonation	activation	408	7834621
SULT1A2	chemical	PAH, metabolite	(−)-1-hydroxyethylpyrene	*O*-sulfonation	activation	394	11535246
SULT1A2	chemical	PAH, metabolite	1-hydroxymethylpyrene	*O*-sulfonation	activation	394, 410	11535246, 12464797
SULT1A2	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	*O*-sulfonation after oxidation	activation	400	22006426
SULT1A2	chemical	arylamine, heterocyclic	2-hydroxylamino-3-methyl-9*H*-pyrido[2,3-*b*]indole (N-OH-MeAαC)	*O*-sulfonation	activation	159	14729582
SULT1A2	chemical	hydroxylamine, heterocyclic	2-hydroxylamino-5-phenylpyridine	*O*-sulfonation	potent activation	394, 410	11535246, 12464797
SULT1A2	chemical	nitroarene	3-acetylaminobenzanthrone	*O*-sulfonation after *N*-hydroxylation, at higher concentrations	potent activation	79	12740904
SULT1A2	chemical	arylamine, metabolite	3-aminobenzanthrone	*O*-sulfonation after *N*-hydroxylation, at higher concentrations	potent activation	79	12740904
SULT1A2	chemical	nitroarene	3-nitrobenzanthrone	*O*-sulfonation after nitroreduction to hydroxylamine	activation	73, 79	16601755, 12740904
SULT1A2	chemical	furaldehyde derivative	5-hydroxymethylfurfural	*O*-sulfonation	activation	400	22006426
SULT1A2	chemical	arylamine, metabolite	*N*-acetyl-*N*-hydroxy-3-aminobenzanthrone	*O*-sulfonation, at higher concentrations	potent activation	79, 388	12740904, 12419844
SULT1A2	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylamino-3-methyl-5-phenylpyridine	*O*-sulfonation	activation	399	11154739
SULT1A2	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*O*-sulfonation	potent activation	169, 394, 410	10720750, 11535246, 12464797

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
SULT1A2	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminol-5-phenylpyridine	*O*-sulfonation	activation	399	11154739
SULT1A2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	*O*-sulfonation	potent activation	393, 399	12067565, 11154739
SULT1A2	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-2-aminofluorene (*N*-OH-2-AF)	*O*-sulfonation	potent activation	401	22072630
SULT1A3	natural compound	alkenylbenzene; occurs in a variety of foods including essential oils of tarragon, sweet basil, sweet fennel, anis, metabolite	1′-hydroxyestragole	*O*-sulfonation	activation	197, 401	21459083, 22072630
SULT1A3	chemical	PAH, metabolite	1-hydroxymethylpyrene	*O*-sulfonation	activation	169, 394, 396	10720750, 11535246, 10657971
SULT1A3	chemical	nitroalkane	2-nitropropane	*O*-sulfonation, propane 2-nitronate formation	activation	169, 396	1072075, 10657971
SULT1A3	natural compound	alkenylbenzene; occurs in a variety of foods including essential oils of tarragon, sweet basil, sweet fennel, anis	estragole	*O*-sulfonation after C1′-hydroxylation	activation	401	22072630
SULT1A3	chemical	nitroarene	nitrofen	*O*-sulfonation after nitroreduction to hydroxylamine	activation	390	14754874
SULT1B1	chemical	PAH, aldehyde	1-formylpyrene	*O*-sulfonation	activation	399	11154739
SULT1B1	chemical	PAH, metabolite	1-hydroxymethylpyrene	*O*-sulfonation	activation	394	11535246
SULT1B1	chemical	arylamine, heterocyclic	2-hydroxylamino-3-methyl-9*H*-pyrido[2,3-*b*]indole (*N*-OH-MeAαC)	*O*-sulfonation	activation	159	14729582
SULT1B1	chemical	hydroxylamine, heterocyclic	2-hydroxylamino-5-phenylpyridine	*O*-sulfonation	activation	394	11535246
SULT1B1	chemical	PAH, metabolite	4-hydroxycyclopenta[*d,e.f*]chrysene	*O*-sulfonation	potent activation	169, 394	10720750, 11535246
SULT1B1	chemical	PAH, metabolite	6-hydroxymethylbenzo[*a*]pyrene	*O*-sulfonation	potent activation	394	11535246

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enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
SULT1B1	natural compound	nephrotoxin, *Aristolochia fangchi* compound, nitroarene	aristolochic acids I and II	*O*-sulfonation after nitroreduction to hydroxylamine	activation	394	16161050
SULT1C1	chemical	PAH, metabolite	(−)-1-hydroxyethylpyrene	*O*-sulfonation	activation	392	11535246
SULT1C1	chemical	arylamine, heterocyclic	2-hydroxylamino-3-methyl-9*H*-pyrido[2,3-*b*]indole (*N*-OH-MeAαC)	*O*-sulfonation	activation	169	14729582
SULT1C1	chemical	nitroarene	nitrofen	*O*-sulfonation after nitroreduction to hydroxylamine	activation	390	14754874
SULT1C2	chemical	PAH, metabolite	(−)-1-hydroxyethylpyrene	*O*-sulfonation	activation	394	11535246
SULT1C2	chemical	PAH, metabolite	1-hydroxymethylpyrene	*O*-sulfonation	activation	394	11535246
SULT1C2	chemical	furan derivative	2,5-(bishydroxymethyl)furan	*O*-sulfonation	activation	411	21825114
SULT1C2	chemical	furan derivative	5-methylfurfural	*O*-sulfonation	activation	411	21825114
SULT1C2	chemical	furan derivative	furfuryl alcohol	*O*-sulfonation	activation	411	21825114
SULT1C3	chemical	PAH, metabolite	(±)-, (+)-, and (−)-1-hydroxyethylpyrene	*O*-sulfonation	activation	397	17936463
SULT1C3	chemical	methylenedioxyphenyl, benzodioxole, metabolite	1′-hydroxysafrole	*O*-sulfonation, at high conc.	activation	397	17936463
SULT1C3	chemical	PAH, metabolite	6-hydroxymethylanthanthrene	*O*-sulfonation	potent activation	397	17936463
SULT1C3	chemical	PAH, metabolite	6-hydroxymethylbenzo[*a*]pyrene	*O*-sulfonation	potent activation	397	17936463
SULT1E1	chemical	PAH, metabolite	(±)-, (+)-, and (−)-1-hydroxyethylpyrene	*O*-sulfonation	potent activation	169, 394, 397	10720750, 11535246, 17936463
SULT1E1	chemical	PAH, metabolite	1-(1-pyrenyl)ethanol	*O*-sulfonation	activation	395	9141497
SULT1E1	chemical	PAH, metabolite	10-hydroxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene	*O*-sulfonation	activation	395	9141497
SULT1E1	chemical	PAH, metabolite	1-hydroxymethylpyrene	*O*-sulfonation	potent activation	394, 396, 397	11535246, 10657971, 17936463
SULT1E1	chemical	PAH, metabolite	4-hydroxycyclopenta[def]chrysene	*O*-sulfonation	activation	169, 394	10720750, 11535246

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
SULT2A1	chemical	PAH, metabolite	(±)-, (+)-, and (−)-1-hydroxyethylpyrene	*O*-sulfonation	activation	169, 394, 397	10720750, 11535246, 17936463
SULT2A1	chemical	PAH, metabolite	1-(1-pyrenyl)ethanol, I-HEP	*O*-sulfonation	activation	395	9141497
SULT2A1	chemical	PAH, metabolite	1-hydroxy-3-methylcholanthrene	*O*-sulfonation	activation	395	9141497
SULT2A1	chemical	PAH, metabolite	1-hydroxymethylpyrene	*O*-sulfonation	potent activation	169, 394, 396	10720750, 11535246, 10657971
SULT2A1	chemical	PAH, metabolite	2-hydroxymethylpyrene	*O*-sulfonation	activation	395	9141497
SULT2A1	drug	pregnane, antiandrogen, metabolite	3α-hydroxycyproterone acetate	*O*-sulfonation	activation	394	11535246
SULT2A1	chemical	PAH, metabolite	6-hydroxymethylbenzo[a]pyrene	*O*-sulfonation	potent activation	169, 394	10720750, 11535246
SULT2A1	chemical	PAH, metabolite	7-hydroxy-12-methylbenz[*a*]anthracene	*O*-sulfonation	activation	394	9141497
SULT2A1	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	α-hydroxytamoxifen	*O*-sulfonation	activation	412, 413	9855017, 15371299
SULT2A1	drug	thioxanthenone; schistosomicide	hycanthone	*O*-sulfonation	potent activation	394, 395	11535246, 9141497
SULT2E1	chemical	PAH	1-acetylpyrene	*O*-sulfonation	potent activation	399	11154739
SULT2E1	drug	thioxanthenone; schistosomicide	hycanthone	*O*-sulfonation	activation	394	11535246

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Table 2

Bioactivation of Natural Compounds

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A1	natural compound	indole, alkylating, pulmonary toxin; higher concentrations in mammalian digestive tract and coal tar	3-methylindole (skatole) epoxidation (3-methyloxindole formation); dehydrogenation (desaturation, 3-methyleneindolenine form), low K_m, medium	activity, high efficiency	activation	75-78	8558432, 11408359, 12563100, 20795680
CYP1A1	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation 8,9-; oxidation	activation	41, 57, 61, 93, 94	8674051, 15279838, 11377247, 7923587, 8200084
CYP1A1	natural compound	phenanthroic acid derivative; nephrotoxin, found in the *Aristolochiaceae* family of plants	aristolochic acid I	nitroreduction	potent activation	96-99	11511187, 15386410, 16125300, 22086975
CYP1A1	natural compound	phenanthroic acid derivative; nephrotoxin, found in the *Aristolochiaceae* family of plants	aristolochic acid II	nitroreduction	activation	96-99	11511187, 15386410, 16125300, 22086975
CYP1A1	physiological compound	estrogen	17β−estradiol	C2-hydroxylation (major reaction, medium K_m, high activity, high efficiency), major metabolite and major extrahepatic enzyme; C4-hydroxylation (minor reaction, medium K_m, medium efficiency, low activity), oxidation, 3,4-quinone formation (lower activity); oxidation, 2,3-quinone formation; C16α-hydroxylation (high K_m, low activity)	potent activation	71, 106, 121-130	9721189, 8037457, 7826886, 9625734, 9054608, 9667077, 8930523, 11555828, 12865317, 15784278, 16112414, 17570247
CYP1A1	physiological compound	estrogen	estrone	C2-hydroxylation (major reaction, medium K_m, low activity), oxidation, 2,3-quinone formation; C4-hydroxylation (medium K_m, low	activation	49, 127, 130, 131	10426814, 12865317, 17570247, 15805301

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
				activity, or medium activity); C16α-hydroxylation (minor reaction, very low activity)			
CYP1A1	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	oxidation	activation	132, 133	11774366, 12214673
CYP1A2	natural compound	furanoterpene produced by sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	oxidation (major enzyme)	activation	172, 173	1651809, 15892579
CYP1A2	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation (both *exo*-8,9- and *endo*-8,9-); oxidation	activation	11, 12, 13, 41, 42, 57, 61, 93, 94, 162, 175-182	2492107 2655891, 2509067, 8674051, 7955101, 15279838, 11377247, 7923587, 8200084, 10023085, 2162057 7766804, 8261428, 12079611, 1902334, 11782366, 16385575, 16608170
CYP1A2	natural compound	phenanthroic acid derivative; nephrotoxin, found in the *Aristolochiaceae* family of plants	aristolochic acid I	nitroreduction	potent activation	96-99	11511187, 15386410, 16125300, 22086975
CYP1A2	natural compound	phenanthroic acid derivative; nephrotoxin, found in the *Aristolochiaceae* family of plants	aristolochic acid II	nitroreduction	potent activation	96-99	11511187, 15386410, 16125300, 22086975
CYP1A2	natural compound	bicyclic monoterpene	Δ^3-carene	epoxidation (high K_m, medium activity)	activation	183	16379671

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1A2	physiological compound	estrogen	17β-estradiol	C2-hydroxylation (major reaction, medium K_m, medium activity, medium efficiency), major metabolite and major enzyme in liver; C4-hydroxylation (minor reaction); C16α-hydroxylation (major enzyme, high K_m, no activity, or low activity)	activation	71, 106, 122-124, 126-129, 190-194	9721189, 8037457, 9625734, 9054608, 9667077, 11555828, 12865317, 15784278, 16112414, 1449532, 9635876, 11454902, 11741520, 14703066
CYP1A2	natural compound	alkenylbenzene; occurs in a variety of foods including essential oils of tarragon, sweet basil, sweet fennel, anis	estragole	C1′-hydroxylation (major enzyme, medium K_m, low activity)	potent activation	195-197	17407329, 15914212, 21459083
CYP1A2	physiological compound	estrogen	estrone	C2-hydroxylation (medium K_m, high activity, major metabolite); C4-hydroxylation (medium K_m, medium activity, very low activity); C16α-hydroxylation (minor reaction, very low activity)	activation	49, 122, 123, 127, 128, 191, 192, 198	10426814, 9625734, 9054608, 12865317, 15784278, 9635876, 11454902, 16537715
CYP1A2	natural compound	phenylpropene, from *Rhizoma acorigraminei*	methyleugenol	C1′-hydroxylation (medium K_m, major enzyme)	activation	196, 199	15914212, 16411663
CYP1A2	natural compound	furanoxanthone; mycotoxin, produced by *Aspergillus* species	sterigmatocystin	oxidation	activation	41	8674051
CYP1B1	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	oxidation	activation	61, 210, 217	11377247, 16551781, 9106248

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP1B1	physiological compound	estrogen	17β-estradiol	C4-hydroxylation (major enzyme, medium K_m, medium activity, medium and low efficiency), oxidation, 3,4-quinone formation; C2-hydroxylation (low activity, minor reaction), oxidation, 2,3-quinone formation; C16α-hydroxylation (minor enzyme, medium and high K_m, low activity)	potent activation	49, 71, 121-130, 194, 211, 221, 225-228	10426814, 9721189, 7826886, 9625734, 9054608, 9667077, 8930523, 11555828, 12865317, 15784278, 16112414, 17570247, 14703066, 11719446, 11465393, 8790407, 7568105, 10862525, 10910054
CYP1B1	physiological compound	estrogen	estrone	C4-hydroxylation (low K_m, major reaction); C2-hydroxylation (low activity, minor reaction), oxidation, 2,3-quinone formation;	potent activation	49, 127, 128, 130, 198	10426814, 12865317, 15784278, 17570247, 16537715
CYP2A6	natural compound	alkenylbenzene; occurs in a variety of foods	including essential oils of tarragon, sweet basil, sweet fennel, anis estragole	C1′-hydroxylation (major enzyme, medium K_m, medium activity)	potent activation	195, 197	17407329, 21459083
CYP2A6	natural compound	furanocoumarin; anti-psoriatic, photosensitizer, found in several species of plants	methoxalen (8-methoxypsoralen, xanthotoxin)	epoxidation (furanoepoxide formation) and hydrolysis	activation	140	17584015
CYP2A6	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	hydroxylation C5′-(lactol formation, medium K_m, high to medium activity); oxidation (major enzyme)	activation	132-134, 244, 256-258	11774366, 12214673, 11600130, 15651850, 10837014, 9276639, 7646564
CYP2A6	natural compound	methylenedioxypheny, benzodioxole	safrole	C1′-hydroxylation (major enzyme at low concentrations), medium Km, medium activity	activation	195, 196, 259, 260	17407329, 15914212, 15377158, 15310247
CYP2A13	natural compound	indole, alkylating, pulmonary toxin; in higher concentrations in mammalian digestive tract and coal tar	3-methylindole, skatole	dehydrogenation (desaturation, 3-methyleneindolenine formation, low K_m, medium activity, high	potent activation	77, 261	20795680, 19608696

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
				efficiency); epoxidation (3-methyloxindole formation)			
CYP2A13	chemical	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation 8,9-; oxidation	potent activation	181, 265	16385575, 16917071
CYP2A13	natural compound	furanocoumarin; anti-psoriatic, photosensitiser, found in bergamot essential oil, in other citrus essential oils, and in grapefruit juice	bergapten (5-methoxypsoralen)	epoxidation and hydrolysis to dihydrodiol	activation	267	20798279
CYP2A13	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	hydroxylation C5′- (lactol formation, medium K_m, high activity) and C2′- (keto alcohol formation, medium K_m, low activity)	activation	258, 266	19074523, 15651850
CYP2C9	natural compound	phenylpropene; from *Rhizoma acorigraminei*	methyleugenol	C1′-hydroxylation (medium activity, high K_m), at high concentration	activation	196, 199	15914212, 16411663
CYP2C19	natural compound	furanoterpene produced in sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	oxidation (major enzyme)	activation	173	15892579
CYP2D6	natural compound	furanoterpene produced in sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	oxidation	activation	173	15892579
CYP2D6	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	oxidation	activation	61	11377247
CYP2E1	natural compound	furanoterpene produced in sweet potatoes infected with *Fusariumsolani*; pulmonary toxin, alkylating	4-ipomeanol	oxidation	activation	173	15892579
CYP2E1	natural compound	carbamic acid derivative;	ethyl carbamate (urethane)	oxidation to vinyl	activation	107, 282, 310-312	1486866, 1664256, 9344892, 9150748, 11181492

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
		fermentation by-product		carbamate epoxide			
CYP2E1	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	hydroxylation C5′-(lactol formation, low activity)	activation	134, 244, 247, 256, 265	11600130, 10837014, 1423839, 9276639, 7646564
CYP2F1	natural compound	indole, alkylating, pulmonary toxin; present in higher concentrations	in mammalian digestive tract and coal tar	3-methylindole, skatole dehydrogenation (desaturation, 3-methyleneindolenine form., low K_m, medium activity, high efficiency), major enzyme	potent activation	75-79, 334, 335	8558432, 11408359, 12563100, 20795680, 10383923, 17962375
CYP2F1	natural compound	furanoterpene produced in sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	oxidation	activation	172	1651809
CYP2W1	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	oxidation	activation	210	16551781
CYP2W1	natural compound	furanoxanthone; mycotoxin, produced by *Aspergillus* species	sterigmatocystin	oxidation	activation	210	16551781
CYP3A4	natural compound	furanoterpene produced in sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	epoxidation; oxidation, minor enzyme	activation	140, 172, 173	17584015, 1651809, 15892579
CYP3A4	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation *exo*-C8,9- (major activating enzyme), oxidation	activation	11, 12, 41, 57, 61, 175-180, 182, 336, 339-341	2492107, 2655891, 7955101, 15279838, 11377247, 2162057, 7766804, 8261428, 12079611, 1902334, 11782366, 16608170, 9328287, 1643250, 7545582, 7850790

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP3A4	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin G_1 (AFG_1)	oxidation	activation	11, 12, 107, 341-343	2492107, 2655891, 1486866, 8082563, 7850790, 352361, 12849689
CYP3A4	physiological compound	estrogen	17β-estradiol	C2-hydroxylation (major reaction, major enzyme, medium K_m, medium efficiency, high activity), major metabolite and major enzyme in liver; oxidation, 2,3-quinone formation (lower activity); C4-hydroxylation (minor reaction, major enzyme, medium K_m, medium activity, medium efficiency); oxidation, 3,4-quinone formation; C16α-hydroxylation (high K_m, low activity)	activation	107, 122-124, 126-130, 190-193, 346, 347	1486866, 9625734, 9054608, 9667077, 11555828, 12865317, 15784278, 16112414, 17570247, 1449532, 9635876, 11454902, 11741520, 10821664, 12124305
CYP3A4	physiological compound	estrogen	estrone	C2-hydroxylation (high K_m, major metabolite, low activity); oxidation, 2,3-quinone formation; C4-hydroxylation (high K_m, low activity, major enzyme); C16α-hydroxylation (high K_m, low activity, major enzyme)	activation	49, 122-124, 127, 128, 130, 191, 192	10426814, 9625734, 9054608, 9667077, 12865317, 15784278, 17570247, 9635876, 11454902
CYP3A4	natural compound	alkaloid, pyrrolizidine, genotoxic	monocrotaline	dehydrogenation	activation	356	15649625
CYP3A4	natural compound	nitrosamine, tobacco-specific	*N*′-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	hydroxylation C2′- (keto alcohol formation); oxidation	activation	132, 133, 256, 257	11774366, 12214673, 9276639, 7646564
CYP3A4	natural compound	pyrrolizidine alkaloid from *Senecio retrorsus*	retrorsine	dehydrogenation	activation	356	15649625
CYP3A4	natural compound	pyrrolizidine alkaloid, food contaminant (meat, milk, and honey)	riddelliine	dehydrogenation	activation	356	15649625
CYP3A4	natural compound	pyrrolizidine alkaloid, genotoxic	senecionine	dehydrogenation	activation	107, 357	1486866, 2009596

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP3A4	natural compound	furanoxanthone; mycotoxin, produced by *Aspergillus* species	sterigmatocystin	oxidation	activation	11, 12, 66, 107, 336, 341	2492107, 2655891, 9685642, 1486866, 9328287, 7850790
CYP3A5	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation *exo*-8,9- (major reaction); oxidation	activation	182, 365	16608170, 7893152
CYP3A5	physiological compound	estrogen	17β-estradiol	C2-hydroxylation; C4-hydroxylation (major reaction); C16α-hydroxylation (low activity)	activation	127, 128, 191, 192, 347	12865317, 15784278, 9635876, 11454902, 12124305
CYP3A5	chemical	tobacco-specific nitrosamine	*N*′-nitrosoanabasine	oxidation	activation	132, 133	11774366, 12214673
CYP3A7	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	epoxidation *exo*-C8,9-; oxidation	activation	107, 182, 336, 338, 341, 366	1486866, 16608170, 9328287, 9493761, 7850790, 9044840
CYP3A7	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin G_1 (AFG_1)	oxidation	activation	341	7850790
CYP3A7	physiological compound	estrogen	17β-estradiol	C2-hydroxylation (medium K_m, low activity, major reaction); C4-hydroxylation (low activity, high K_m); C16α-hydroxylation (very low activity, high K_m)	activation	127, 128, 347	12865317, 15784278, 12124305,
CYP3A7	physiological compound	estrogen	estrone	C2-hydroxylation (medium K_m, medium activity); C4-hydroxylation (low activity, medium K_m); C16α-hydroxylation (medium K_m, medium activity)	activation	127, 128	12865317, 15784278
CYP3A7	natural compound	furanoxanthone; mycotoxin, produced by *Aspergillus* species	sterigmatocystin	oxidation	activation	336, 338, 341	9328287, 9493761, 7850790

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP4B1	natural compound	furanoterpene produced in sweet potatoes infected with *Fusarium solani*; pulmonary toxin, alkylating	4-ipomeanol	oxidation	activation	172	1651809
CYP19A1 (aromatase)	physiological compound	estrogen	estradiol 17β-	C2-hydroxylation (medium K_m)	activation	125, 369	8930523, 8476762
CYP19A1 (aromatase)	physiological compound	estrogen	estrone	C2-hydroxylation (medium K_m)	activation	125, 369	8930523, 8476762
SULT1A1	natural compound	1-methoxy-3-indolylmethyl glucosinolate breakdown product, in many *Brassica* vegetables	1-methoxy-3-indolylmethyl-alcohol	*O*-sulfonation	activation	398	20846518
SULT1A1	natural compound	nephrotoxin, *Aristolochia fangchi* compound, nitroarene	aristolochic acids I and II	*O*-sulfonation after nitroreduction to hydroxylamine	potent activation	404	16161050
SULT1A3	natural compound	alkenylbenzene; occurs in a variety of foods including essential oils of tarragon, sweet basil, sweet fennel, anis, metabolite	1′-hydroxyestragole	*O*-sulfonation	activation	197, 401	21459083, 22072630
SULT1A3	natural compound	alkenylbenzene; occurs in a variety of foods including essential oils of tarragon, sweet basil, sweet fennel, anis	estragole	*O*-sulfonation after C1′-hydroxylation	activation	401	22072630
SULT1B1	natural compound	nephrotoxin, *Aristolochia fangchi* compound, nitroarene	aristolochic acids I and II	*O*-sulfonation after nitroreduction to hydroxylamine	activation	394	16161050

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Table 3

Activation of Drugs

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
COX-1	drug	pyrido-carbazole; antineoplastic, alkaloid, Apocyanaceae plant compound, topoisomerase II inhibitor, and DNA binding	ellipticine	oxidation	activation	39, 40	16936898, 21753906
CYP1A1	drug	imidazole; anticancer, alkylating	dacarbazine	*N*-demethylation (major extrahepatic enzyme)	activation	111	10473105
CYP1A1	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	oxidation (at high conc.)	activation	87	20507880
CYP1A2	drug	imidazole; anticancer, alkylating	dacarbazine	*N*-demethylation (major enzyme)	potent activation	111	10473105
CYP1A2	drug	pyrido-carbazole; antineoplastic, alkaloid, apocyanaceae plant compound, topoisomerase II inhibitor and DNA binding	ellipticine	hydroxylation, C12- and C13- (low activity)	activation	39, 40, 185-189	16936898, 21753906, 11755121, 12123750, 15548707, 17197724, 21683692
CYP1A2	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	oxidation (at high concentration)	activation	87	20507880
CYP1B1	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plant compound, topoisomerase II inhibitor and DNA binding	ellipticine	oxidation	activation	39, 185-188	16936898, 11755121, 12123750, 15548707, 17197724
CYP2A6	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation (minor enzyme, high K_m); oxidation	activation	101, 108, 251-254	11377097, 19501186, 8242617, 9010702, 10348794, 10692561
CYP2A6	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation (minor reaction, high K_m); oxidation (at high concentration)	activation	87, 251, 253	20507880, 8242617, 10348794
CYP2B6	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation (major enzyme, major reaction, high K_m, high activity); oxidation	potent activation	74, 101, 108, 251-254, 271, 275	11360624, 11377097, 19501186, 8242617, 9010702, 10348794, 10692561, 9280407, 15919850

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP2B6	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation stereoselective for (*S*)-(high K_m, major enzyme); oxidation (at high concentrations)	activation	87, 251-254, 275-277, 355	20507880, 8242617, 10348794, 10692561, 15919850, 10534317, 15821045, 16854777
CYP2C8	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation (minor enzyme, high K_m), oxidation (at high concentrations)	activation	87, 251, 253	20507880, 8242617, 10348794
CYP2C9	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation (low K_m, low activity, major enzyme at low concentration); oxidation	activation	101, 108, 251-254	11377097, 19501186, 8242617, 9010702, 10348794, 10692561
CYP2C9	Drug	Oxazaphosporine; Anticancer, Nitrogen mustard alkylating	Ifosfamide	C4-hydroxylation (low K_m), Oxidation (at high concentrations)	activation	87, 251	8242617, 20507880
CYP2C9	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation (low K_m), oxidation (at high concentration)	activation	86, 251	20507880, 8242617
CYP2C19	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation stereoselective for (*S*)- (minor reaction, high K_m), oxidation (at high concentration)	activation	87, 251, 253, 276	20507880, 8242617, 10348794, 10534317
CYP2D6	drug	pyrido-carbazole; antineoplastic, alkaloid, Apocyanaceae plant compound, topoisomerase II inhibitor and DNA binding	ellipticine	oxidation N^2-; hydroxylation, C13-(low activity)	activation	39, 40, 187, 188	16936898, 21753906, 15548707, 17197724
CYP2D6	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	oxidation (at high concentration)	activation	87	20507880
CYP2E1	drug	platinum-containing; anticancer	cisplatin	oxidation	activation	303, 304	16251482, 17761302
CYP2E1	drug	imidazole; anticancer, alkylating	dacarbazine	*N*-demethylation	activation	111	10473105
CYP3A4	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation; oxidation	activation	108, 251-254, 275, 344	19501186, 8242617, 9010702, 10348794, 10692561, 9923542, 15919850

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
CYP3A4	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	ellipticine	hydroxylation, C13- (major enzyme) and C12- (minor reaction); oxidation N2- (major enzyme)	potent activation	39, 40, 287-290, 345	16936898, 21753906, 11755121, 12123750, 15548707, 17197724, 20576524
CYP3A4	drug	estradiol derivative; estrogen, contraceptive	17α-ethynylestradiol (ethinylestradiol 17α-)	oxygenation (2-hydroxylation, 17α-inactivation)	activation	140, 348	17584015, 17251390
CYP3A4	drug	antimitotic, epipodophyllotoxin, topoisomerase II inhibitor	etoposide (VP-16)	*O*-demethylation (catechol formation), high K_m, high activity, major enzyme	activation	349-351	8114683, 9456308, 17168690
CYP3A4	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation stereoselective for (*R*)- (high K_m, high activity); oxidation at high concentration	potent activation	87, 251, 275-277, 344, 352-355	20507880, 8242617, 10692561, 15919850, 10534317, 15821045, 9923542, 8161344, 10101149, 10348794, 16854777
CYP3A4	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator	tamoxifen	Cα-hydroxylation (major enzyme); catechol formation; oxidation, at high concentration	activation	87, 354, 358-364	20507880, 10348797, 12018981, 12971802, 14678348, 15159443, 16533026, 12124303, 12419838
CYP3A5	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation (very low activity) activation to cytotoxic metabolites	activation	253	10348794
CYP3A5	drug	estradiol derivative; estrogen, contraceptive	17α-ethynylestradiol (ethinylestradiol, 17α-)	oxygenation (2-hydroxylation, 17α-mechanism-based inactivation)	activation	140, 348	17584015, 17251390
CYP3A5	drug	antimitotic, epipodophyllotoxin, topoisomerase II inhibitor	etoposide (VP-16)	*O*-demethylation (catechol formation), medium K_m, high activity, minor enzyme	activation	349	8114683
CYP3A5	drug	oxazaphosporine; anticancer, nitrogen	ifosfamide	C4-hydroxylation, stereoselective for (*R*)-	activation	253, 276,	10348794, 10534317, 15821045, 10101149, 16854777

enzyme	category	subcategory	compound	reaction	remarks	references	PubMed ID
		mustard alkylating				277, 353, 355	
CYP3A7	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating	cyclophosphamide	C4-hydroxylation	activation	253, 275	10348794, 15919850
CYP3A7	drug	oxazaphosporine; anticancer, nitrogen mustard alkylating	ifosfamide	C4-hydroxylation stereoselective for (*R*)- (high K_m, medium (*S*-) and high (*R*-) activity, minor enzyme and reaction)	activation	253, 275	10348794, 15919850
Lactoperoxidase (LPO)	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	Ellipticine	oxidation	activation	39, 40	16936898, 21753906
Myeloperoxidase (MPO)	drug	pyrido-carbazole; antineoplastic, alkaloid, apocyanaceae plants compound, topoisomerase II inhibitor and DNA binding	ellipticine	oxidation	activation	39, 40	16936898, 21753906
NADPH-cytochrome P450 reductase (POR)	drug	dihydroxyanthraquinone, laxative	danthron	reduction	activation	385	11697035
SULT1A1	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-sulfonation	activation	402, 403	12034366, 21537383
SULT2A1	drug	pregnane, antiandrogen, metabolite	3α-hydroxycyproterone acetate	*O*-sulfonation	activation	394	11535246
SULT2A1	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	α-hydroxytamoxifen	*O*-sulfonation	activation	412, 413	9855017, 15371299
SULT2A1	drug	thioxanthenone, schistosomicide	hycanthone	*O*-sulfonation	potent activation	394, 395	11535246, 9141497
SULT2E1	drug	thioxanthenone, schistosomicide	hycanthone	*O*-sulfonation	activation	394	11535246

Table 4

Detoxication Reactions

enzyme	category	subcategory	compound	reaction	references	PubMed ID
AKR1B1	natural compound	carbonyl, unsaturated	4-hydroxynonenal	reduction	414	21329684
AKR1B1	natural compound	carbonyl, unsaturated	acrolein	reduction (low activity)	414	21329684
AKR1B1	natural compound	carbonyl, unsaturated	crotonaldehyde	reduction (low activity)	414	21329684
AKR1B1	natural compound	GSH conjugate, metabolite	GS-2-hexenal	reduction (high activity)	414	21329684
AKR1B1	natural compound	carbonyl, unsaturated	GS-4-hydroxynonanal	reduction (high activity)	414	21329684
AKR1B1	natural compound	carbonyl, unsaturated	GS-butanal	reduction (high activity)	414	21329684
AKR1B1	natural compound	carbonyl, unsaturated	GS-propanal	reduction	414	21329684
AKR1B1	natural compound	GSH conjugate, metabolite	GS-trans-2-hexenal	reduction	414	21329684
AKR1B1	natural compound	carbonyl, unsaturated	trans-2,4-hexedinal	reduction	414	21329684
AKR1B1	natural compound	carbonyl, unsaturated	trans-2-hexenal	reduction	414	21329684
AKR1B10	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	reduction	415	16381663
AKR1B10	natural compound	carbonyl, unsaturated	4-hydroxynonenal	reduction (high activity)	414, 416, 417	21329684 19013440, 19563777,
AKR1B10	natural compound	carbonyl, unsaturated	4-methylpentanal	reduction	416	19013440
AKR1B10	natural compound	carbonyl	4-oxonon-2-enal	reduction	416	19013440
AKR1B10	natural compound	carbonyl	acrolein	reduction	414, 417	21329684 19563777
AKR1B10	natural compound	carbonyl	crotonaldehyde	reduction (high activity)	414, 417	21329684 19563777
AKR1B10	natural compound	GSH conjugate, metabolite	GS-2-hexenal	reduction	414	21329684

enzyme	category	subcategory	compound	reaction	references	PubMed ID
AKR1B10	natural compound	GSH conjugate, metabolite	GS-acrolein	reduction	417	19563777
AKR1B10	natural compound	carbonyl, unsaturated	GS-butanal	reduction	414	21329684
AKR1B10	natural compound	GSH conjugate, metabolite	GS-crotonaldehyde	reduction	417	19563777
AKR1B10	natural compound	carbonyl, unsaturated	GS-propanal	reduction (low activity)	414	21329684
AKR1B10	natural compound	GSH conjugate, metabolite	GS-trans-2, 4-hexadienal	reduction	417	19563777
AKR1B10	natural compound	GSH conjugate, metabolite	GS-trans-2-hexenal	reduction (high activity)	414, 417	21329684 19563777
AKR1B10	natural compound	carbonyl, unsaturated	trans-2, 4-hexadienal	reduction	417	19563777
AKR1B10	natural compound	carbonyl, unsaturated	trans-2,4-hexedinal	reduction	414	21329684
AKR1B10	natural compound	carbonyl, unsaturated	trans-2-hexenal	reduction (high activity)	414, 417	21329684 19563777
AKR1C1	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	reduction	418, 419	11037109, 11306090
AKR1C2	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	reduction	418, 419	11037109, 11306090
AKR1C4	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	reduction	418, 419	11037109, 11306090
AKR7A2	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 dialdehyde	reduction	420, 421	10383892, 17537398
AKR7A3	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products, metabolite	aflatoxin B_1 dialdehyde	reduction	420-422	10383892, 17537398, 18416522
CYP1A1	chemical	nitroarene	2-nitroanisole	demethylation, *O*-hydroxylation, C2-, C2-C5-, and C2-C6-	423, 424	15144223, 17159769
CYP1A1	natural compound	nephrotoxin, *Aristolochia fangchi* compound, nitroarene	aristolochic acid I	hydroxylation, C8- (major enzyme)	99	22086975

enzyme	category	subcategory	compound	reaction	references	PubMed ID
CYP1A1	chemical	PAH	benzo[a]pyrene	hydroxylation, 3- (low K_m, or medium K_m, medium activity, or high activity)	44, 46, 48, 104-106, 425-427	11238186, 7581497, 8293790, 9806168, 11513247, 8037457, 7766605, 9152602, 7703357
CYP1A1	chemical	PAH	benzo[*a*]pyrene	hydroxylation 3- (low activity)	44, 138	11238186 9014198
CYP1A1	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor, and DNA binding	ellipticine	hydroxylation, C7- and C9- (major enzyme, low activity)	39, 187, 189	16936898, 15548707, 21683692
CYP1A1	chemical	aza-aromatic	Sudan I	hydroxylation, C4′- (high activity), hydroxylation, C6- (low activity); oxidation, major enzyme	136, 137	12384524, 17159775
CYP1A2	chemical	heterocyclic amine	2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx)	C8-oxidation (carboxylic acid form.)	428, 429	10220313, 11258970
CYP1A2	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	hydroxylation (AFM_1 formation, major enzyme and reaction); hydroxylation, C3α- (AFQ_1 formation, low activity); demethylation, O- (AFP_1 formation, very low activity)	176-178	7766804, 8261428, 12079611
CYP1A2	natural compound	nephrotoxin, *Aristolochia fangchi* compound, nitroarene	aristolochic acid I	hydroxylation, C8- (major enzyme)	99	22086975
CYP1A2	chemical	PAH	benzo[*a*]pyrene	3- hydroxylation (low activity)	46, 104, 106, 425-427, 430	7581497, 9806168, 8037457, 7766605, 9152602, 7703357, 1551116

enzyme	category	subcategory	compound	reaction	references	PubMed ID
CYP1A2	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	ellipticine	hydroxylation, C7- and C9- (major enzyme in liver, low activity)	39, 187, 189	16936898, 15548707, 21683692
CYP1A2	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	ellipticine	C7- hydroxylation (major enzyme)	187	15548707
CYP1B1	chemical	PAH	benzo[*a*]pyrene	3-hydroxylation	104, 222, 426	9806168, 15958554, 9152602
CYP1B1	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	ellipticine	hydroxylation, C7- (very low activity) and C9-	187	15548707
CYP2A6	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	oxidation, *N*-	265	12975327
CYP2A6	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	oxidation, N-	265	12975327
CYP2A6	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	hydroxylation (AFM1 formation, low activity); hydroxylation, C3α- (AFQ_1 formation, low activity); demethylation, O- (AFP1 formation, major reaction), at high substrate concentrations	181	16385575
CYP2A13	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	oxidation, *N*-	265	12975327
CYP2A13	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	hydroxylation (AFM_1 formation, low activity); hydroxylation, C3α- (AFQ_1	181	16385575

enzyme	category	subcategory	compound	reaction	references	PubMed ID
				formation, low activity); demethylation, O- (AFP_1 formation, very low activity)		
CYP2B6	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	oxidation, N-	265	12975327
CYP2C19	chemical	PAH	benzo[*a*]pyrene	hydroxylation 3-	138, 425, 427	9014198, 7766605, 7703357,
CYP2C8	chemical	PAH	benzo[*a*]pyrene	hydroxylation 3-	425, 427, 430	7766605, 7703357, 1551116
CYP2C9	chemical	PAH	benzo[*a*]pyrene	hydroxylation 3- (major enzyme)	138, 425, 427, 430	9014198, 7766605, 7703357, 1551116
CYP2D6	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	ellipticine	hydroxylation, C7- (low activity) and C9-	187	15548707
CYP2E1	chemical	nitroarene	2-nitroanisole	demethylation, *O*- hydroxylation, C2-, C2-C5-, and C2-C6- (major enzyme)	423, 424	15144223, 17159769
CYP2E1	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	oxidation, N-	265	12975327
CYP2E1	chemical	PAH	benzo[*a*]pyrene	hydroxylation 3- (low activity)	425, 427	7766605, 7703357
CYP3A4	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	hydroxylation, C3α- (AFQ_1 form.), medium K_m, medium activity, major reaction, major enzyme	176-178, 339	7766804, 8261428, 12079611, 1643250
CYP3A4	chemical	PAH	benzo[*a*]pyrene	hydroxylation 3- (major enzyme)	138, 425-427, 430	9014198, 7766605, 9152602, 7703357, 1551116

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enzyme	category	subcategory	compound	reaction	references	PubMed ID
CYP3A4	drug	pyrido-carbazole; antineoplastic, alkaloid, *Apocyanaceae* plants compound, topoisomerase II inhibitor and DNA binding	ellipticine	hydroxylation, C9- (very low activity)	187	15548707
CYP3A4	chemical	aza-aromatic	Sudan I	hydroxylation, C4′- and C6 (low activity)	136	12384524
CYP3A5	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	hydroxylation, C3α- (AFQ_1 form.)	182, 365	16608170, 7893152
CYP3A7	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products	aflatoxin B_1 (AFB_1)	hydroxylation, C3α - (AFQ1 formation)	182	16608170
Epoxide hydrolase, EH	chemical	haloalkene, metabolite	chloroprene epoxide (1-chloroethenyl oxirane)	hydrolysis	431	14565770
Epoxide hydrolase, EH	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products, metabolite	aflatoxin B_1-8,9-epoxide	hydrolysis, aflatoxin-8,9-dihydrodiol formation	432, 433	8781383, 9115980
Epoxide hydrolase, EH	chemical	PAH, metabolite	benzo[*a*]pyrene-7,8-oxide	hydrolysis to benzo[*a*]pyrene-7,8-diol	52, 220	21028851, 10409402
GST	physiological compound	estrogen, metabolite	4-hdroxyestrone-*o*-quinone	covalent binding	434	18588320
GST	chemical	acrylic amide	acrylamide	GSH conjugation	435	19904761
GSTM	chemical	aromatic hydrocarbon, alkyl benzene, metabolite	styrene 7,8-oxide	GSH conjugation	436, 437	3224538, 3692493
GSTA1	chemical	PAH	dibenzo[*a,l*]pyrene	GSH conjugation after oxidation	119	17509623
GSTA1	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	GSH conjugation after oxidation	119, 438	17509623, 9855012
GSTA1-1	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-dihydrodiol 9,10-epoxide	GSH conjugation (high activity)	439-441	8706254, 11849043, 12067250

enzyme	category	subcategory	compound	reaction	references	PubMed ID
GSTA1-1	drug	oxazaphosporine; anticancer, mitrogen mustard, alkylating, metabolite	4-hydroxycyclophosphamide	GSH conjugation	442	7954469
GSTA1-1	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products, metabolite	aflatoxin B_1-8,9-epoxide	GSH conjugation	375, 443	8330352, 9675258
GSTA1-1	chemical	PAH, metabolite	benzo[*c*]chrysene-9,10-diol 11,12-epoxide	GSH conjugation	439	8706254
GSTA1-1	chemical	PAH, metabolite	benzo[*c*]phenanthrene-3,4-diol 1,2-epoxide	GSH conjugation	439	8706254
GSTA1-1	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol 13,14-epoxide	GSH conjugation	439	8706254
GSTA1-1	chemical	PAH, metabolite	chrysene-*trans*-1,2-dihydrodiol-3,4-epoxide	GSH conjugation	439	8706254
GSTA1-1	chemical	PAH, metabolite	dibenz[*a,h*]anthracene-3,4-dihydrodiol 1,2-epoxide	GSH conjugation	439	8706254
GSTA1-1	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol 13,14-epoxide	GSH conjugation (high activity)	441	12067250
GSTA1-1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-acetoxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-acetoxy-PhIP)	reduction in reaction with GST (major enzyme)	406, 444	11535243, 8069858
GSTA1-1	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	GSH conjugation	375	8330352
GSTA1-1	drug	phosphoramide mustard ; anticancer, alkylating, metabolite of cyclophosphamide	phosphoramide mustard	GSH conjugation	442	7954469
GSTA1-2	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating, metabolite	4-hydroxycyclophosphamide	GSH conjugation	442	7954469
GSTA1-2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-acetoxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-acetoxy-PhIP)	reduction in reaction with GST (low activity)	444	8069858
GSTA2-2	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products, metabolite	aflatoxin B_1-8,9-epoxide	GSH conjugation	420	10383892

enzyme	category	subcategory	compound	reaction	references	PubMed ID
GSTA2-2	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-acetoxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-acetoxy-PhIP)	Reduction in reaction with GST (low activity)	406	11535243
GSTA2-2	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol 13,14-epoxide	GSH conjugation (low activity)	441	12067250
GSTA3-3	chemical	PAH, metabolite	dibenzo[a,l]pyrene-11,12-diol 13,14-epoxide	GSH conjugation	441	12067250
GSTM1	chemical	PAH, metabolite	phenanthrene-9,10-epoxide	GSH conjugation	445	16978029
GSTM1-1	natural compound	difuranocoumarin; mycotoxin, produced by *Aspergillus* species on food products, metabolite	aflatoxin B_1-8,9-epoxide	GSH conjugation, major enzyme	432, 443, 433	8781383, 9675258, 9115980
GSTM1-1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-acetoxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (**N**-acetoxy-PhIP)	reduction in reaction with GST (low activity)	404	11535243
GSTM1-1	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol 9,10-epoxide	GSH conjugation	440, 446	11849043, 9403173
GSTM1-1	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol	GSH conjugation after oxidation	51, 447	17525473, 12507920
GSTM1-1	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating, metabolite	4-hydroxycyclophosphamide	GSH conjugation	442	7954469
GSTM1-1	chemical	PAH	benzo[*a*]pyrene	GSH conjugation after oxidation	51	17525473
GSTM1-1	chemical	PAH, metabolite	benzo[c]chrysene-9,10-diol 11,12-epoxide	GSH conjugation	446	9403173
GSTM1-1	chemical	PAH, metabolite	benzo[g]chrysene-11,12-diol 13,14-epoxide	GSH conjugation	446	9403173
GSTM1-1	chemical	PAH, metabolite	chrysene-*trans*-1,2-diol-3,4-epoxide	GSH conjugation	446	9403173
GSTM1-1	chemical	PAH	dibenz[*a,h*]anthracene-3,4-diol-1,2-epoxide	GSH conjugation	446	9403173
GSTM1-1	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol 13,14-epoxide	GSH conjugation	446	9403173
GSTP1-1	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-	GSH conjugation	438, 440, 446, 448, 449	9855012, 11849043 9403173, 9299520, 9525277

enzyme	category	subcategory	compound	reaction	references	PubMed ID
			7,8-diol 9,10-epoxide			
GSTP1-1	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol	GSH conjugation after oxidation	50, 450	16885195, 10344744
GSTP1-1	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating, metabolite	4-hydroxycyclophosphamide	GSH conjugation	442	7954469
GSTP1-1	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating, metabolite	4-hydroxyifosfamide	GSH conjugation	451	8555414
GSTP1-1	chemical	quinoline	4-nitroquinoline 1-oxide (NQO)	GSH conjugation	452, 453	11108662, 15766272
GSTP1-1	chemical	PAH	5-methylchrysene	GSH conjugation after oxidation	83	18992797
GSTP1-1	chemical	PAH, metabolite	5-methylchrysene-1,2-diol	GSH conjugation after oxidation	83	18992797
GSTP1-1	chemical	PAH, metabolite	5-methylchrysene-1,2-diol 3,4-epoxide	GSH conjugation	454	9771942
GSTP1-1	chemical	PAH, metabolite	6-methylchrysene-1,2-diol 3,4-epoxide	GSH-conjugation	454	9771942
GSTP1-1	chemical	PAH	benzo[*a*]pyrene	GSH conjugation after oxidation	50	16885195
GSTP1-1	chemical	PAH, metabolite	benzo[*c*]chrysene-9,10-diol 11,12-epoxide	GSH conjugation	446, 455	9403173, 9827546
GSTP1-1	chemical	PAH, metabolite	benzo[*c*]phenanthrene-3,4-diol-1,2-epoxide	GSH conjugation	438, 446, 455, 456	9855012, 9403173, 9827546, 9850062
GSTP1-1	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol-13,14-epoxide	GSH conjugation	438, 446, 455, 456	9855012, 9403173, 9827546, 9850062
GSTP1-1	chemical	PAH, metabolite	chrysene-trans-1,2-dihydrodiol-3,4-epoxide	GSH conjugation	446, 448, 449	9403173, 9299520, 9525277
GSTP1-1	chemical	PAH, metabolite	dibenz[*a,h*]anthracene-3,4-diol-1,2-epoxide	GSH-conjugation	446, 449	9403173, 9525277
GSTP1-1	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol-13,14-epoxide	GSH conjugation	438, 446, 455, 457	9855012, 9403173, 9827546, 9687571

enzyme	category	subcategory	compound	reaction	references	PubMed ID
GSTP1-1	drug	oxazaphosporine; anticancer, nitrogen mustard, alkylating, metabolite	ifosfamide mustard	GSH conjugation	451	8555414
GSTP1-1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-acetoxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-acetoxy-PhIP)	reduction in reaction with GST (low activity)	406, 444	11535243, 8069858
GSTP1-1	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	GSH conjugation	375	8330352
GSTP1-1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	reduction in reaction with GST	458	11196146
GSTT1-1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-acetoxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-acetoxy-PhIP)	reduction in reaction with GST (low activity)	406	11535243
GSTT2-1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-acetoxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-acetoxy-PhIP)	reduction in reaction with GST (low activity)	406	11535243
NAD(P)H-dependent quinone oxidoreductase, NQO1	physiological compound	estrogen, metabolite	4-hydroxyestrone-*o*-quinone	reduction (low activity)	434	18588320
NADH cytochrome b_5 reductase, b5R; cytochrome b_5, CYB5	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	reduction	459	17040106
NADH cytochrome b5 reductase, b_5R; cytochrome b5, CYB5	chemical	arylamine, tobacco smoke compound, metabolite	*N*-hydroxy-4-aminobiphenyl (*N*-OH-4-ABP)	reduction (low activity)	459, 460	17040106, 21447608

enzyme	category	subcategory	compound	reaction	references	PubMed ID
NAT1	chemical	heterocyclic amine	2-amino-3-methylimidazo[4,5-*f*]quinolone (IQ)	*N*-acetylation (low activity)	389	8353847
NAT1	chemical	arylamine	2-aminofluorene (2-AF)	*N*-acetylation (low activity)	389	8353847
NAT1	chemical	PAH	2-naphthylamine	*N*-acetylation (low activity)	389	8353847
NAT1	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl (4-ABP)	*N*-acetylation (low activity)	389	8353847
NAT1	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminobiphenyl (*N*-acetoxy-4-ABP)	*N*-acetylation (low activity)	389	8353847
NAT1	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*N*-acetylation (low activity)	389	8353847
NAT1	chemical	arylamine, tobacco smoke compound, metabolite	*N*-hydroxy-4-aminobiphenyl (*N*-OH-4-ABP)	*N*-acetylation (low activity)	389	8353847
NAT1	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-2-aminofluorene (*N*-OH-2-AF)	*N*-acetylation (low activity)	389	8353847
NAT2	chemical	heterocyclic amine	2-amino-3-methylimidazo[4,5-*f*]quinolone (IQ)	*N*-acetylation	389	8353847
NAT2	chemical	arylamine	2-aminofluorene (2-AF)	*N*-acetylation	389	8353847
NAT2	chemical	arylamine	2-naphthylamine	*N*-acetylation	389	8353847
NAT2	chemical	arylamine, tobacco smoke compound	4-aminobiphenyl (4-ABP)	*N*-acetylation	389	8353847
NAT2	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminobiphenyl (*N*-acetoxy-4-ABP)	*N*-acetylation	389	8353847
NAT2	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*N*-acetylation	389	8353847
NAT2	chemical	arylamine, tobacco smoke compound, metabolite	*N*-hydroxy-4-aminobiphenyl (*N*-OH-4-ABP)	*N*-acetylation	389	8353847
NAT2	chemical	hydroxylamine, arylamine, metabolite	*N*-hydroxy-2-aminofluorene (*N*-OH-2-AF)	*N*-acetylation	389	8353847
S-COMT	physiological compound	estrogen, metabolite	2-hydroxyestradiol	*O*-methylation, 2-OH and 3-OH	461, 462	11606384, 12360102

enzyme	category	subcategory	compound	reaction	references	PubMed ID
S-COMT	physiological compound	estrogen, metabolite	2-hydroxyestrone	*O*-methylation, 2-OH and 3-OH	462	12360102
S-COMT	physiological compound	estrogen, metabolite	4-hydroxyestradiol	*O*-methylation, 4-OH	462	12360102
S-COMT	physiological compound	estrogen, metabolite	4-hydroxyestrone	*O*-methylation, 4-OH	462	12360102
S-COMT	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol	*O*-methylation	463	21622560
S-COMT	chemical	PAH, metabolite	12-methylbenz[*a*]anthracene-3,4-diol	*O*-methylation	463	21622560
S-COMT	chemical	PAH, metabolite	5-methylchrysene-1,2-diol	*O*-methylation	463	21622560
S-COMT	chemical	PAH, metabolite	5-methylchrysene-7,8-diol	*O*-methylation	463	21622560
S-COMT	chemical	PAH, metabolite	7,12-dimethylbenz[*a*]anthracene-3,4-diol	*O*-methylation	463	21622560
S-COMT	chemical	PAH, metabolite	7-methylbenz[*a*]anthracene-3,4-diol	*O*-methylation	463	21622560
S-COMT	chemical	PAH, metabolite	benz[*a*]anthracene-3,4-diol	*O*-methylation (low activity)	463	21622560
S-COMT	chemical	PAH, metabolite	benzo[*c*]phenanthrene-3,4-diol	*O*-methylation	463	21622560
S-COMT	chemical	PAH, metabolite	benzo[*g*]chrysene-11,12-diol	*O*-methylation	463	21622560
S-COMT	chemical	PAH, metabolite	chrysene-1,2-diol	*O*-methylation	463	21622560
S-COMT	chemical	PAH, metabolite	chrysene-3,4-diol	*O*-methylation (low activity)	463	21622560
SULT	chemical	heterocyclic amine	2-amino-3-methylimidazo[4,5-*f*]quinolone (IQ)	*N*-sulfamate formation (low activity)	464	7744696
SULT	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (*N*-OH-MeIQx)	*N*-sulfation after *N*-hydroxylation	429, 465	11258970 8844796
UGT	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (*N*-OH-MeIQx)	*N*-glucuronidation	429, 465	11258970 8844796
UGT1A1	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol	*O*-glucuronidation	466	11929814
UGT1A1	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	N2- (major metabolite) and N3-glucuronidation	467, 468	11408353, 17638922

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enzyme	category	subcategory	compound	reaction	references	PubMed ID
UGT1A1	physiological compound	estrogen, metabolite	2-hydroxyestradiol	*O*-glucuronidation	469	15117964
UGT1A1	physiological compound	estrogen, metabolite	2-hydroxyestrone	*O*-glucuronidation	469	15117964
UGT1A1	physiological compound	estrogen, metabolite	4-hydroxyestrone	*O*-glucuronidation	469	15117964
UGT1A1	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	*O*-glucuronidation	470	21780761
UGT1A1	physiological compound	estrogen	17β-estradiol	*O*-glucuronidation	469	15117964
UGT1A1	physiological compound	estrogen	estrone	*O*-glucuronidation	469	15117964
UGT1A1	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	N2- (major metabolite) and N3-glucuronidation, major enzyme	146, 467, 468, 471, 472	11375903, 11408353, 17638922, 15310245, 15708579
UGT1A1	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-glucuronidation (low activity)	402, 473, 474	12034366, 16480962, 17664247
UGT1A3	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	N2- and N3-glucuronidation	475	10357796
UGT1A3	physiological compound	estrogen, metabolite	2-hydroxyestradiol	*O*-glucuronidation (low activity)	469	15117964
UGT1A3	physiological compound	estrogen, metabolite	2-hydroxy-estrone	*O*-glucuronidation (low activity)	469	15117964
UGT1A3	physiological compound	estrogen, metabolite	4-hydroxyestrone	*O*-glucuronidation	469	15117964
UGT1A3	physiological compound	estrogen	17β-estradiol	*O*-glucuronidation	469	15117964
UGT1A3	physiological compound	estrogen	estrone	*O*-glucuronidation	469	15117964
UGT1A3	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*N*-glucuronidation (low activity)	146	11375903
UGT1A3	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	N2- and N3-glucuronidation (major metabolite)	146, 467, 468, 471	11375903, 11408353, 17638922, 15310245

enzyme	category	subcategory	compound	reaction	references	PubMed ID
UGT1A4	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	N2- and N3-glucuronidation (major metabolite), low activity	467, 468	11408353, 17638922
UGT1A4	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	*N*-glucuronidation	476-478	14871856, 14709623, 18238858
UGT1A4	drug	triphenylethyleneamine ; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*N*-glucuronidation	278, 402, 473, 474, 479	16884532, 12034366, 16480962, 17664247, 15135306
UGT1A4	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	*O*-glucuronidation	470	21780761
UGT1A4	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	N2- (major metabolite) and N3-glucuronidation	467, 468, 471	11408353, 17638922, 15310245
UGT1A4	chemical	tobacco-specific nitrosamine	*N*′-nitrosoanabasine	*O*-glucuronidation	478	18238858
UGT1A4	drug	triphenylethyleneamine ; antiestrogen, estrogen receptor modulator	tamoxifen	*N*-glucuronidation	278	16884532
UGT1A6	drug	triphenylethyleneamine ; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-glucuronidation (low activity)	473	16480962
UGT1A6	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2AAF)	*N*-glucuronidation (low activity)	146	11375903
UGT1A6	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	*N*-glucuronidation (low activity)	146	11375903
UGT1A7	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol	*O*-glucuronidation	466	11929814
UGT1A7	physiological compound	estrogen, metabolite	2-hydroxyestradiol	*O*-glucuronidation	469	15117964
UGT1A7	physiological compound	estrogen, metabolite	2-hydroxyestrone	*O*-glucuronidation	469	15117964
UGT1A7	physiological compound	estrogen, metabolite	4-hydroxyestrone	*O*-glucuronidation	469	15117964
UGT1A7	drug	triphenylethyleneamine ; antiestrogen, estrogen receptor modulator,	4-hydroxytamoxifen	*O*-glucuronidation (low activity)	473, 474	16480962, 17664247

enzyme	category	subcategory	compound	reaction	references	PubMed ID
		metabolite				
UGT1A7	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	*O*-glucuronidation	470	21780761
UGT1A7	physiological compound	estrogen	17β-estradiol	*O*-glucuronidation (low activity)	469	15117964
UGT1A7	physiological compound	estrogen	estrone	*O*-glucuronidation (low activity)	469	15117964
UGT1A7	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*N*-glucuronidation (high activity)	146	11375903
UGT1A7	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	N2- and N3-glucuronidation (low activity)	146, 467, 468, 471	11375903, 11408353, 17638922, 15310245
UGT1A8	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	N2- and N3-glucuronidation	466	10357796
UGT1A8	physiological compound	estrogen, metabolite	2-hydroxyestradiol	*O*-glucuronidation	469	15117964
UGT1A8	physiological compound	estrogen, metabolite	2-hydroxyestrone	*O*-glucuronidation	469	15117964
UGT1A8	physiological compound	estrogen, metabolite	4-hydroxyestrone	*O*-glucuronidation	469	15117964
UGT1A8	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-glucuronidation (low activity)	473, 474	16480962, 17664247
UGT1A8	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	*O*-glucuronidation	470	21780761
UGT1A8	physiological compound	estrogen	17β-estradiol	*O*-glucuronidation	469	15117964
UGT1A8	physiological compound	estrogen	estrone	*O*-glucuronidation (low activity)	469	15117964
UGT1A8	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*N*-glucuronidation (low activity)	146	11375903
UGT1A8	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	N2- (major metabolite) and N3-glucuronidation	146, 467, 468, 471	11375903, 11408353, 17638922, 15310245

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enzyme	category	subcategory	compound	reaction	references	PubMed ID
UGT1A9	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol	*O*-glucuronidation	466	11929814
UGT1A9	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	N2- (major metabolite) and N3-glucuronidation, low activity	467, 468, 475	11408353, 17638922, 10357796
UGT1A9	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	*O*-glucuronidation	477, 480	14709623, 11038164
UGT1A9	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-glucuronidation (low activity)	402, 473, 474	12034366, 16480962, 17664247
UGT1A9	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	*O*-glucuronidation (high activity)	470	21780761
UGT1A9	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*N*-glucuronidation (high activity)	146	11375903
UGT1A9	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	N2- and N3-glucuronidation (major metabolite)	146, 467, 468, 471, 475	11375903, 11408353, 17638922, 15310245, 10357796
UGT1A10	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol	*O*-glucuronidation (major enzyme)	466, 481	11929814, 16510539
UGT1A10	chemical	heterocyclic amine	2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)	N2- and N3-glucuronidation	468, 475	17638922, 10357796
UGT1A10	physiological compound	estrogen, metabolite	2-hydroxyestradiol	*O*-glucuronidation (high activity)	469	15117964
UGT1A10	physiological compound	estrogen, metabolite	2-hydroxyestrone	*O*-glucuronidation	469	15117964
UGT1A10	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	*O*-glucuronidation	482	20007297
UGT1A10	physiological compound	estrogen, metabolite	4-hydroxyestrone	*O*-glucuronidation (high activity)	469	15117964
UGT1A10	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-glucuronidation (low activity)	473, 474	16480962, 17664247
UGT1A10	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	*O*-glucuronidation	468	21780761

enzyme	category	subcategory	compound	reaction	references	PubMed ID
UGT1A10	physiological compound	estrogen	17β-estradiol	*O*-glucuronidation (high activity)	467	15117964
UGT1A10	physiological compound	estrogen	estrone	*O*-glucuronidation (high activity)	467	15117964
UGT1A10	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*N*-glucuronidation (low activity)	146	11375903
UGT1A10	chemical	hydroxylamine, heterocyclic amine, metabolite	*N*-hydroxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (*N*-OH-PhIP)	N2- (major metabolite) and N3-glucuronidation, high activity	146, 465, 466, 469	11375903, 11408353, 17638922, 15310245
UGT2A1	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol	*O*-glucuronidation	483	21164388
UGT2A1	chemical	PAH, metabolite	5-methylchrysene-1,2-diol	*O*-glucuronidation	481	21164388
UGT2B10	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	*O*-glucuronidation	478	18238858
UGT2B10	chemical	tobacco-specific nitrosamine	*N*'-nitrosoanabasine	*O*-glucuronidation	478	18238858
UGT2B10	chemical	tobacco-specific nitrosamine	*N*'-nitrosoanatabine	*O*-glucuronidation	478	18238858
UGT2B10	chemical	tobacco-specific nitrosamine	*N*'-nitrosoanatabine	*O*-glucuronidation	468, 478	17638922, 18238858
UGT2B10	natural compound	nitrosamine, tobacco-specific	*N*'-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	*O*-glucuronidation	478	18238858
UGT2B10	natural compound	nitrosamine, tobacco-specific	*N*'-nitrosonornicotine (*N*-nitrosonornicotine, NNN)	*O*-glucuronidation	468, 478	17638922, 18238858
UGT2B15	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-glucuronidation	402, 473, 474	12034366, 16480962, 17664247
UGT2B17	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	*O*-glucuronidation	484	17416778
UGT2B17	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-glucuronidation	474	17664247
UGT2B7	chemical	PAH, metabolite	(+)- and (−)-benzo[*a*]pyrene-7,8-diol	*O*-glucuronidation	466	11929814

enzyme	category	subcategory	compound	reaction	references	PubMed ID
UGT2B7	chemical	tobacco-specific nitrosamine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	*O*-glucuronidation	476, 477, 480	14871856, 14709623, 11038164
UGT2B7	chemical	PAH, metabolite	dibenzo[*a,l*]pyrene-11,12-diol	*O*-glucuronidation	470	21780761
UGT2B7	chemical	hydroxamic acid, heterocyclic amine, metabolite	*N*-hydroxy-2-acetylaminofluorene (*N*-OH-2-AAF)	*N*-glucuronidation	146	11375903
UGT2B7	drug	triphenylethyleneamine; antiestrogen, estrogen receptor modulator, metabolite	4-hydroxytamoxifen	*O*-glucuronidation	474	17664247