Human *In vitro* Drug Metabolism Dataset
Transforming scientific data into clinical knowledge

The Drug Metabolism Dataset contains results from *in vitro* metabolism studies, where a drug is tested as an inhibitor/activator/inducer (precipitant) or a substrate (object) for a given human drug metabolizing enzyme (including variants).

**Metabolism parameters** ($IC_{50}$, $K$, $K_I$, $k$, % inhibition, % activation, % or fold increase, $EC_{50}$, $E_{max}$, $K_{m}$, $V_{max}$, and $CL_{int}$), along with detailed experimental conditions, are extracted from published articles (citations) and NDA/BLA reviews.

**Study results** are organized according to the overall effect and mechanism of the interaction:
- Enzyme inhibition entry: drug as inhibitor or non-inhibitor
- Enzyme activation entry: drug as activator or non-activator
- Enzyme induction entry: drug as inducer, down-regulator, or non-inducer
- Enzyme substrate entry: drug as substrate

**Multiple queries** allow users to retrieve an *in vitro* dataset by drug name, enzyme name, or mechanism of the interaction (drug as precipitant or as object).

**Results** can be viewed, customized, and downloaded in multiple formats, allowing users to compile and organize the large body of information available.
FROM A CITATION OR NDA/BLA REVIEW

The latest, most relevant, peer-reviewed publications and regulatory documents are identified and fully analyzed. Study protocol and results are manually curated to update the knowledgebase on a daily basis.
TO A FULLY CURATED DATASET

Prior to integration, all data are carefully and critically evaluated. The richness of each citation, including relevant insights, is exploited, generating a highly detailed dataset.

Tree View of Citation Data

Mechanism: valsartan as a substrate of CYP2C9

Test system and test concentrations

Study results: $K_m$, $V_{max}$, and $CL_{int}$ values

Other experimental details

Mechanism: diacerein as an inhibitor of CYP2C9-mediated valsartan 4-hydroxylation

Study results: $K_i$ value and mode of inhibition

Study results: $IC_{50}$ value

Diacerein inhibits CYP2C9 with an $IC_{50}$ value of 32.23 µM and a $K_i$ value of 30.80 µM. What other drugs inhibit the CYP2C9 index substrate diclofenac?
POWERFUL TOOL FOR DATA INTEGRATION: FROM ONE CITATION TO METADATA ANALYSIS

The data are formatted for immediate use and can be filtered and re-arranged to allow meta-analysis of multiple results.

Query all CYP2C9 inhibitors

Table View of Query Results

Obtain a complete list of *in vitro* inhibitors of CYP2C9
IN VITRO METABOLISM DATASET IN NUMBERS
(as of October 16, 2023)

- **6,206** citations
- **404** NDAs/BLAs
- **24,269** substrate entries
- **51,831** inhibition entries
- **735** activation entries
- **8,905** induction entries
- **69,926** positive entries
- **14,517** negative entries
- **36** *in vitro* metabolism queries
- **117** possible searches
- **186** drug metabolizing isozymes & **72** variants
- **2,764** compounds as substrates
- **5,306** compounds as inhibitors
- **265** compounds as activators
- **1,975** compounds as inducers
- **705** food products & **1,960** herbal medications

APPLICATIONS OF THE IN VITRO METABOLISM DATASET

- PROVIDES CONTEXT for RESULTS OBTAINED for candidate compounds
- ALLOWS ASSESSMENT of MEASUREMENT VARIABILITY (inter-lab, substrate- and system-dependency, etc.)
- SUPPORTS STATIC PREDICTIONS and PBPK MODELING with input parameters
- HELPS OPTIMIZE IN VITRO STUDY DESIGN (cell system, incubation conditions, test concentrations, choice of substrate/inhibitor, etc.)
- ASSISTS with DOSE SELECTION for clinical trials
- PROVIDES IN VITRO EVIDENCE to EXPLAIN CLINICAL RESULTS and improve understanding of drug interaction mechanisms
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