Metabolism & Transport Drug Interaction Database (DIDB)

REFERENCE MANUAL

I- INTRODUCTION

The purpose of this document is to guide first-time users through the web interface and the functionalities of the Metabolism and Transport Drug Interaction Database (DIDB). First-time users may also wish to read the User Guide section of the website, which includes terminology definitions and scientific assumptions used in the database.

II- WEB SITE PRESENTATION

The web site (www.druginteractioninfo.org) contains the following sections:

Home/Contact Us/User guide: general presentation
Tools/Queries: two entry gateways to access drug interactions articles
Examples of use: two sets of selected scenarios
P-gp Info: section on P-glycoprotein-related drug interactions
Terms of use: licensing information

III- ACCESSING THE INFORMATION

A. General presentation:

The database currently includes more than 4000 published articles referenced in Medline, related to in vivo and in vitro drug interaction studies in humans. The content of the database is updated on a monthly basis.

- Database information is indexed not only by generic drug names and therapeutic classes, but also by key data categories such as enzymes, study design, studied population/system, etc. (see Index Search).
- Drugs are listed alphabetically, starting with the enantiomers.
- The unit of information of the database is the research article. Each article is indexed by its Accession Number (AN), which matches Medline’s Unique Identifier number (UI). The information extracted from each article is structured in the database according to a defined hierarchy.
- Information from each article is accessible by opening (clicking) the yellow folders on the left side of the screen. The blue hypertext links provide the search engine functionalities defined as the “hopping” ability; clicking on these links opens articles with related data.
B. Query Types:

Four sets of questions allow searching the database from the following perspectives: Enzyme, Drug, Parameters, and Metabolic/Pharmacokinetic. While Enzyme and Drug Queries give qualitative answers (lists of substrates, enzymes, studies...), Parameters and Metabolic/PK Queries are designed to select quantitative parameters (Ki values, AUC changes, Plasma concentrations...).

EXAMPLES OF QUERIES:

1- “Drug Queries” section / Query #1

The aim of this query is to find all the studies with a particular object (substrate). The user selects an object from the list (for example midazolam), a study condition (in vitro, in vivo, or both) and submits the query...

IMPORTANT!
In order to optimize the speed of the database retrieval system, predefined short lists of drug names are presented by default. If the compound of
interest is not in these standard lists, the user may need to check the box at the bottom of the query page, in order to load the FULL LISTS of objects and precipitants available in the database.

Query 1 gives a list of articles (indexed by type of study), in which midazolam was studied as an object. By clicking on any AN, the user displays the full content of the article (TIP: Right click on the AN / Click on “Open in a new window”).
Two functionalities are available next to the Accession Number:

- The "Abstract" button provides a direct link to the article abstract on the Medline web site.
- The "Drug Info" button provides access to available reference information on all of the compounds listed in the article. The information is extracted from reference textbooks:
  1) Goodman & Gilman. 10th Edition 2001
  2) Physicians' Desk Reference
2- “Parameter Queries” section / Query #1

The aim of this query is to display in vitro quantitative parameters determined with a given substrate, alone (Km/Vmax) or with different inhibitors (Ki, IC50, % inhibition). The user selects a parameter of interest, a particular object and submits the query. For example: “Find precipitant Ki values with object (S)-mephenytoin in vitro”.

The display gives a list of precipitants (inhibitors) tested with (S)-mephenytoin, ordered alphabetically. By clicking on each yellow folder, the user accesses the experimental conditions used to determine the Ki value(s). Each set of result is linked to its source-article by the AN. As described in the previous example, the user can display the full content of the article by clicking on the AN.
3- “Hopping” Ability

In all displays, there are numerous hyperlinks: names of drugs, enzymes, Ki values...etc. These hyperlinks allow the user to “hop” on any data type. By just clicking on a data type (such as Human Kidney Microsomes), all the information in the database related to this particular data type is retrieved.

Note: this functionality gives the same information than the “Index Search” described in the Tools section.

C. Tools Section:

1- Index Search

This section provides an alternative way to search the database using a specific data category, such as Journal, Author, Object, Enzyme, etc. For example, the user may wish to find information related to a given Therapeutic Class.
Step 1: Select “Therapeutic class” from the list of Data types.

Step 2: Selection of the class of interest (“HMG CoA reductase Inhibitor” in this example).

Step 3: Using, if necessary, the “refine search” box option.

Step 4: The result is displayed in a new window; clicking on the yellow folders can access the information on each drug from this class.

2- Advanced Search

In this section, the user can build original queries using the CCM query language as described in the CCM query guide.
3- Links: Selected links to other useful web sites are available in this section.
D- Examples of Use Section

Getting a final answer to questions in drug interaction area, using the database may involve more than one step.

Two examples of practical approaches that use the database features in a defined order are provided: **CYP3A4 Inhibitors** and **Finding PK data**.

The user will find a short description of the context and the steps to follow for each scenario.
E- P-gp Section / Information on transporters

1- For P-gp, supporting evidence (in vitro, animal and ex-vivo studies) on the compounds that are P-gp substrates/modulators is available in the P-gp section.

Two lists of compounds are presented and each compound is linked to individual chart tables.

The chart’s cells are hyper linked to details of each study.
2- When the role of transporters is discussed in an *in vivo* drug interaction study (currently mainly P-gp and OATP), this information is available in the section “transporter” of the article.

These particular articles can be accessed through the *Index Search*, using *Transporter* as selected *data type* (see below).

![Index Search](image.png)

**IV- CONTACT US**

For any feedback or question, please contact the Database Project Manager:

Dr Isabelle Ragueneau-Majlessi  
E-mail: didbase@u.washington.edu  
Phone: 206-543-4669.