

## HERpred Instruction

**HERpred** is a user-friendly, easy-to-access web server that can be used to predict the hepatoenteric recycling (HER) rates of compounds with their SMILES as the input. HER is a new drug disposition mechanism we identified, for which intestine is the organ for metabolism and liver is the organ for recycling, as opposed to in enterohepatic recycling (EHR), where liver is the organ for metabolism while intestine is the organ for recycling.

Such processes significantly affect drug bioavailability, in particular, for instance, drug local exposure to colon cells vs. systematic exposure. Since experimental determination of HER involves metabolism, circulation, etc., thus it is very labor-intensive, time-consuming, and costly, especially for a large number of compounds. To this end, we developed **HERpred** which can serve the scientific community to screen compounds with high HER rates in an ultra-fast manner. The model was constructed based on a novel supervised Octave residual convolutional neural network (ORCNN) method with a new image-based representation scheme to characterize compound structures. The web server is implemented using the Flask framework, with Python 3.8.10, Torch 1.11.0, and Flask 2.4.

### 1. Input to HERpred

The input from users is simple and straightforward: just the names and SMILES strings of compounds to be predicted. There are two ways to input them: 1). Direct input in the online form, and 2). Upload a file containing a list of compounds with their names and SMILES strings, as shown below:

**Input for Prediction (compound name followed by a space and then SMILES)**

**1.** directly input compound names and SMILES strings, separated by a blank space

```
wogonin7_A
COC1=C(C=C(C2=C1OC(=CC2=O)C3=CC=CC=C3)O)OC4C(C(C(O4)C(=O)O)O)O
Genistein7_D
C1=CC(=CC=C1C2=COC3=CC(=CC(=C3C2=O)O)O)OC4C(C(C(O4)C(=O)O)O)O
Phenol Oc1ccccc1
```

**2.** upload a file containing a list of compounds with their names and SMILES strings separated by a blank space (example: HERpred.csv)

or Upload a File ([Example](#)):

No file chosen

**SUBMIT****INSTRUCTION**

The input compounds must consist of names and SMILES strings separated by a blank space. Otherwise, the input will be considered as “illegal”. If this happens, an error message will show up in the input Form. Here are some examples with incorrect input:

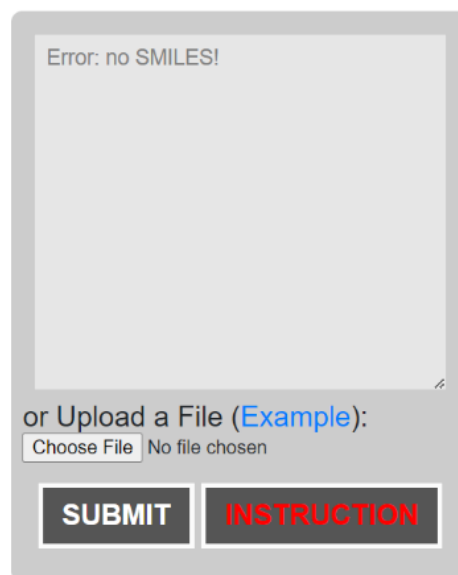
### 1). No SMILES

Phenol  
Oc1ccccc1

An error message will show up to indicate there is no SMILES (for either Phenol or Oc1ccccc1 [treated as a name] here).

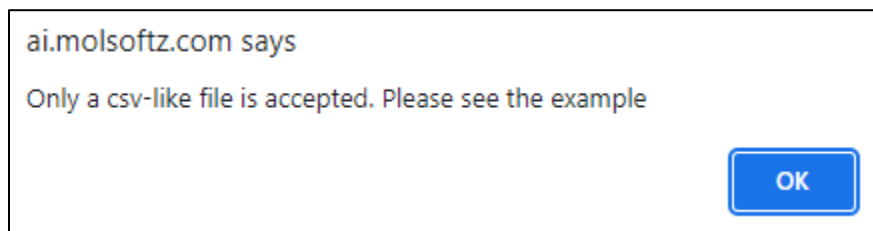
The correct format should be:

Phenol Oc1ccccc1



### 2). The uploading file extension is wrong

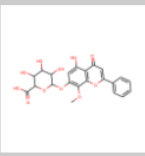
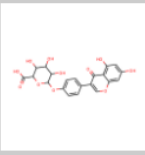
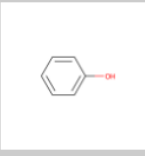
Of note, for safety purposes, the uploaded file must use .csv extension, although the compound name and SMILES are actually separated by a space. Otherwise, the following error will occur.



## 2. Output of HERpred

The output of **HERpred** is also easy to understand, with 4 columns in a table. The first column is the compound names, as provided by users in the input; The 2<sup>nd</sup> and 3<sup>rd</sup> columns are the predicted minimum and maximum HER rates, respectively; The 4<sup>th</sup> column is the color image of each compound structure used by our model for prediction. Please refer to our manuscript for more details. The below shows some examples of predictions.

## Output of Predicted HER (Download Data)

Name	HER_Min	HER_Max	Structure
wogonin7_A	34%	52%	
Genistein7_D	34%	41%	
Phenol	31%	44%	

In addition to visualizing the result in a table, we also dynamically provide users with an option to download the data (the Download Data link). This is particularly useful if the input number of compounds is large (e.g., >50). The format of the downloadable table is as follow:

Compound Name	HER_Min	HER_Max
wogonin7_A	34%	52%
Genistein7_D	34%	41%

### 3. Frequently Asked Questions

This FAQ section is quite self-explanatory. It provides brief answers to the most frequently asked questions, along with some more information about the use of our tools and services.