# Generated Unwanted Substructures

November 5, 2022

## 1 Remove Unwanted Substructures

Aim: remove unselective substructures (PAINS) and other unwanted substructures

## 2 Load Modules

[1]:
```
from pathlib import Path

import pandas as pd
from tqdm.auto import tqdm
from rdkit import Chem
from rdkit.Chem import PandasTools
from rdkit.Chem.FilterCatalog import FilterCatalog, FilterCatalogParams
```

[2]:
```
# define paths
HERE = Path(_dh[-1])
DATA = HERE / "data"
```

[8]:
```
PTP1B_data = pd.read_csv(DATA / "PTP1B_generated_lipinski.csv")
PTP1B_data = PTP1B_data.iloc[:,1:]

# Drop unnecessary information
print("Dataframe shape:", PTP1B_data.shape)
PTP1B_data.drop(columns=["molecular_weight.1", "n_hbd.1", "n_hba.1", "logp.1",␣
 ↪"molecular_weight", "n_hbd", "n_hba", "logp"], inplace=True)
PTP1B_data.head()
```

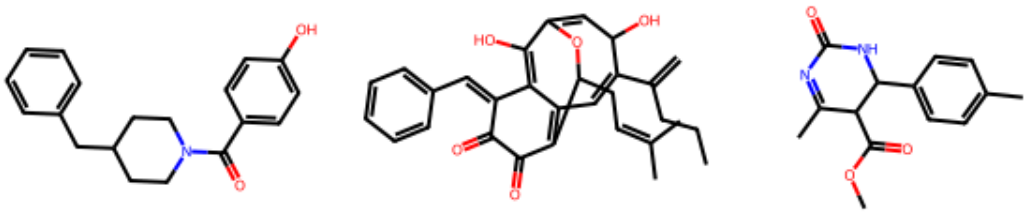
```
Dataframe shape: (872, 10)
```

[8]:

| | SMILES | ro5_fulfilled |
|---|---|---|
| 0 | O=C(c1ccc(O)cc1)N1CCC(Cc2ccccc2)CC1 | True |
| 1 | C=C(CCC)C1=CC2=C3C(=O)C(=O)C(=Cc4ccccc4)C2=C(O… | True |
| 2 | COC(=O)C1C(C)=NC(=O)NC1c1ccc(C)cc1 | True |
| 3 | O=C(O)C(=O)Nc1ccc(OCc2c(F)cccc2Br)cc1 | True |
| 4 | O=C(O)COc1c(C(=O)O)sc(-c2ccccc2)c1Br | True |

[11]:
```
# Add molecule column
PandasTools.AddMoleculeColumnToFrame(PTP1B_data, smilesCol="SMILES")
# Draw first 3 molecules
Chem.Draw.MolsToGridImage(
    list(PTP1B_data.head(3).ROMol)
)
```

[11]:




[12]:
```
# initialize filter
params = FilterCatalogParams()
params.AddCatalog(FilterCatalogParams.FilterCatalogs.PAINS)
catalog = FilterCatalog(params)
```

[15]:
```
# search for PAINS
matches = []
clean = []
for index, row in tqdm(PTP1B_data.iterrows(), total=PTP1B_data.shape[0]):
    molecule = Chem.MolFromSmiles(row.SMILES)
    entry = catalog.GetFirstMatch(molecule)  # Get the first matching PAINS
    if entry is not None:
        # store PAINS information
        matches.append(
            {
                "chembl_id": row.SMILES,
                "rdkit_molecule": molecule,
                "pains": entry.GetDescription().capitalize(),
            }
        )
    else:
        # collect indices of molecules without PAINS
        clean.append(index)

matches = pd.DataFrame(matches)
PTP1B_data = PTP1B_data.loc[clean]  # keep molecules without PAINS
```

```
  0%|          | 0/872 [00:00<?, ?it/s]
```

[17]:
```python
# NBVAL_CHECK_OUTPUT
print(f"Number of compounds with PAINS: {len(matches)}")
print(f"Number of compounds without PAINS: {len(PTP1B_data)}")

PTP1B_data.to_csv("PAINS_removed_generated.csv")
```

```
Number of compounds with PAINS: 84
Number of compounds without PAINS: 788
```

### 2.1 Unwanted Substructures

[18]:
```python
substructures = pd.read_csv(DATA / "unwanted_substructures.csv", sep="\s+")
substructures["rdkit_molecule"] = substructures.smarts.apply(Chem.MolFromSmarts)
print("Number of unwanted substructures in collection:", len(substructures))
# NBVAL_CHECK_OUTPUT
```

```
Number of unwanted substructures in collection: 104
```

[20]:
```python
# search for unwanted substructure
matches = []
clean = []
for index, row in tqdm(PTP1B_data.iterrows(), total=PTP1B_data.shape[0]):
    molecule = Chem.MolFromSmiles(row.SMILES)
    match = False
    for _, substructure in substructures.iterrows():
        if molecule.HasSubstructMatch(substructure.rdkit_molecule):
            matches.append(
                {
                    "chembl_id": row.SMILES,
                    "rdkit_molecule": molecule,
                    "substructure": substructure.rdkit_molecule,
                    "substructure_name": substructure["name"],
                }
            )
            match = True
    if not match:
        clean.append(index)

matches = pd.DataFrame(matches)
PTP1B_data = PTP1B_data.loc[clean]
```

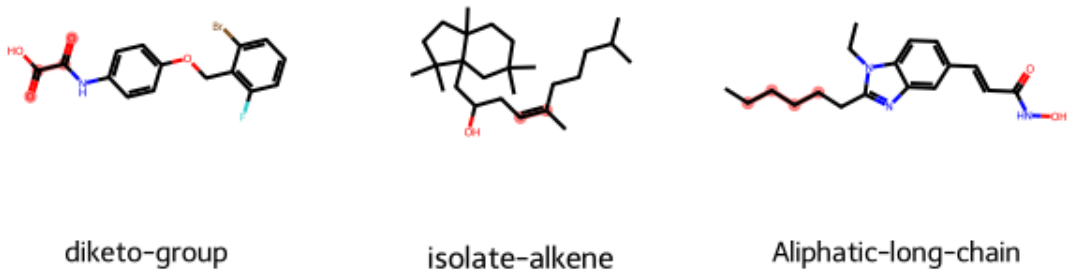
```
  0%|          | 0/788 [00:00<?, ?it/s]
```

[21]:
```python
# NBVAL_CHECK_OUTPUT
print(f"Number of found unwanted substructure: {len(matches)}")
print(f"Number of compounds without unwanted substructure: {len(PTP1B_data)}")
```

```
Number of found unwanted substructure: 584
Number of compounds without unwanted substructure: 391
```

[22]:
```
to_highlight = [
    row.rdkit_molecule.GetSubstructMatch(row.substructure) for _, row in␣
 ↪matches.head(3).iterrows()
]
Chem.Draw.MolsToGridImage(
    list(matches.head(3).rdkit_molecule),
    highlightAtomLists=to_highlight,
    legends=list(matches.head(3).substructure_name),
)
```

[22]:




[23]:
```
PTP1B_data.to_csv(DATA / "PAINSandUNWANTED_removed_generated.csv")
```

39.1% of the original De Novo set is left, the compounds will now be evaluated whether they are active

[ ]: