Supplementary Information

CoviRx: A User-Friendly Interface for Systematic Down-Selection of Repurposed Drug Candidates for COVID-19

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S1. Table listing Python libraries used for the development of CoviRx

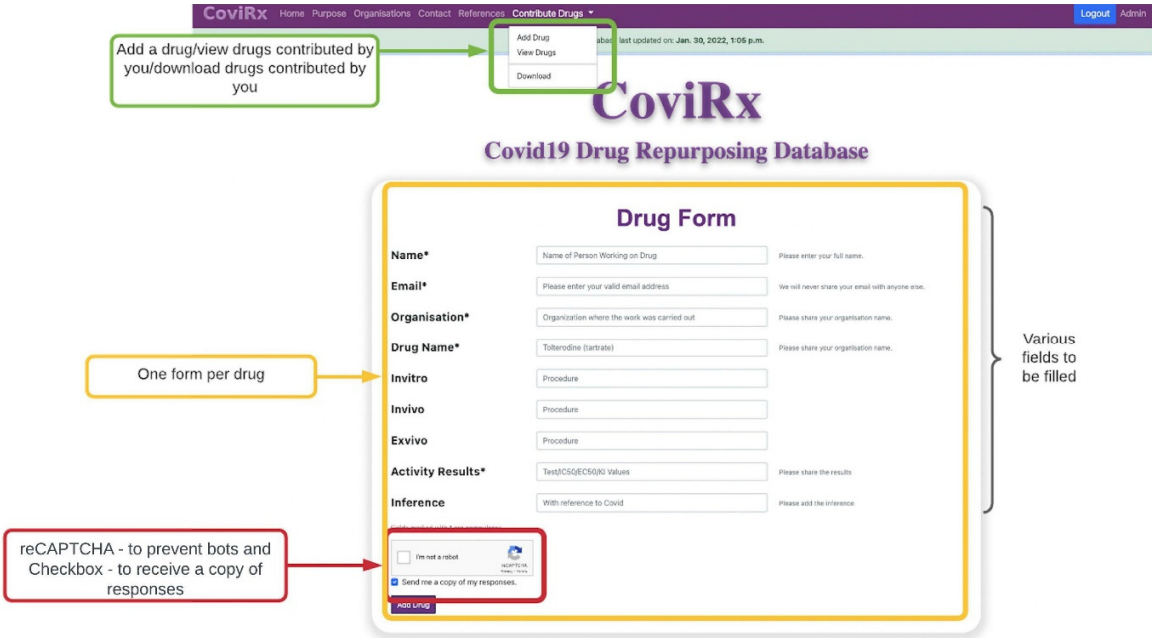
No.	Library name	Version	Used for	References
1	django	3.2.6	Webframework	[1]
2	google_auth	2.3.0	Authentication services	[2]
3	rdkit-pypi	2021.9.2.1	Determining drug similarity	[3]
4	django-flat-json-widget	0.1.3	Styling Custom Fields	[4]
5	django-admin-interface	0.16.3	Styling django admin	[5]
6	premailer	3.10.0	Styling the mailing templates	[6]
7	celery		To be used in the future to ensure data persistency on failures	[7]

S2. List of external APIs used by CoviRx

No.	External service	Used for	References
1	Google Charts	Creating graphical visualisations	[8]
2	Google Translate	Translating web page	[9]
3	Google reCAPTCHA	Preventing bots from submitting forms	[10]
4	Google OAuth	Authentication services	[2]
5	Google SMTP	Mailing services	[11]

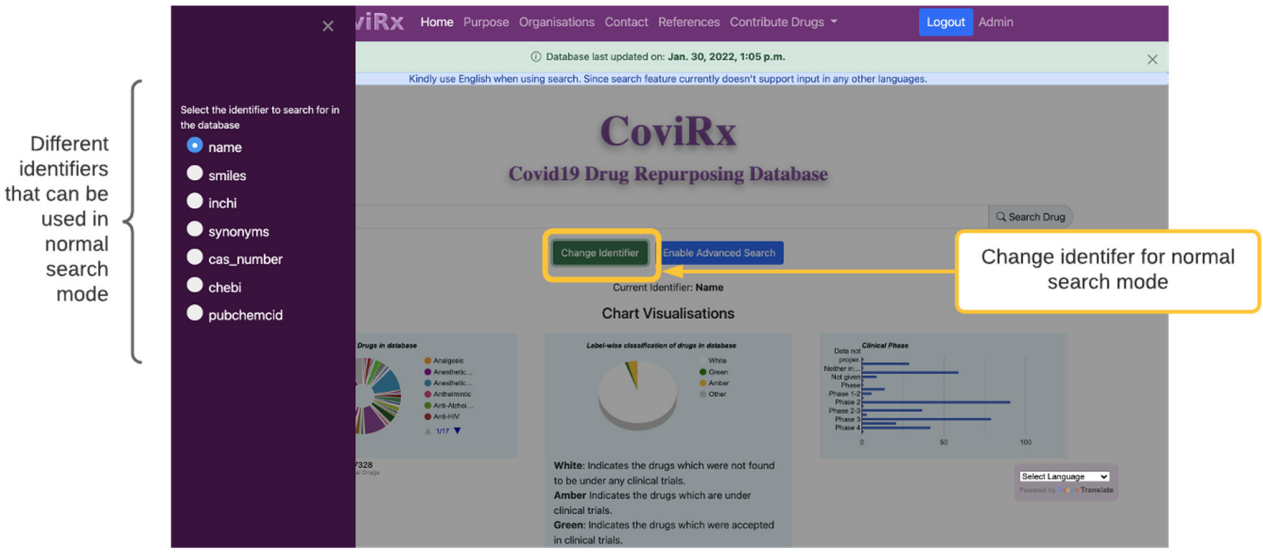
S3. User Interface

S3.1 Drug upload form

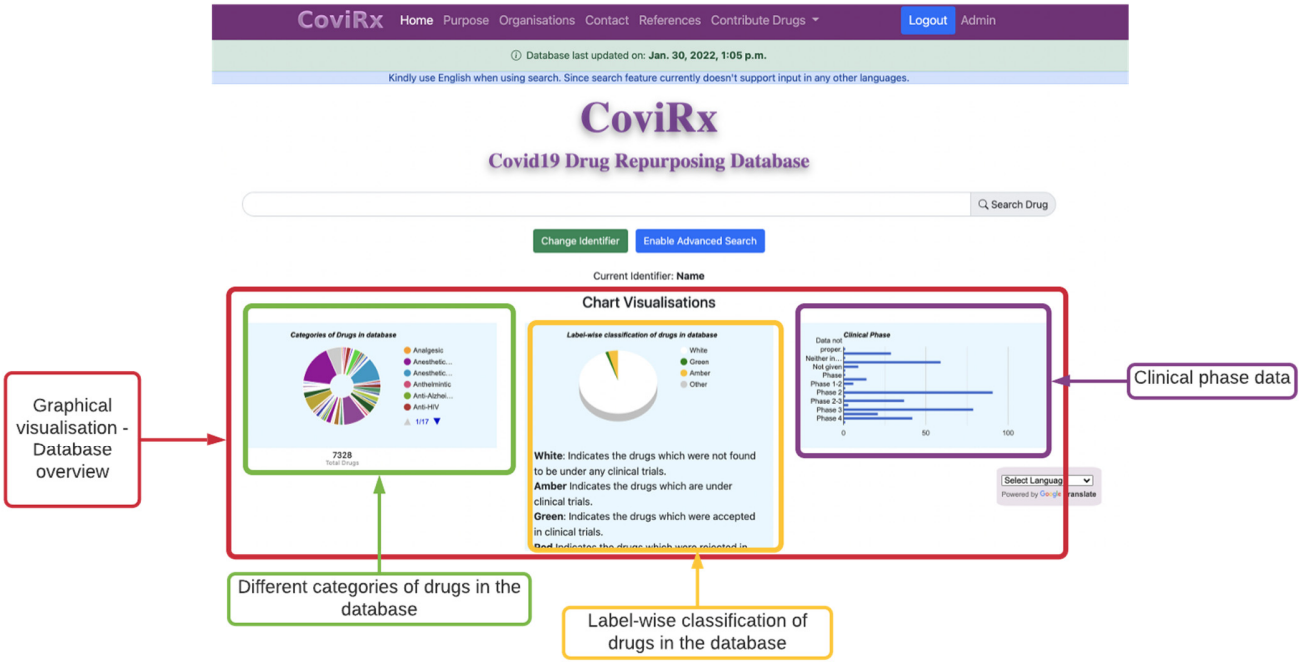


S3.2 Contact form

S3.3 Identifiers available for normal search mode

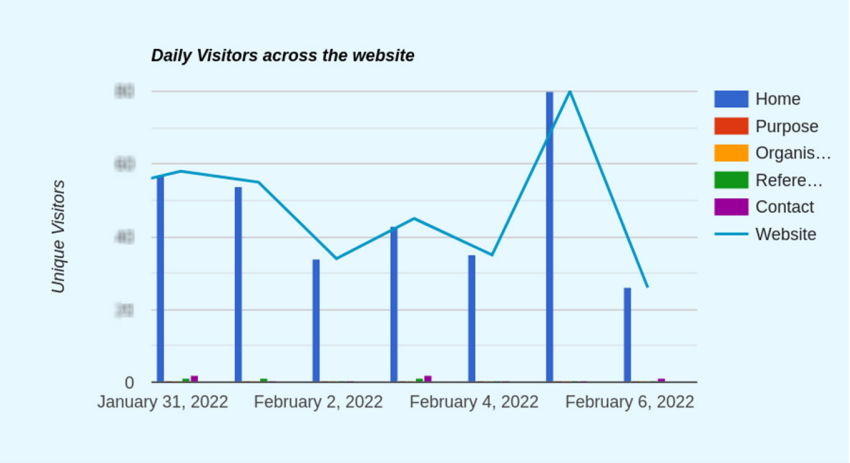


S3.4: Graphical visualization giving database overview

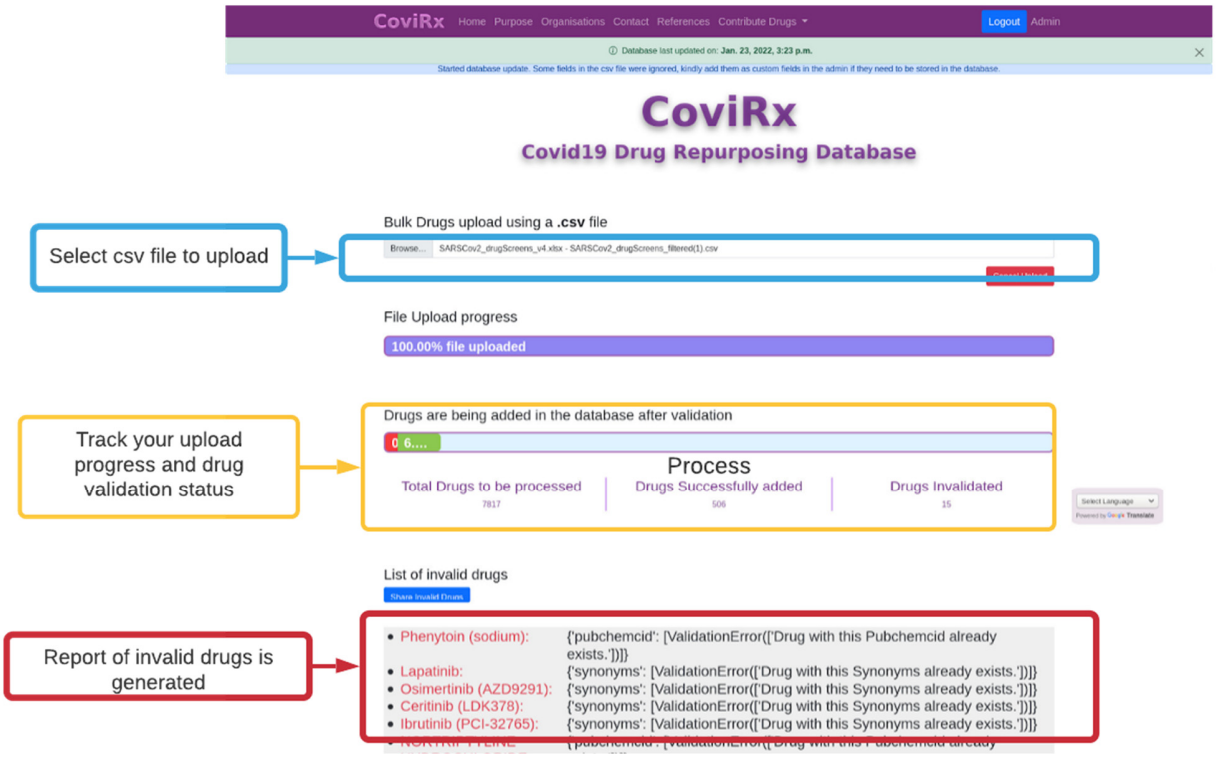


S4. Admin panel

S4.1 Website Analytics



S4.2 Drug bulk upload feature, invalidated drugs are shared via email as depicted in S4.3



S4.3 Email sent by CoviRx to correct invalidated drugs

List of invalid drugs in latest drug upload on CovirX Inbox ×

to [redacted], me

CovirX

Covid19 Drug Repurposing Database

During the latest drug upload on CovirX, many drugs couldn't get added into the database. A list for the same has been shared with you.

Drug Name	Reason for rejecting addition to database
[redacted]	{'synonyms': [ValidationError(['Drug with this Synonyms already exists.'])]}
[redacted]	{'synonyms': [ValidationError(['Drug with this Synonyms already exists.'])]}
[redacted]	{'inchi': [ValidationError(['Drug with this Inchi already exists.'])]}
[redacted]	{'inchi': [ValidationError(['Drug with this Inchi already exists.'])]}

S4.4 Invitation email

You have been invited to join CoviRx admin Inbox ×

covirxwebapp@gmail.com
to

CoviRx

Covid19 Drug Repurposing Database

You have been invited to the CoviRx admin panel by *H J*.

To become an admin member, visit our website Home Page and click on the Google button in the header pane to login.

Please login within 7 days to accept the invite. This invite will expire in 7 days from the time of receiving this email.

S4.5 Tech stack used for development

Font scripts

- Bootstrap Icons 1.5.0

Web frameworks

- Django

Web servers

- Apache 2.4.29

JavaScript graphics

- Google Charts

Programming languages

- Python

Operating systems

- Ubuntu

CDN

- Unpkg
- jsDelivr
- cdnjs

JavaScript libraries

- jQuery UI 1.12.1
- jQuery 3.6.0

UI frameworks

- Bootstrap 5.0.2

Authentication

- Google Sign-in

S5 Formulas

Calculation of Tanimoto Coefficient [12, 13]

$$S_{A,B} = \frac{\left[\sum_{j=1}^{n} x_{jA}\, x_{jB}\right]}{\left[\sum_{j=1}^{n}\left(x_{jA}\right)^2 + \sum_{j=1}^{n}\left(x_{jB}\right)^2 - \sum_{j=1}^{n} x_{jA}\, x_{jB}\right]}$$

x_{jA} means the j-th feature of molecule A. a is the number of *on* bits in molecule A, b is the number of *on* bits in molecule B.

S6.Website general information

- For contributing drugs to CoviRx:
  - Individuals who want to contribute drugs to CoviRx can reach out to our team using the contact form, and necessary privileges and access would be made available.
  - The submitted drugs will undergo a manual review by our team to ensure reliability and uniformity of data so that they won't get merged into the database right away.
- Privacy concerns:
  - We declare that any details collected from users using the website are purely to provide core functionalities.
  - Any identifying information related to website users is not stored in our database unless the user contacted us via the contact form or a drug has been contributed and sent for verification.
  - All the cookies used by our website have been listed and well explained in our cookie policy.

S7. Code Repository

GitHub Repository [Private currently]

S8. Code Usage

- The technical documentation detailing the various files in the code can be referred to.
- For instructions regarding setting up the web app on your local computer, please refer to the README instructions provided in the repository.

S9. API calls available

Besides using the CoviRx web app, individuals can also get the data by using multiple API endpoints provided by the CoviRx platform.
Every drug in the CoviRx database is stored with a unique ID, referred to as <drug_id>. This <drug_id> can be obtained from the URL to the drug. For example, in https://www.covirx.org/drug/b2d6cf7d-17e4-4f72-b073-974fd17106fc, **b2d6cf7d-17e4-4f72-b073-974fd17106fc** is the <drug_id>.

S9.1. Drugs Metadata API

This API endpoint can be used to perform search operations.

a. Parameters supported:
   i. suggestions: the number of tips needed (a maximum of 20)
   ii. keyword: the keyword to be searched for and the identifier
   iii. filters: the filters that need to be satisfied separated by commas
b. Endpoint: api/drugs-metadata
c. Method: GET
d. Response contains:
   i. A maximum of 5 drugs
e. Example request:

```
curl -G -d 'keyword={"name":"a"}' "https://www.covirx.org/api/drugs-metadata?suggestions=2"
```

f. Example response:


```
{
 "0": {
        "name": "Abiraterone acetate",
        "smiles":
"CC(=O)O[C@H]1CC[C@@]2(C)C(=CC[C@H]3[C@@H]4CC=C(c5cccnc5)[C@@]4(C)CC[C@@
H]32)C1",
        "inchi": null,
        "synonyms": "CB7630",
        "cas_number": "154229-18-2",
        "chebl": null,
        "pubchemcid":
"139597119|87055577|87055578|9821849|152986093|144748333|75201460|11670322|86582960|1448
78649|71696658",
        "indication_class": "Antineoplastic",
        "label": "1",
        "id": "5e03cd3b-efb1-5732-9e7e-f6aec090d005"
```

```
 },
 "1": {
        "name": "Azatadine (dimaleate)",
        "smiles":
"CN1CCC(=C2c3ccccc3CCc3cccnc32)CC1.O=C(O)/C=C\\C(=O)O.O=C(O)/C=C\\C(=O)O",
        "inchi": null,
        "synonyms": "Azatadine maleate",
        "cas_number": "3978-86-7",
        "chebl": null,
        "pubchemcid":
"66273|16052003|75373670|53486409|21158508|19861|91114266|59910424|5281066|69650887|21933
722",
        "indication_class": "Antiallergic",
        "label": "1",
        "id": "3cb3b3bd-32ad-5749-90c1-4ec6fa164787"
 }
}
```


S9.2 Similar Drugs API

CoviRx provides an endpoint that can get a maximum of 5 similar drugs based on the Tanimoto coefficient by providing the <drug_id> associated with the drug.

g. Parameters required: None
h. Endpoint: api/similar/<drug_id>
i. Method: GET
j. Response contains:
    i. A JSON containing a maximum of 5 drugs
    ii. For every drug, its id, name, and SMILES value
k. Example request:

```
curl "https://www.covirx.org/api/similar/5982620b-1cf2-54de-945a-0f6e1319d859"
```

l. Example response:


```
{
  "0": {
      "id": "95b145ea-f19c-5e4d-8ea8-f27dff256ec5",
      "name": "METHOXSALEN",
      "smiles": "COc1c2oc(=O)ccc2cc2ccoc12"
  },
  "1": {
      "id": "bb020607-4a1a-5e88-8fc2-fed627a1880f",
      "name": "Aminophylline",
```

```
      "smiles":
"Cn1c(=O)c2[nH]cnc2n(C)c1=O.Cn1c(=O)c2[nH]cnc2n(C)c1=O.NCCN"
  },
  "2": {
      "id": "47c3bd83-f6bb-5531-8064-56c53a300372",
      "name": "(R)-(-)-Ibuprofen",
      "smiles": "CC(C)Cc1ccc([C@@H](C)C(=O)O)cc1"
  },
  "3": {
      "id": "2882f16f-5cb6-5b94-801c-034388e21129",
      "name": "D-(+)-MALTOSE",
      "smiles":
"OC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1O[C@H]1O[C@H](CO)[C@@H](O)[C@H](
O)[C@H]1O"
  },
  "4": {
      "id": "e865272e-7579-5702-8ac2-6fccf37c08e8",
      "name": "Irisflorentin",
      "smiles": "COc1cc(-c2coc3cc4c(c(OC)c3c2=O)OCO4)cc(OC)c1OC"
  }
}
```


S9.3 Charts API

All the graphical visualisations in CoviRx use the data provided by this endpoint. An overview of the dataset can be obtained from the same.

m. Parameters required:
   i. data: an array of strings containing the name of charts whose data is needed. Currently, options include 'categories,' 'label,' 'phase. '
n. Endpoint: api/charts-json
o. Method: GET
p. Response Contains:
   i. A JSON containing the charts that have been requested
   ii. Every chart data is presented in the form of a 2D array
q. Example request: for labels and phase data

```
curl --request GET "https://www.covirx.org/api/charts-json?charts[]=labels"
```

r. Example response:

```
{
```

```
  "labels": [
    [
      "Drug Labels",
      "Number of drugs"
    ],
    [
      "White",
      392
    ],
    [
      "Green",
      35
    ],
    [
      "Red",
      1
    ],
    [
      "Amber",
      78
    ]
  ]
}
```


S9.4 Download drug data API

Will return all the data for a drug present in CoviRx database in JSON format.

s. Endpoint: drug/<drug_id>?download-json=True
t. Method: GET
u. Response contains: all the identifiers, drug-likeness, original indication, assays, PK / PD, Covid clinical trials, and red flags data along with the references for the data.
v. Example request:

```
curl "https://www.covirx.org/drug/5e03cd3b-efb1-5732-9e7e-f6aec090d005?download-json=True"
```

w. Example response:


```
{
        "name": "Abiraterone acetate",
        "chembl": "CHEMBL271227",
        "smiles":
```

"CC(=O)O[C@H]1CC[C@@]2(C)C(=CC[C@H]3[C@@H]4CC=C(c5cccnc5)[C@@]4(C)CC[C@@H]32)C1",
"inchi": **null**,
"drug_likeness": {
"Molecular Weight": "391.555",
"No. of Chiral Centres": "6",
"logP": "5.9694",
"HBA": "3",
"HBD": "0",
"PSA": "39.19",
"Rotation bonds": "2",
"Administration route": "Oral",
"Indication class/ category": "Antineoplastic"
},
"original_indication": {
"Indication": "",
"Indication (1)": "Antineoplastic",
"status": "|Launched",
"Pathway": "Metabolic Enzyme/Protease",
"Pathway (1)": "Steroid hormone biosynthesis",
"Target": "Cytochrome P450",
"Target (1)": "CYP11B1, CYP17A1",
"moa": "",
"MOA(1)": "androgen biosynthesis inhibitor",
"source": "",
"Biological Description": "Abiraterone acetate (CB7630) is an oral, potent, selective, and irreversible inhibitor of CYP17A1 with antiandrogen activity. Abiraterone acetate is a prodrug form of Abiraterone (CB7598).\nIC50 & Target: CYP17A1[2]\nIn Vitro: Abiraterone (Abi) acetate is an ester prodrug of the anticancer agent Abiraterone, which shows IC50 values of 15 nM and 2.5 nM for the 17,20-lyase and 17\u03b1-hydroxylase (CYP17 is a bifunctional enzyme with both 17\u03b1-hydroxylase and 17,20-lyase activity). Abiraterone inhibits human 17,20-lyase and 17\u03b1-hydroxylase with IC50 of 27 and 30 nM respectively[1]. \nSignificant inhibition of proliferation of the AR-positive prostate cancer cell lines LNCaP and VCaP with doses of Abiraterone \u22655 \u03bcM is confirmed[2]. Abiraterone inhibits recombinant human 3\u03b2HSD1 and 3\u03b2HSD2 activity with competitive Ki values of 2.1 and 8.8 \u03bcM. 10 \u03bcM Abiraterone is sufficient to completely block synthesis of 5\u03b1-dione and DHT in both cell lines.Treatment with Abiraterone significantly inhibited CRPC progression in the robustly growing subset, effectively putting a ceiling on tumor growth over 4 weeks of treatment (P[3].\nIn Vivo: Abiraterone (Abi) acetate prolongs survival in castration-resistant prostate cancer (CRPC). [3H]-dehydroepiandrosterone (DHEA) depletion and \u03944-androstenedione (AD) accumulation are inhibited by Abiraterone in LNCaP, with an IC50[3].",
"Research Area": "Cancer"
},

"identifiers": {
"CAS Number": "154229-18-2",
"Formula": "C26H33NO2",
"Synonyms": "CB7630",
"ChEBL": **null**,
"PubChem ID": "139597119|87055577|87055578|9821849|152986093|144748333|75201460|11670322|86582960|144878649|71696658",
"ChemBank": **null**,
"Drug Bank": **null**
},
"activity_rank": "0.08687820135",
"target_models": {
"Caco2 Ellinger": {
"% inhibition": "47.15",
"IC50 (nM)": "",
"CC50 (nM)": "",
"Caco2 Selectivity index": ""
},
"3CLPro Kuzikov": {
"% inihibition": "18.05",
"IC50 (nM)": ""
},
"SARS-CoV Pseudotyped particle entry Vero E6 - NCATS and PubChem (AID:1479145)": {
"AC50 (\u03bcM)": "0",
"AUC": "-1.884845252",
"Potency (\u03bcM)\nConcentration at which compound exhibits half-maximal efficacy, AC50. Extrapolated AC50s also include the highest efficacy observed and the concentration of compound at which it was observed.": "0",
"Efficacy (%) \nMaximal efficacy of compound, reported as a percentage of control. These values are estimated based on fits of the Hill equation to the dose-response curves. ": "0",
"Activity": "Inactive"
},
"SARS-CoV Pseudotyped particle entry Vero E6 (Tox counterscreen)- NCATS and PubChem (AID:1479150)": {
"AC50 (\u03bcM)": "0",
"AUC": "16.64367159",
"Potency (\u03bcM) Concentration at which compound exhibits half-maximal efficacy, AC50. Extrapolated AC50s also include the highest efficacy observed and the concentration of compound at which it was observed.": "0",
"Efficacy (%) Maximal efficacy of compound, reported as a percentage of control. These values are estimated based on fits of the Hill equation to the dose-response curves. ": "0",
"Activity": "Inactive",

"Tox": "Inactive"
},
"MERS Pseudotyped particle entry Huh7 - NCATS and PubChem (AID:1479149)": {
"AC50 (\u03bcM)": "0",
"AUC": "1.634591441",
"Potency (\u03bcM) Concentration at which compound exhibits half-maximal efficacy, AC50. Extrapolated AC50s also include the highest efficacy observed and the concentration of compound at which it was observed.": "0",
"Efficacy (%) Maximal efficacy of compound, reported as a percentage of control. These values are estimated based on fits of the Hill equation to the dose-response curves. ": "0",
"Activity": "Inactive"
},
"MERS Pseudotyped particle entry Huh7 (Tox counterscreen) - NCATS and PubChem (AID:1479147)": {
"AC50 (\u03bcM)": "0",
"AUC": "0",
"Potency (\u03bcM) Concentration at which compound exhibits half-maximal efficacy, AC50. Extrapolated AC50s also include the highest efficacy observed and the concentration of compound at which it was observed.": "0",
"Efficacy (%) Maximal efficacy of compound, reported as a percentage of control. These values are estimated based on fits of the Hill equation to the dose-response curves. ": "0",
"Activity": "Inactive",
"Tox": "Inactive"
},
"SARS-CoV-2 cytopathic effect (CPE) - NCATS, PubChem (AID:1508606) and Chen": {
"AC50 (\u03bcM)": "0",
"AUC": "10.94748344",
"Potency (\u03bcM) Concentration at which compound exhibits half-maximal efficacy, AC50. Extrapolated AC50s also include the highest efficacy observed and the concentration of compound at which it was observed.": "",
"Efficacy (%) Maximal efficacy of compound, reported as a percentage of control. These values are estimated based on fits of the Hill equation to the dose-response curves. ": "",
"Activity": "",
"CPE EC50 (uM)": "",
"CPE % Efficacy": ""
},
"SARS-CoV-2 cytopathic effect (CPE)(Tox counterscreen) - NCATS, PubChem (AID:1508605) and Chen": {
"AC50 (\u03bcM)": "4.466835922",
"AUC": "-55.95373116",
"Potency (\u03bcM) Concentration at which compound exhibits half-maximal efficacy, AC50. Extrapolated AC50s also include the highest efficacy observed and the concentration of compound at which it was observed.": "",

"Efficacy (%) Maximal efficacy of compound, reported as a percentage of control. These values are estimated based on fits of the Hill equation to the dose-response curves. ": "",
"Activity": "",
"Tox": "",
"Cytotox CC50 (uM)": "",
"% Cytotox": ""
}
},
"covid_trials": {
"Covid trials": "No",
"Phase": "",
"Application (Treatment/Management)": "",
"Outcome": "",
"References": ""
},
"pk_pd": {
"Administration route": "Oral",
"Absorption": "",
"Cmax": "",
"Notes on absorption": "",
"protein-binding": ">99%",
"BDDCS (Biopharmaceutical Drug Disposition Classification System)": "",
"S (Water solubility)": "",
"EoM (Fraction excreted unchanged in urine)": "",
"MRTD (Maximum Recommended Therapeutic Daily Dose)": "",
"Vd (Volume of distribution)": "",
"CL (Clearance)": "",
"fu (Fraction unbound in plasma)": "",
"t_half (Half-life)": "5-14h",
"BA (Bioavailability)": "",
"Ccalc (uM)": ""
},
"red_flags": {
"Drug interactions": "Ombitasvir/paritaprevir/ritonavir & dasabuvir",
"Contraindications": "Cardiovascular diseases",
"Pregnancy concerns": "Category D",
"Breast feeding ": "Not recommended",
"Notes (Breast feeding)": "ZYTIGA is not for use in women. It is unknown if either abiraterone or its metabolites are excreted in human breast milk. (TGA)",
"Side effects": "None",
"Predicted CAD (Cationic amphiphile) induced phospholipidosis": ""
},
"filters_passed": 4,

"references": "[1] Stein MN, et al. Androgen synthesis inhibitors in the treatment of castration-resistant prostate cancer. Asian J Androl. 2014 May-Jun;16(3):387-400. [2] Richards J, et al. Interactions of abiraterone, eplerenone, and prednisolone with wild-type and mutant androgen receptor: a rationale for increasing abiraterone exposure or combining with MDV3100. Cancer Res. 2012 May 1;72(9):2176-82. [3] Li R, et al. Abiraterone inhibits 3\u03b2-hydroxysteroid dehydrogenase: a rationale for increasing drug exposure in castration-resistant prostate cancer. Clin Cancer Res. 2012 Jul 1;18(13):3571-9. [4] Lee GT, et al. Intracrine androgen biosynthesis in renal cell carcinoma. Br J Cancer. 2017 Mar 28;116(7):937-943. [5] A O'Donnell, et al. Hormonal impact of the 17\u03b1-hydroxylase/C17,20-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer. British Journal of Cancer volume 90, pages2317\u20132325 (2004) "
}

S10. Additional information regarding reusability of CoviRx web app

- The CoviRx platform was designed to be highly customizable, and thus, most components are reusable and not hard-coded. CoviRx was built as a SarCov2 drug repurposing database; however, it can be extended to other diseases in the future by using functionalities such as custom fields.
- Every data field of a drug displayed on the CoviRx platform maps to an attribute in the database. This implies that the code needs to be altered if a field is added, deleted, or modified for a particular drug. To overcome this problem of changing the code repeatedly, custom fields were introduced. Custom Fields feature is one of the critical components in the admin panel. It is a **JSON field** in the database that stores key-value pairs with the key holding the name of the drug field and the value holding the value for that field. This feature would make CoviRx extensible and flexible in the long run.
- Other functionalities which can be customized are located in the **CoviRx/main/utils.py** file in the repository. Some variables that can be used to customize CoviRx include the Search fields to customize the identifiers used in the search engine, Target model names to change the assay data to be stored in the database, verbose names, extra references, etc.
- To extend the CoviRx database to import datasets for other diseases, the csv_upload.py file needs to be edited, and the data would be stored for the new fields in the database. The use of custom fields ensures that no other changes are needed in tables.
- For changing the frontend of the website, the individual_drug.html file needs to be changed, and the necessary data be supplied by changing the views.py file.
- Django template language, modular structure, minimum dependencies, and other design principles ensure that extending CoviRx remains simple.

S11. References

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