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

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**Abstract:** Although various vaccines are now commercially available, they have not been able to stop the spread of COVID-19 infection completely. An excellent strategy to get safe, effective, and affordable COVID-19 treatments quickly is to repurpose drugs that are already approved for other diseases. The process of developing an accurate and standardized drug repurposing dataset requires considerable resources and expertise due to numerous commercially available drugs that could be potentially used to address the SARS-CoV-2 infection. To address this bottleneck, we created the CoviRx.org platform. CoviRx is a user-friendly interface that allows analysis and filtering of large quantities of data, which is onerous to curate manually for COVID-19 drug repurposing. Through CoviRx, the curated data have been made open source to help combat the ongoing pandemic and encourage users to submit their findings on the drugs they have evaluated, in a uniform format that can be validated and checked for integrity by authenticated volunteers. This article discusses the various features of CoviRx, its design principles, and how its functionality is independent of the data it displays. Thus, in the future, this platform can be extended to include any other disease beyond COVID-19.

**Dataset:** www.covirx.org

**Dataset License:** CC-BY

**Keywords:** COVID-19; drug fingerprints; drug repurposing; open-source dataset; search engine; web application development; web scraping

## 1. Introduction

COVID-19 pandemic, caused by the SARS-CoV-2 virus, has created significant impacts throughout the entire world [1,2]. As of 5 November 2022, more than 632 million cases have been reported, resulting in about 6.5 million deaths globally [3]. Despite recent advances in drug discovery, the treatment of viral infections remains a significant challenge for scientists worldwide. Although various vaccines are now available on the market, they have not been sufficient to stop the spread of COVID-19, which is further complicated by variants of SARS-CoV-2 emerging continuously. An efficient and economic strategy for satisfying the urgent requirement for safe, effective, and affordable COVID-19 treatments is to repurpose the drugs already approved for other diseases [4,5]. A wide range of approaches is available for repurposing a drug, such as computational and bio-experimental approaches. With the use of various drug databases it is feasible to determine the biological function of a protein computationally and validate the process statistically. This technique, however, comes with its own set of challenges. One such challenge is data availability. Public access to high-quality, valuable information such as clinical trials data is still limited. Although there are a few open-access databases, such as the Drug Repurposing Hub [6], which provide drug repurposing candidates, very few are specific to COVID-19, such as Excelra [7] and NCATS [8].

Additionally, the significant sizes of these databases often create computational bottlenecks. Through this study we explored the problems of data accessibility, availability, and interpretability by developing CoviRx, a robust web-based application. The name CoviRx is a portmanteau of the terms COVID-19 and Rx (a medical prescription).

CoviRx provides users with an interactive interface to access 7817 drugs for COVID-19 drug repurposing. The web application (henceforth mentioned as either App or app) presents each drug's physical and chemical properties, original indication, available data from multiple assays, COVID-19 clinical trials, and any red flags (pregnancy concerns and contraindications, among others) for these drugs. It calculates dynamically any drugs similar to the query drug using the Tanimoto coefficient [9], a popular metric used for finding similarity between molecules using their fingerprint descriptors. It displays the output along with the number of filters passed out of the total eleven designed by the research team. This computer science paper should be read in conjunction with research by MacRaild et al., 2022 [10], which describes the pharmacological methodology for systematic down-selection of repurposed drug candidates for COVID-19. To increase collaboration with the other researchers, features have been incorporated in CoviRx that allow registered users to submit their findings on any drug candidate to the CoviRx web app. Following a thorough peer review process, these submissions will be merged with the primary database, which we herein report. The user can download the available data as JSON (JavaScript Object Notation) or PDF (Portable Document Format) file, and unique URLs. This provides an elegant solution to the problem of data non-standardization and lack of data mining, interpretation, and manipulation-friendly datasets [11].

CoviRx has been designed according to current industry standards. Stringent checks are placed to ensure data consistency, security, and uniformity. Unique identifiers have been added for the individual drugs to ensure that they are easy to search and data for all the drugs are easily accessible. Modern frameworks such as Django [12,13], jQuery [14], and Bootstrap5 [15] have been used for development on a cloud hosting service (Azure) to ensure that the web app is scalable, i.e., able to process an increase in website traffic. It supports different user profiles to protect the integrity of data. Only registered users can submit to the website, to maintain data uniformity and reliability and prevent the malicious activities suffered by some prominent open-source platforms. Only the users with adminis-

tration rights have modification privileges. Numerous graphical representations [16] are present throughout the web app to give the users an overview of the dataset and enhance their experience. Its modular architecture ensures that it is flexible enough to be extended to any other disease without disrupting its underlying functionality. CoviRx thus is a one-stop application for accessing high-quality data related to COVID-19 drug repurposing and, in the future, any other epidemic. CoviRx can be accessed at www.covirx.org.

## 2. Data Description

Drug data (with assays) were manually curated by our team from various research journals and publicly available drug databases. Regulatory approval data were obtained from the U.S. Food and Drug Administration (FDA) [17], Therapeutic Drug Administration, Australia (TGA) [18], and Inxight Drugs websites [19], while clinical trials data were acquired from clinicaltrials.gov [20] for 7817 drugs.

These drugs were then passed through a series of 11 filters, and the resultant drugs were screened for possible action against COVID-19 to narrow down to twelve drugs for further studies on COVID-19 drug repurposing [21].

Manual curation of data and datasets requires considerable time, labor, and financial resources. Therefore, to economise these resources, it was decided to open source this dataset and make it available with a user-friendly graphical interface so that other researchers working on their own filters for down-selecting drugs can use it as shown in Figure 1.

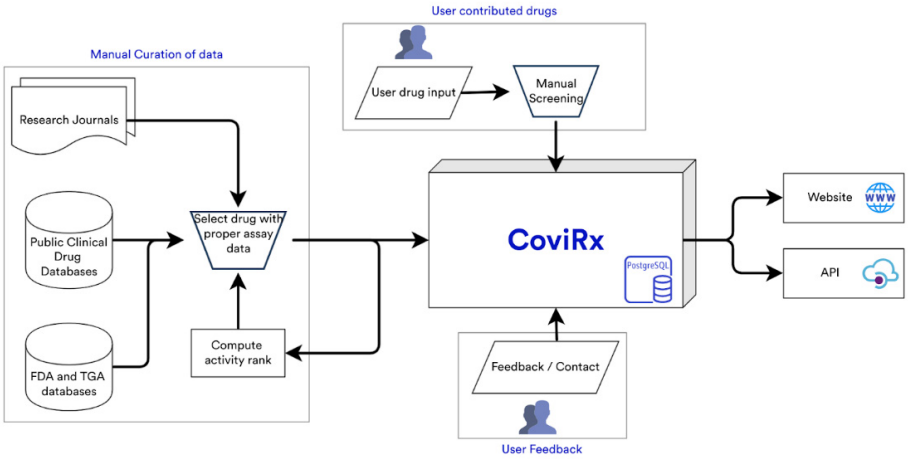


**Figure 1.** CoviRx components and workflow.

The CoviRx website consists of various identifiers such as synonyms, Chemical Abstract Service (CAS) number, and PubChem ID, ChEMBL ID, amongst others, which are hyperlinked to provide a seamless transition across different databases. Various drug-likeness properties such as molecular weight, Partition Coefficient (logP), hydrogen bond donors (HBD) and hydrogen bond acceptors (HBA) are also included for each compound to assist with early drug discovery programs. A drug's original indication, mechanism of action (MOA), relevant pathways it interferes with, and associated targets are also included to provide a brief background about its original application. CoviRx provides users with SARS-CoV-2 drug repurposing data from several COVID-19 drug repurposing studies and the status of such drugs in COVID-19 trials. The website's pharmacokinetics (PK) section includes information regarding a compound's route of administration, the volume of distribution, clearance, protein binding, etc. The CoviRx website also consists of a specially curated section called "red flags", which sheds light on drug–drug interactions, contraindications, pregnancy category of a drug, breastfeeding concerns, and severe side effects or black box warnings. To avoid early confounders in drug repurposing programs, information such as CAD (Cationic Amphiphilic Drugs) induced phospholipidosis and PAINS (Pan Assay Interference Compounds) are also included in the red flags section.

The data have been segmented into different tables for efficient storage. Figure 2 depicts different tables and the data fields used to store the drug data, and Figure 3 illustrates the same for data on users. The data types of each field and the type of constraints enforced (if any) are also highlighted.

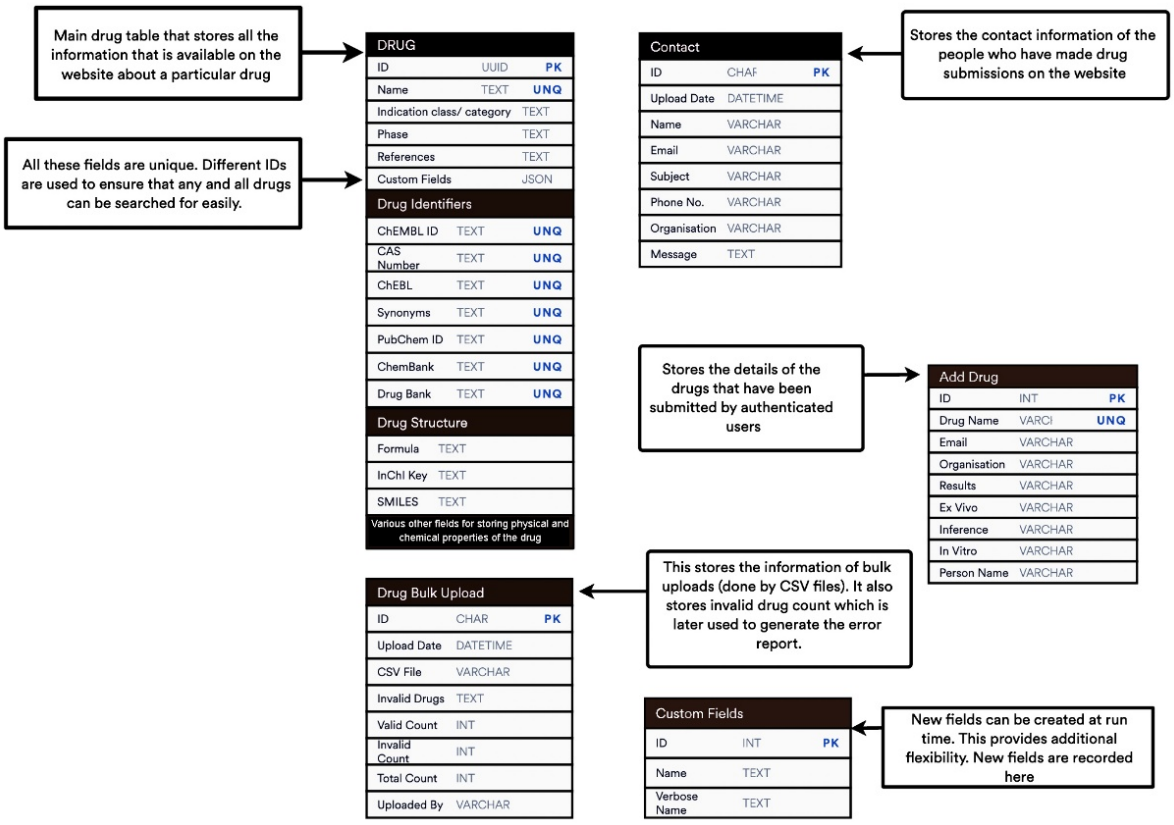


**Figure 2.** Tables and data fields used for storing drug information.

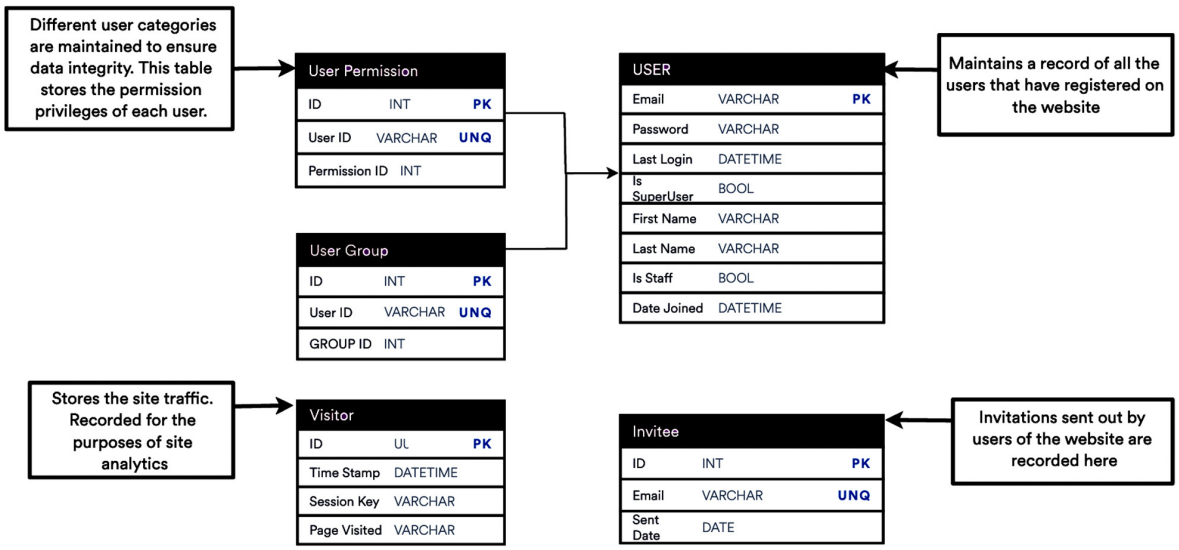


**Figure 3.** Tables and data fields used for storing user information.

## 3. Methods

### *3.1. Tech Stack and Design Principles*

Modern technologies were employed to develop the front-end and back-end of the web app. Figure 4 demonstrates the interaction between different components like front-end and

back-end servers, and the frameworks we have used to develop these. These frameworks are open-source, well documented, and highly flexible to use. Back-end servers, such as Apache [22] and cloud hosting platforms including Azure or AWS, were preferred over other alternatives as these provided support for both vertical and horizontal scalability. Currently, SQLite [23], a relational database management system, is being used to process website data; however, it will be migrated to PostgreSQL soon [24,25] as it offers better concurrency control [26]. Google OAuth [27] (login/logout), Google reCAPTCHA [28], and Google simple mail transfer protocol (SMTP) [29] have been used during development. CoviRx sends emails to its users for various purposes, such as a copy of responses filled by them in contact and "contribute drug" forms; an invitation to the admin panel; and reporting errors that occur during drug upload. A python library called Premailer was used because emails do not support CSS or JS files, and it is important to deliver well-styled HTML emails to our users [30].

Few properties of database systems and websites [31–33] form the foundation for CoviRx's architecture. These design principles have been discussed in detail in Table 1.

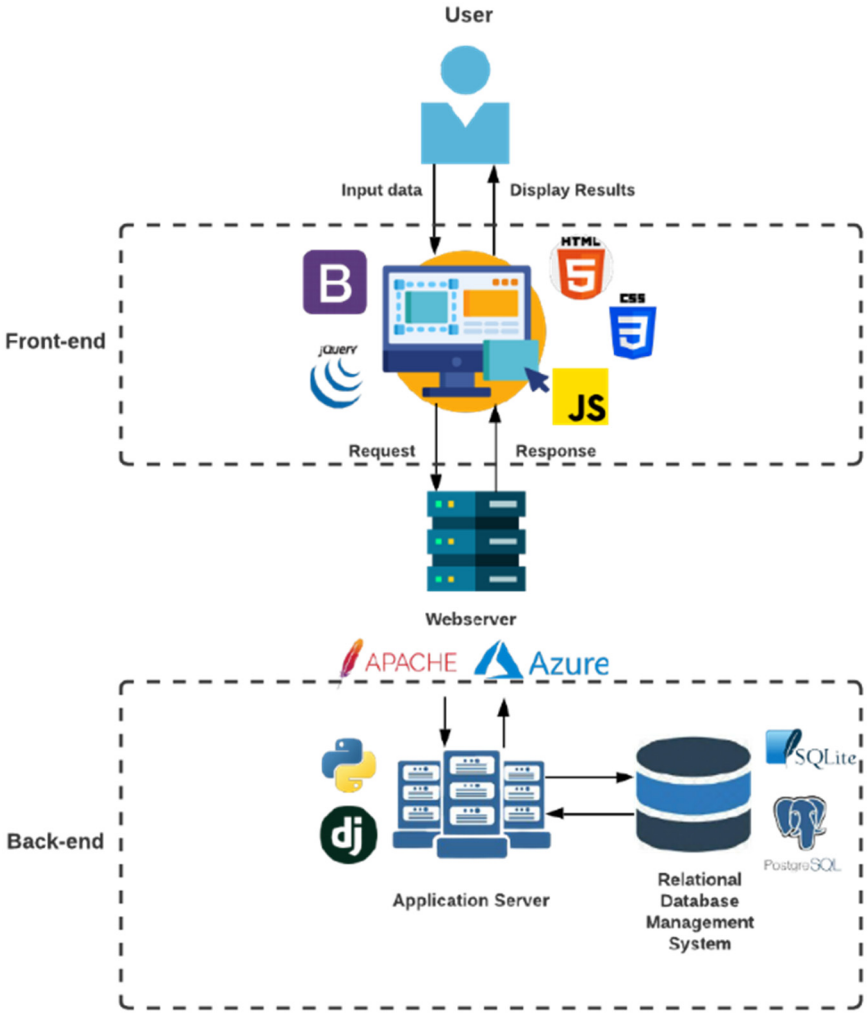


**Figure 4.** Tech stack used for developing CoviRx and the interaction between these frameworks. User interacts with the front-end, built using HTML, CSS, JQuery3 [14], Bootstrap 5 [15], to request data. Front-end then interacts with the webservers, e.g., Azure, AWS, and Apache. These fetch data from the application servers powered by Django [12,13,34], which in turn interact with the database management system, i.e., SQLite [23]. Once these Data are extracted, it follows a reverse path back to the user.

**Table 1.** Design Principles adopted during the development of CoviRx.

| Design Principles | Implementation | Advantages | Framework Support |
|---|---|---|---|
| Access Management | To ensure that no unauthorized access happens, users were divided into three broad categories:<br>1. Unauthenticated users: this type of user can read from the database but cannot modify the database.<br>2. Users with limited privileges: this type of user can read and submit drugs that users with admin privileges will verify before merging.<br>3. Admin users: this type of user has all the privileges, i.e., read, write, update, delete. | • Ensures data security.<br>• Maintains data quality and data consistency by allowing only trained admin users to commit to the database.<br>• Ensures system reliability. | — |
| Data Security | Protection against cross-site scripting (XSS), cross-site request forgery (CSRF), SQL injection, and clickjacking is provided by Django. Secure communication between the web app and the server is established as only encrypted Data are shared via the HTTPS protocol. | • Protects the data from attack.<br>• Ensures data privacy. | Django, HTTPS Protocols |
| Scalability | Modern cloud hosting providers and back-end servers support both vertical and horizontal scaling. | • Ability to manage increasing website traffic without disturbing end users.<br>• Hosting becomes less expensive.<br>• Provides multiuser support. | Django, Apache back-end server, AWS, Azure, Google Cloud Platform (GCP) |
| Modularity | The entire website has been broken down into multiple independent components which are interchangeable. The database components are well encapsulated from program components of the web app. | It adds a layer of abstraction that provides data program independence.<br>• The underlying database can be changed without altering the code.<br>• Easy to maintain.<br>• Easy to recognise and fix bugs. | Django |
| Integrity Constraints | Various constraints are in place to ensure that only data that pass all quality checks are merged with the primary database. Unique identifier constraint is enforced in multiple fields like drug name, ID, etc., Char fields with maximum length constraints over text fields are used to optimize memory usage. | • Maintains correctness of data.<br>• Maintains data uniformity. | — |

**Table 1.** *Cont.*

| Design Principles | Implementation | Advantages | Framework Support |
|---|---|---|---|
| Auto Versioning of Static Files | A string specifying the version of the static file is appended to the URL pointing to the static files. This version is updated, forcing the browser to load the latest version instead of the one from the cache. | • Quicker developmental iterations.<br>• Faster load time. | — |
| Flexibility and Responsiveness | The web app is responsive to a wide range of screen sizes. Django template language makes designing dynamic front-end components easy. | • Multi-device support makes it accessible to a broader audience.<br>• Better user experience. | Django, Bootstrap5, jQuery3, jQuery3 UI |
| Backup and Recovery | Data backups are done weekly. | Protects the data from system failure, both hardware and software. | — |
| Concurrency Control | SQLite is not optimized for performing concurrent operations and often results in Database is locked exceptions. So, we intend to shift to PostgreSQL in the future so that simultaneous operations do not lead to abnormalities. | • Reduces wait time.<br>• Reduces response time.<br>• Increases resource utilization.<br>• Increases performance and efficiency.<br>• Maintains data consistency. | SQLite (shifting to PostgreSQL in future) |
| Data Persistency | If an exception happens between a transaction (write operation), the data to be written might get destroyed. We plan to protect our system in rare cases of failure like this to ensure durability. | Data is never at risk. | Celery [35] (to be implemented) |

### *3.2. CoviRx Architecture*

An iterative software development model was followed [36] while designing CoviRx. First, this was achieved by creating a wireframe [37] for every front-end page, followed by a basic application implementation. The design components were then modified in each version by adding new features and functionalities. Each component was tested individually [38] before merging with the main framework. Upon its completion, the entire application was tested [39]. Figure 5 depicts various pages/features of CoviRx.

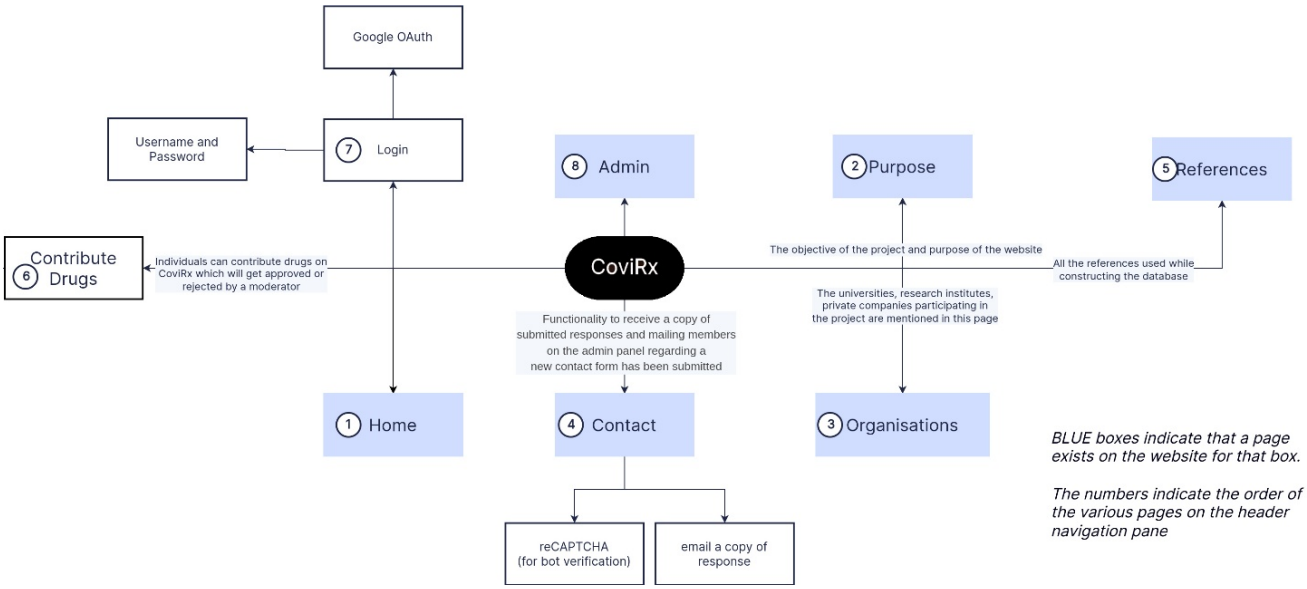


**Figure 5.** Overview of CoviRx architecture.

The CoviRx web app's top hierarchy consists of the admin panel [40] and the user interface. It was a design decision to keep the user interface interactive and straightforward. Users can interact with our tool using features such as the search engine, drug overviews, contact forms, drug submission forms, etc. Features of the website's home page are depicted in Figure 6.

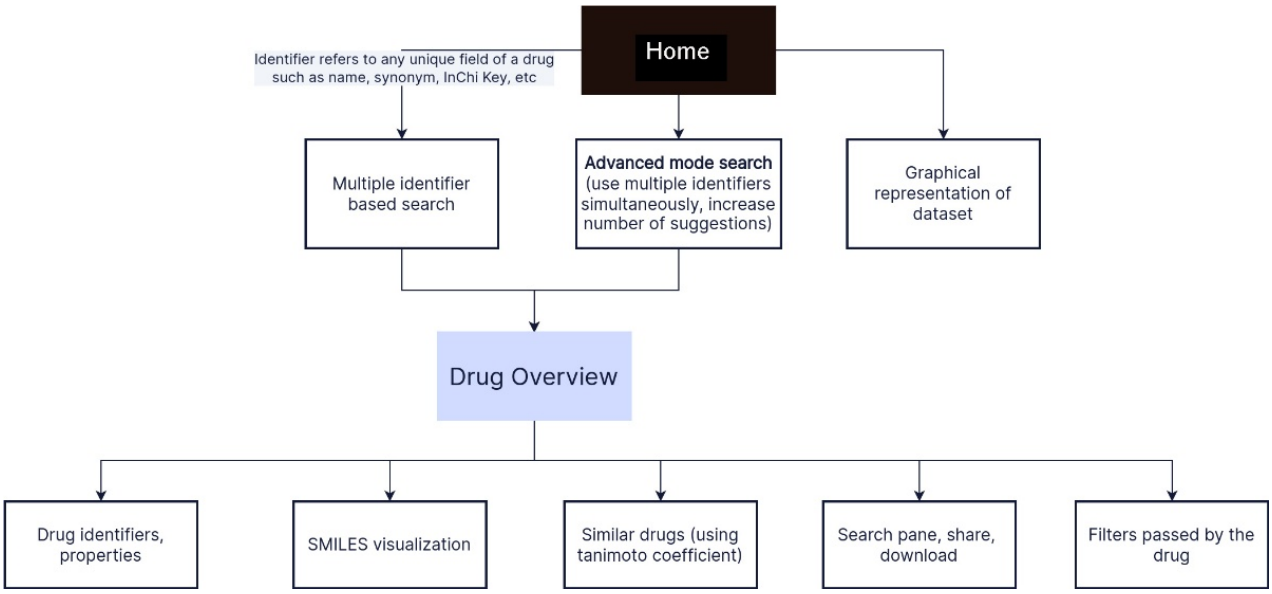


**Figure 6.** Home page overview.

The admin panel is for users with admin rights for the web app. It has two sections: accounts (associated with the users) and main. Admins can use the main section to contribute/upload drugs access website analytics data and custom fields. A feature to invite other users to the admin panel has been added, and admins can use it to send out invites with a seven-day expiry. Features of the admin panel are depicted in Figure 7.

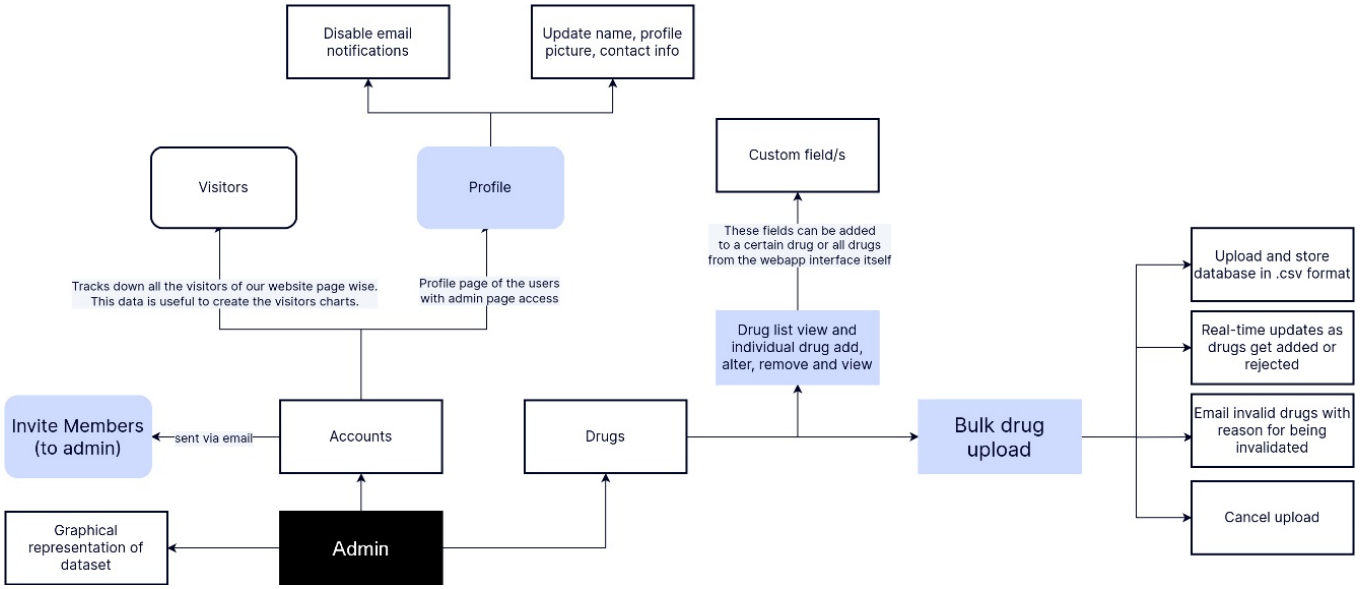


**Figure 7.** Admin panel overview.

Graphical representations have been used throughout the website to give the users a visual representation of the database, enhancing the user experience. CoviRx offers multi-language support [41] so that our open-source dataset is accessible to a broader range of users [42].

#### 3.2.1. User Interface

The Search Engine

The standard and advanced search modes are two modes of usage, as depicted by Figures 8 and 9, respectively. Both modes offer search-as-you-type [43] functionality. The significant difference between the modes is that only one identifier can be used to search for a drug in the case of normal mode. In the advanced search, multiple identifiers can be used simultaneously. The search results have been capped at five for the normal mode to reduce search time, and this limit is adjustable in the advanced search mode. The researchers can also choose a combination of different filters in the advanced search mode to restrict the drugs being displayed as per their requirement. The search results comprise drug metadata, i.e., drug synonyms, indication class, Simplified molecular-input line-entry system (SMILES) [44] representation, etc.

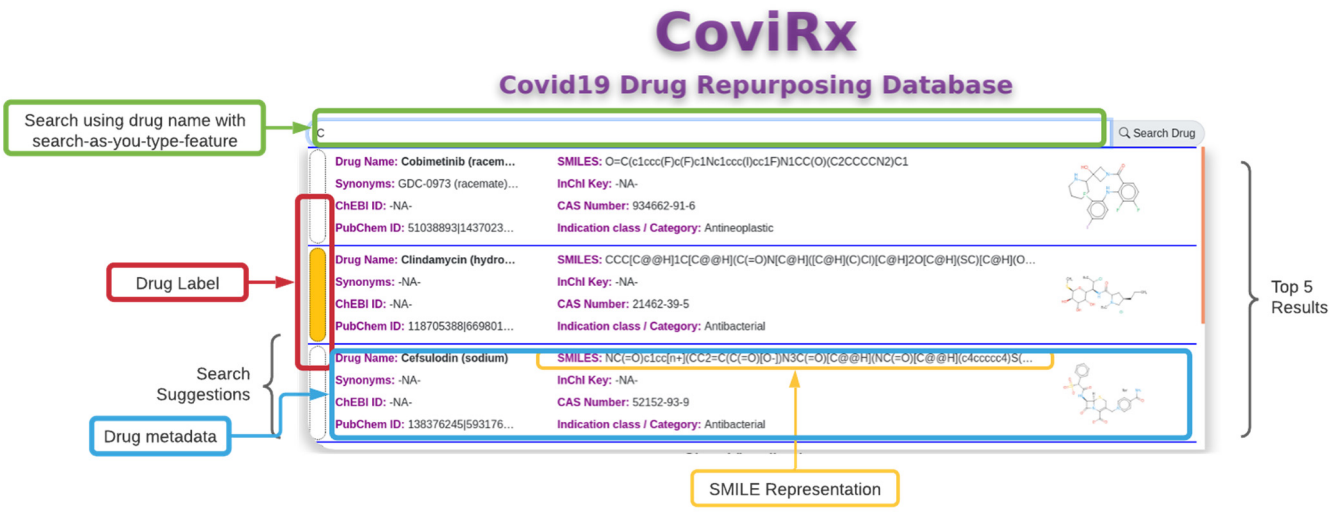


**Figure 8.** Standard search mode.

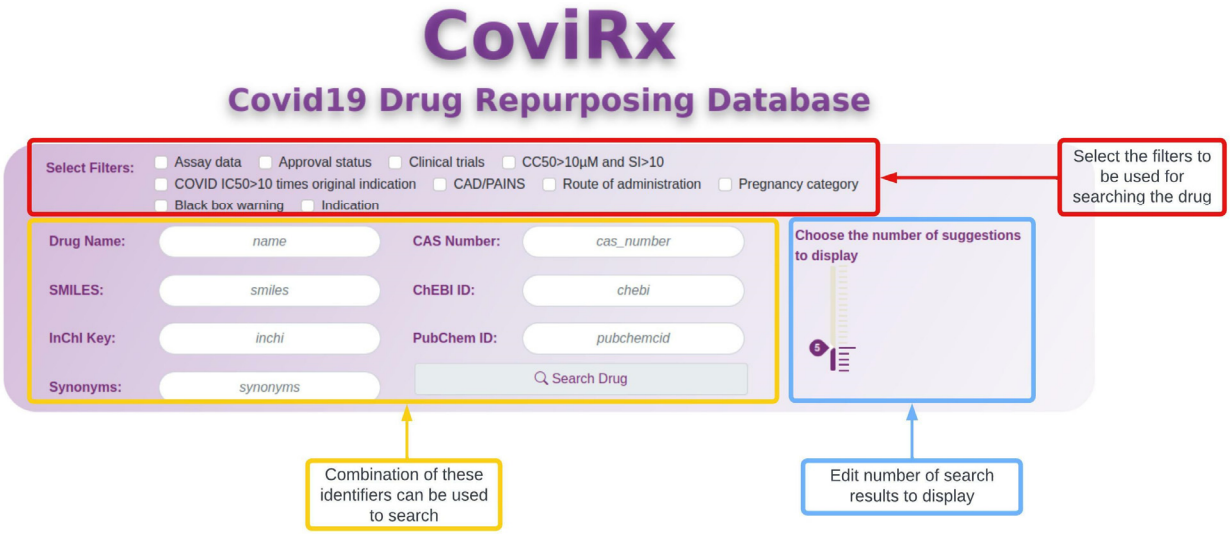


**Figure 9.** Advanced search mode.

Drug Overview Page

This section of the website displays information about the query drug. The data have been divided into distinct categories like identifiers, drug-likeness, original indication, target models, clinical trials, red flags, filters passed, etc. The structure of the webpage is depicted in Figure 10. Specific data points related to drug activity on the original target have not been included; they do not have well-defined values or data uniformity but can be added in the future. Data points such as original indications and red flags have been added to aid researchers. In contrast, other fields like pharmacokinetics (PK) would be helpful to individuals who wish to model their filters and down-select drugs. Visual representation of the filters used to down-select drugs and the filters passed by each drug has been added for those who would like to investigate this further. Drugs are ranked based on activity scores calculated using the assay data as described in MacRaild et al., 2022 [10].

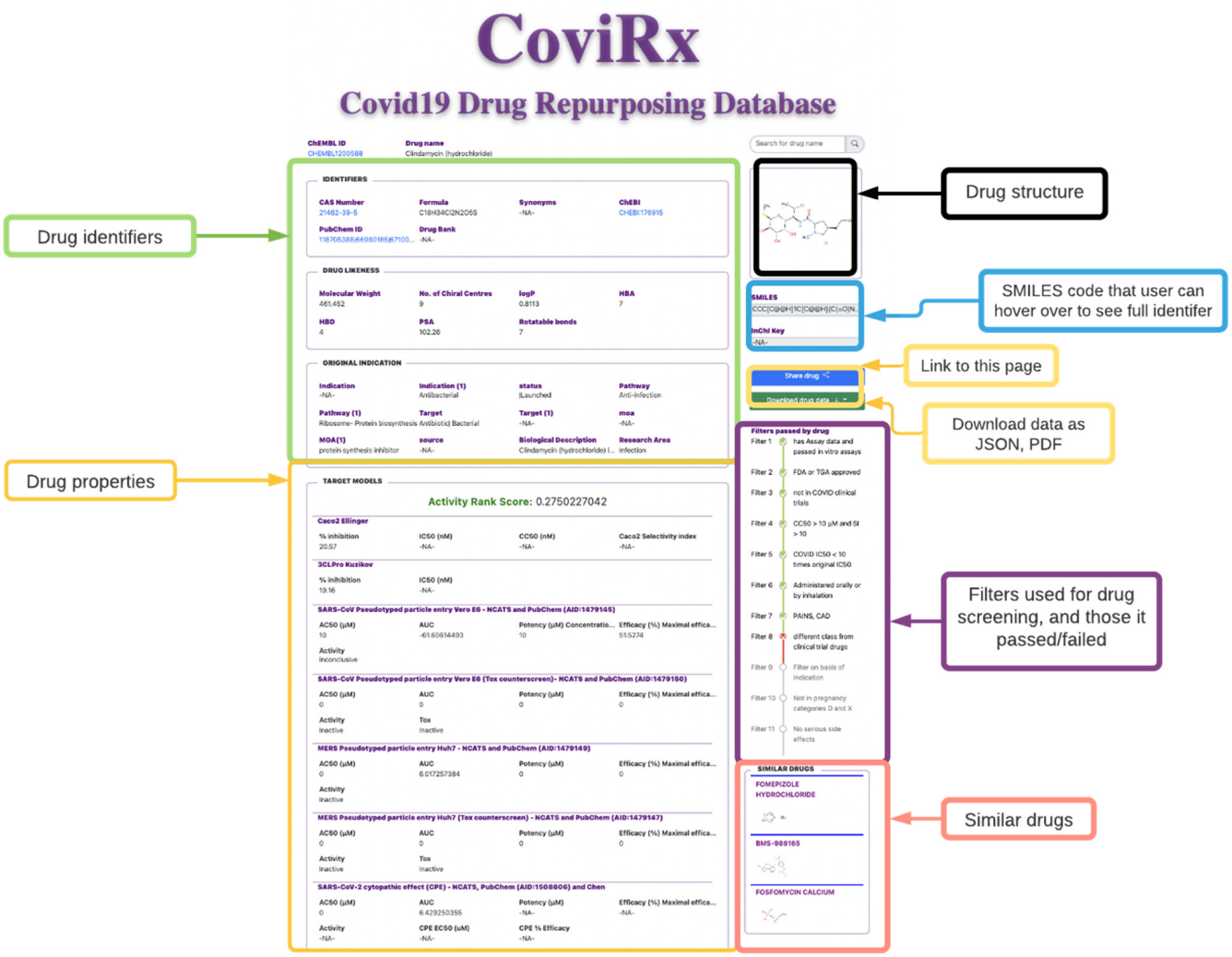


**Figure 10.** Drug overview webpage.

Another important feature of this page is the dynamic calculation and display of similar drug candidates. Drug similarity is calculated using the Tanimoto coefficient [9,45], which is the ratio of common fingerprints and the number of total fingerprints. The RDKit python library [46] was used to generate the fingerprints of the drugs and calculate the Tanimoto similarity between them [47]. The threshold for similarity is kept at a value of 0.7, less than the suggested value of 0.85 [48], to increase the number of similar drugs. Once the similarity is calculated, the page displays the top 5 (i.e., highest five Tanimoto coefficients) candidates.

## Contribute Drug

CoviRx supports and encourages the community to help us enlarge this open-source database. Authenticated individuals can contribute to the web app using the "contribute drug" feature, an overview of which is depicted in Figure 11. Only registered users can make these contributions to ensure data integrity and uniformity. All contributed drugs would be verified manually by a team of admin users to ensure data authenticity and reliability.

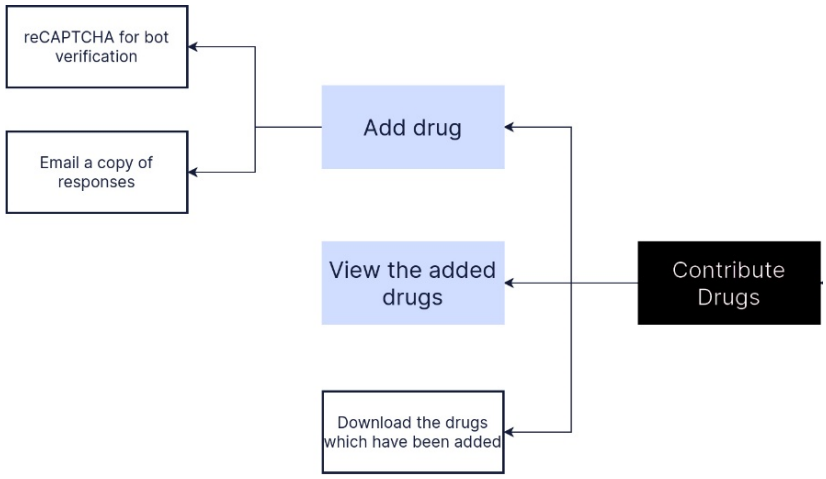


**Figure 11.** Contribute Drugs Feature.

Contact

Using the contact page, users can contact administrators to give any feedback or to request access to contribute drugs. A reCAPTCHA [28,49] check has been added to prevent robots from submitting the form.

### 3.2.2. Admin Panel

Bulk Upload Support

To facilitate the process of bulk drug upload, CoviRx has a feature which enables the admin users to upload large amounts of drug data in one go by directly submitting a CSV file. A single drug upload/delete/modify functionality is also available. CoviRx evaluates every drug against multiple constraints before adding it to the primary database. These constraints ensure the validity of the drugs, so drugs that fail them are considered "invalidated" and shared with the admin users to reverify the data. Figure 12 depicts the various sub-features of the bulk upload feature.

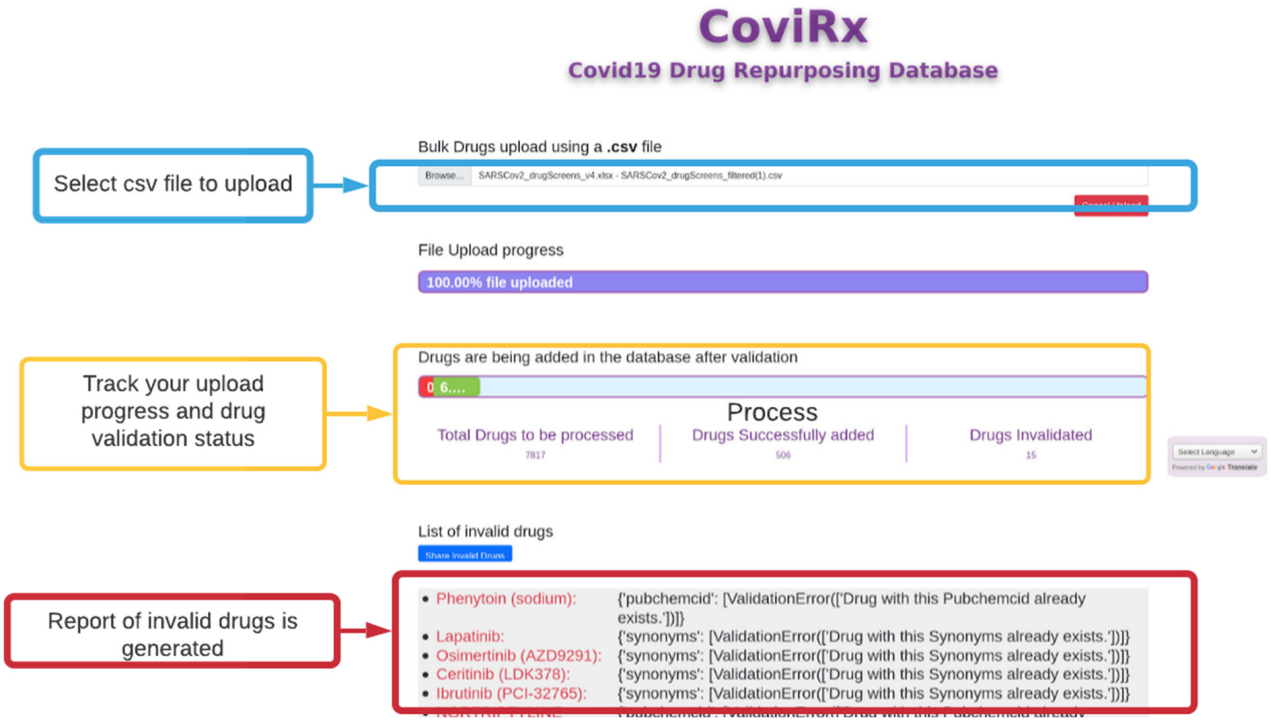


**Figure 12.** Bulk upload webpage.

Website Analytics

Mechanisms have been developed to measure the website traffic, the details of which are available in the admin panel. According to the website load, this was added to plan the resources for hosting the web application. It will also help track the trends about the most popular drugs in the database. While monitoring the website traffic, only a session ID cookie [50] is used, and no other details like IP address are saved to ensure users' privacy [51].

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. Custom fields have been added to overcome this problem of repeatedly changing the code and are 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 [52]. This feature would make CoviRx extensible and flexible in the long run.

### *3.3. Articles Scraping*

To ensure CoviRx does not end up being a static database after its creation, we have introduced a new feature to keep the database up to date with new articles published by peer-reviewed journals and reputed preprint servers such as bioRxiv and medRxiv. CoviRx looks up for new articles periodically (at present every month) to find new assay data for drugs present in the CoviRx database. The papers found are then assigned to admin users for verification. We selected Google Scholar [53] as a platform to find new articles as it covers a very wide range of publications including preprints. A paper can be found at multiple places (preprint server, peer reviewed journal, etc.), in different formats (html, pdf, etc.), therefore CoviRx ensures that only the most recent version gets scraped to prevent duplicate entries of the same article.

The scraped articles are then equitably assigned to admin users, who, as domain experts, verify the article and update the database. When an admin user becomes inactive or leaves, the articles assigned to them are distributed amongst the remaining admin users automatically. Articles are grouped drug-wise to ease verification as shown in Figure 13. The admin users can then view a list of the articles scraped, along with the drug, target model associated, and other keywords used for scraping as shown in Figure 14. If the articles found are relevant, the drug's COVIDvid-19 assay data can be updated with the help of the "Update form" as shown in Figure 15.

Since CoviRx crowd-sources the article verification job to pharmacy students, it becomes imperative to monitor the articles being verified, as shown in Figure 16. CoviRx also allows admin superusers (the highest administration privilege) to revert the changes made by admin users so that any incorrect change can be undone, as shown in Figure 17. In the future, the manual verification process of scraped articles can be automated using NLP techniques [54].

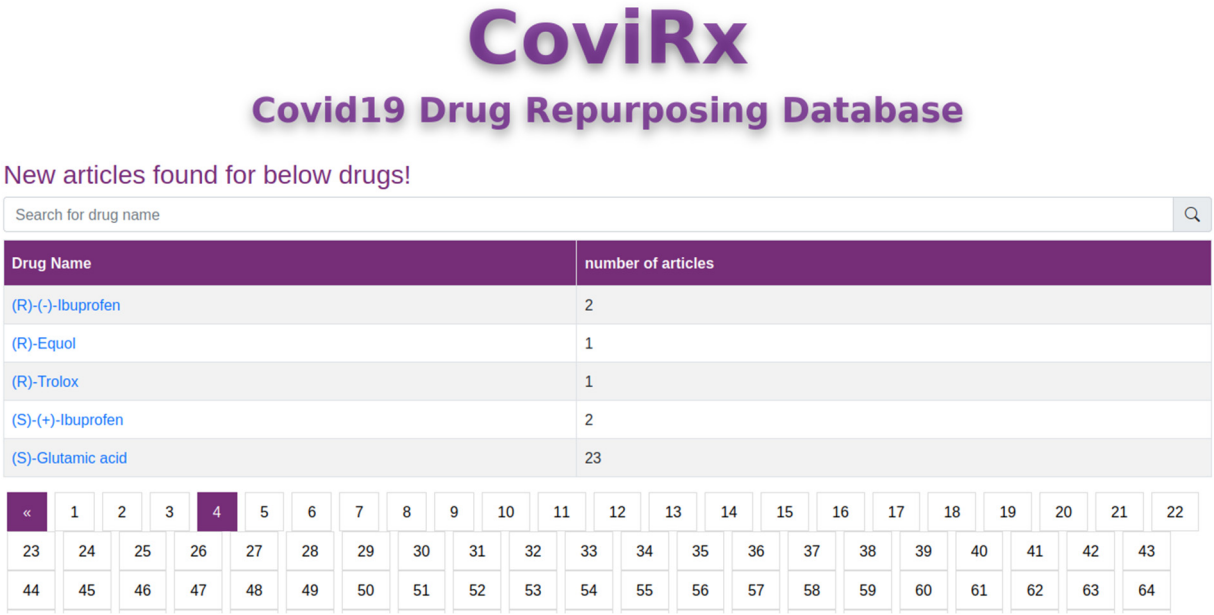


**Figure 13.** Articles are clubbed drugwise, and 5 drugs are displayed on every page to ease verification.

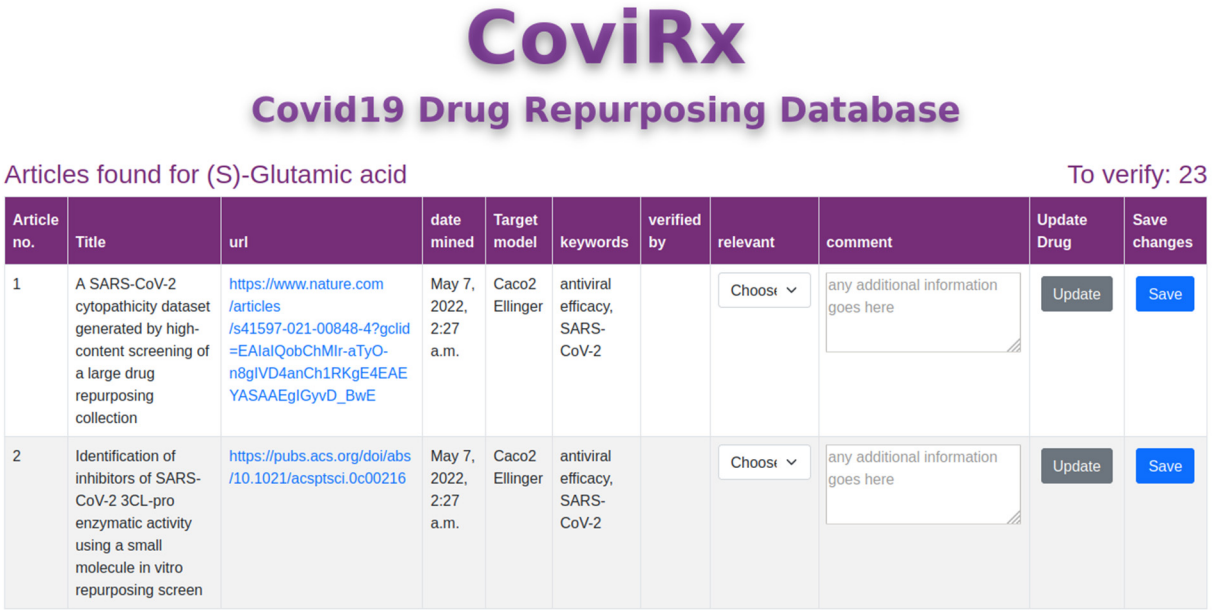


**Figure 14.** The URL, target model and drug associated with every article are listed.

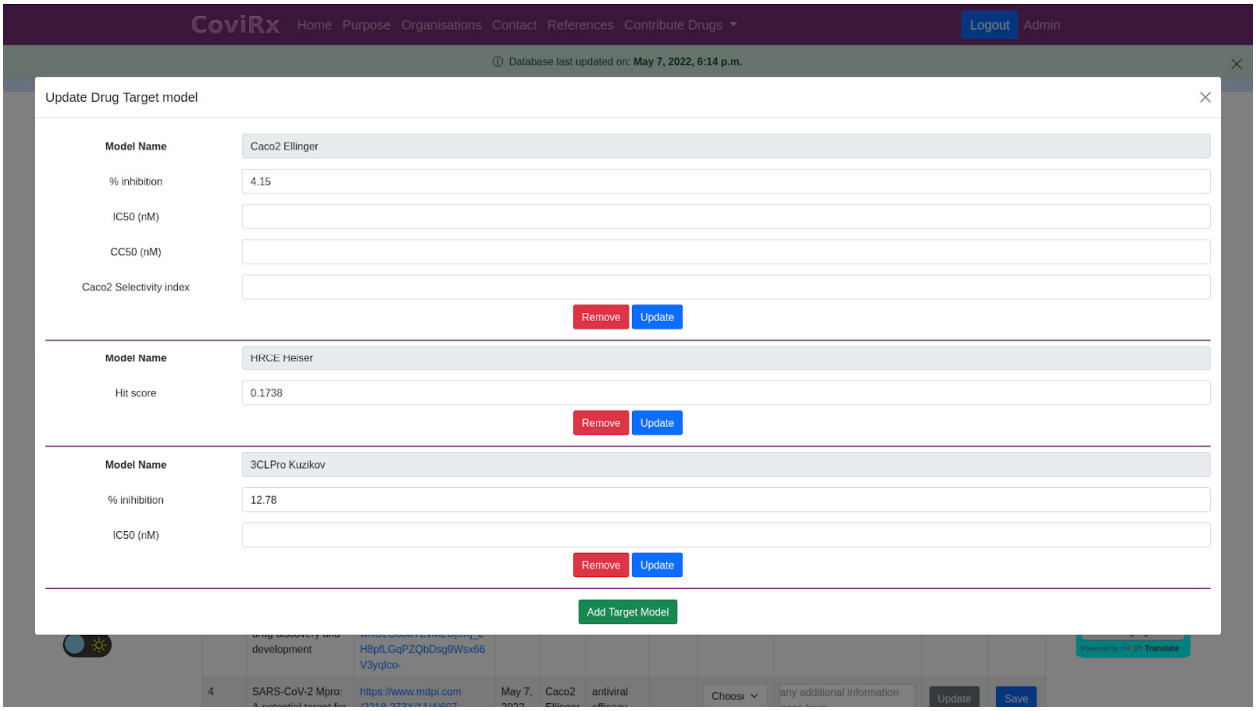


**Figure 15.** The update form can be used by the verifier to update or add new target model data based on the evidence presented in the respective journal article.

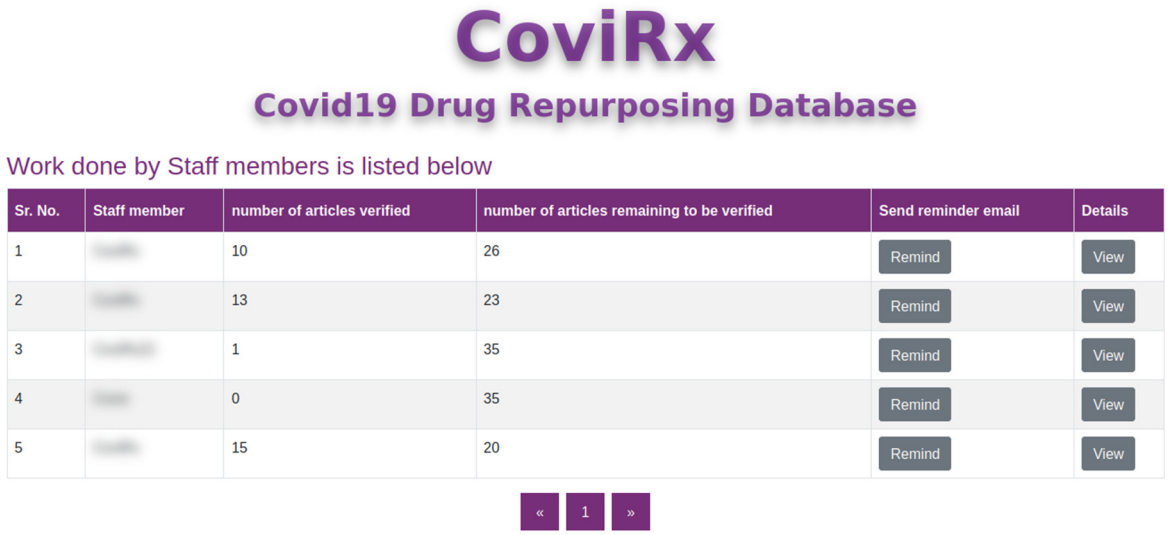


**Figure 16.** The articles verified by the pharmacy students can be tracked by the admin superusers.

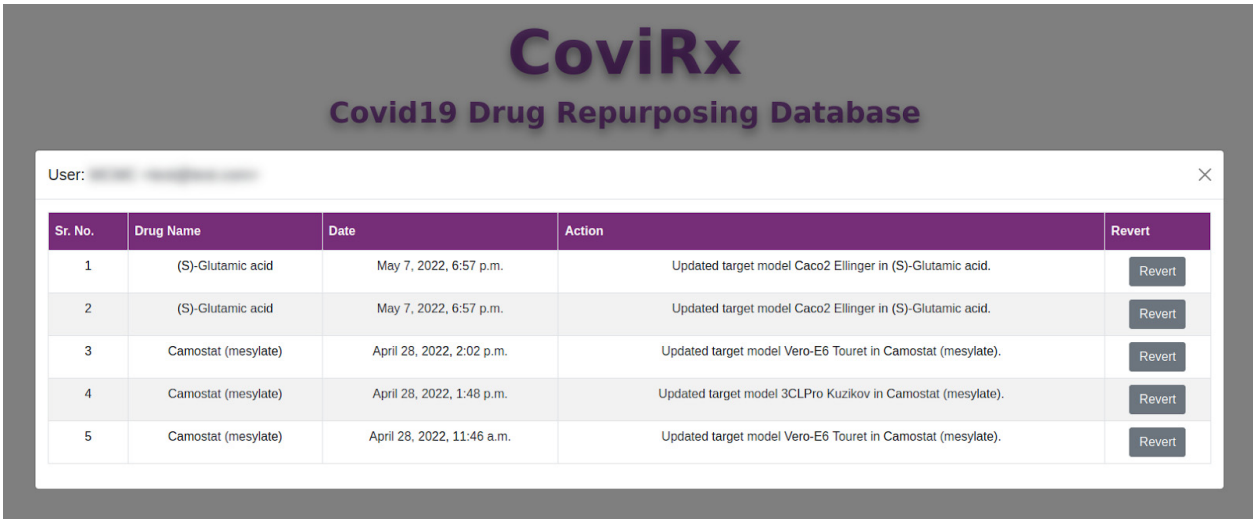


**Figure 17.** Feature to monitor the changes made by every user in detail and revert them if needed.

## 4. User Notes

The supplementary information provides additional information to the users. The external libraries and external APIs used are listed in Tables S1 and S2, respectively. A few more screenshots of the user interface, admin panel and the formulas used are provided in Figure S3, Figure S4 and Text S5, respectively. Additional information for contributing drugs and privacy policy of CoviRx is covered in Text S6, and URL S7 includes a link to the GitHub repository for CoviRx; URL S8 links to more detailed technical documentation, and Text S10 provides information on reusability for developers. All the API endpoints provided by CoviRx are covered in detail, with example in Text S9.

## 5. Conclusions

CoviRx provides users with repurposed drugs that could have anti-viral activity against SARS-CoV-2, based on pharmacological information, assay activity, and drug status in COVID-19 clinical trials. Its user-friendly interface and multi-language support improve data accessibility. Various drug-likeness properties such as molecular weight, logP, hydrogen bond donors (HBD), and hydrogen bond acceptors (HBA), amongst others, are included for each compound to assist with early drug discovery programs. The users who wish to design their own filters for drug down-selection can benefit from the website's pharmacokinetics (PK) section, which provides information regarding a compound's route of administration, the volume of distribution, clearance, protein binding, etc. This platform also encourages its users to help expand this open-source dataset by submitting their drug repurposing data, and to register as volunteer administrators to keep the database error free and up to date. CoviRx has a wide variety of applications, and thus will help advance the field of drug repurposing for the current pandemic as well as future epidemics.

**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/data7110164/s1. Table S1: Table listing Python libraries used for the development of CoviRx, Table S2: List of external APIs used by CoviRx, Figure S3.1: Drug upload form, Figure S3.2: Contact form, Figure S3.3: Identifiers available for normal search mode, Figure S3.4: Graphical visualization giving database overview, Figure S4.1: Website Analytics, Figure S4.2: Drug bulk upload feature, Figure S4.3: Email sent by CoviRx to correct invalidated drugs, Figure S4.4: Invitation email, Figure S4.5: Tech stack used for development, S5: Tanimoto Coefficient formula, S6:Website general information, Link S7: Code Repository, Link S8: Code Usage, S9: API calls available, S10. Additional information regarding reusability of CoviRx, S11: Supplementary references are included in "CoviRx-supplementary-information" file; "Total list of 214 drugs-table" is shared as a separate file which lists the drugs with the highest activity scores in CoviRx.

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