CSTNPD: A Database for Cancer Specific Toxic Natural Products

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Abstract

Objective: To compile an open access central resource database for cancer specific toxic natural products. **Methods:** The literature survey using PubMed was made manually in order to collect the natural product that exhibit anticancer activity but not or least toxic to normal cell, and were curated by in an open access central resource database. **Result:** The compound database provides opportunities for researchers to obtain various information required for the successful identification of pharmaceutically relevant substances. **Application:** The bioactive natural products with anticancer therapeutic potential are abundantly reported, but majority of them are toxic to normal cells too. All those novel natural product molecules failed to proceed towards further detailed research or to reach into clinical trial and pharmaceutical drug development and drug approval.

Keywords: Cancer, Database, Natural Products, Plants, Toxic, CSTNPD

1. Introduction

Cancer (-a very complex genetic or metabolic disease) is well-recognized as a global health problem¹, accounts for approximately 7.6 million deaths (about 13% of all deaths or 1 in every 7 deaths) worldwide^{2,3}. Billions of dollar invested on the advanced, sophisticated and multidisciplinary research works on the cancer has resulted into the identification of varieties of therapeutic targets of cancer as well as the development of vast number of anticancer drugs⁴ which have reduced the death rates owing to cancer during last two decades; however, the perfect drug to combat the cancer is still a nightmare⁵.

Further, the use of chemotherapy as well as the radiotherapy used for the treatment of cancer causes serious side effects⁶. The plant natural products have continuously being explored for the new leads in pharmaceutical development^{7,8} including cancer^{9,4,10}. The *in vitro* cell-based cytotoxicity assays of bioactivity-guided fractionation of plant extracts resulted into the varieties of alkaloids, flavonoids,

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polysaccharides, saponins and terpenoids, and others lead molecules, and have been documented as natural anticancer bioactive products¹¹⁻¹⁵ which inhibits the cell proliferation mainly by inducing apoptosis^{13,16} or autophagy^{17,18} act through regulating immune function, and thus have considerably less side effects as compared to synthetic anticancer drug lead⁶. The reports of novel natural product toxic to various cancer cells are continuously coming¹⁹ resulted into the presence of voluminous biomedical literature, but such novel natural product molecules failed to proceed towards further detailed research or to reach into clinical trial and pharmaceutical drug development and drug approval because of the least or not having the cancer cell specific toxicity²⁰. The compound database provides opportunities for researchers to obtain various information required for the successful identification of pharmaceutically relevant substances²¹. The natural compound online databases like SuperNatural^{22,23} CancerResource^{24,25}, HerbIngredients' Targets²⁶, NPACT⁸, TCMID²⁷, TCMSP²⁸, CancerHSP²⁹, Phytochemica³⁰, NPCARE³¹ or, NPASS³² exists that focuses on plant-based naturally occurring compounds; however,

to our knowledge, online database resources related to cancer specific toxic natural products is lacking. Therefore, to capture the information regarding those plant based anticancer compounds exhibit anticancer activity but not or least toxic to normal cell, we have designed and developed an open access central online resource termed 'Cancer Specific Toxic Natural Products Database' (CSTNPD) currently hosted at http://www.cstnp.co.in.

2. Data Collection

The literature survey using PubMed were made manually in order to collect the natural product that exhibit anticancer activity but not or least toxic to normal cell. Overall, for each and every entry, in addition with submitter information (name of the submitter, affiliation and date), the brief information about the compound, source (novel/literature), reference, reference link and chemical structure of the compound in the form of the image have been curated with a unique ID of CSTNPD under the Tab 'Browse' (Figure 1).



Figure 1. Screenshot of the Cancer Specific Toxic Natural Products Database' (CSTNPD) Web interface.

3. Architecture of the Database and Web Interface

Once we gathered all the information associated to the specific compound we integrate the data in MYSQL, which is freely available open source Relational Database Management System (RDBMS), it functions at the backend. The web interface and the front end were built in PHP, HTML, and Java Script. We have built CSTNPD website on Apache HTPP Server with MYSQL server and PHP, HTML, and Java Script. We have used these Software's or technologies because these all technologies are platform independent and are open source software/technologies.

4. Open Access Submission

The main limitation in development of such databases is that it requires extensive literature search to generate entries and expand the database; therefore, development of such database need global support from the scientific community. Keeping this in mind, CSTNPD also offers an online facility of new submission.

The submitter can make entry of new compound information by filling the entry form. For the new submission, the detailed information of the submitter, Source (novel report by the submitter/literature/other), brief information of the compound, reference, reference link, Structure of the compound in the image form are required. The entries are then added to the database after successful validation.

5. Availability

The 'Cancer Specific Toxic Natural Products Database' (CSTNPD) is currently freely available at http://www. cstnp.co.in. To access the database, the user needs to register through email ID.

6. Discussion

The drugs discovery for any disease is a complex, costly and time taking endeavor. Furthermore, it is well know that only few number of drug candidate undergo for the clinical trial, and then at the last reached to patient after successfully clinical trial. 'In silico' studies such as molecular docking and molecular dynamics simulation are now become the basic component of the drug discovery process for variety of disease including cancer³³. The public and commercial databases storing information on chemical compounds allow scaffolds for the design and development novel drugs²¹. The database like 'CancerResource' (http://bioinformatics. charite.de/care) deals compound-target interaction; mRNA expression and mutation data from cancer genomics experiments²⁵. Herb Ingredients' Targets (http://lifecenter. sgst.cn/hit/) curated herbal ingredients with the information protein target²⁶. The 'SuperNatural' database (http:// bioinformatics.charite.de/supernatural) is a resource contains 3D structures and conformers of about 50,000 natural compounds²². The natural products database 'Super Natural II' (http://bioinformatics.charite.de/supernatural) contains about the corresponding 2d structures, physicochemical properties, predicted toxicity class and information of the potential vendors²³. The 'Naturally Occurring Plant-based Anti-cancer Compound-Activity-Target database' (http:// crdd.osdd.net/raghava/npact/) plant derived natural compounds exhibiting anti-cancerous activity²⁰. The present literature based online freely access database 'CSTNPD' (Cancer Specific Toxic Natural Products Database) contains toxicity information on several of natural product such UttrosideB, Quercetin, 3,5,7,3',5'-pentahydroxy flavanonol-3-O-a-L-rhand 3,5,7-Trihydroxychromone-3-O-a-L-rhamnopyranoside. The compound Uttroside B isolated from the leaves of Solanumnigrum L is cytotoxic to the liver cancer cell line, HepG2 (IC50: 0.5 µM) but nontoxic to normal immortalized hepatocytes³⁴. Quercetin (3,3',4',5,7-pentahydroxy-flavone) (-a flavonoids occurs in fruits and Vegetables), induced cytotoxicity in leukemic cells and in breast cancer cells; however, its cytotoxicity to the normal cells was least or limited³⁵. The compounds 3,5,7,3',5'-pentahydroxyflavanonol-3-O-α-L-rh and 3,5,7-Trihydroxychromone-3-O-a-Lrhamnopyranoside isolated from stem and root of Bauhinia strychnifolia Craib (Fabaceae) shows very potent activity against KB, HT-29, MCF-7 and HeLa cells, but did not show cytotoxicity with normal cells at the concentration of $1 \mu g/mL^{36,37}$.

Moreover, the CSTNPD complements with the other database viz., SuperNatural^{22,23}, CancerResource^{24,25}, Herb Ingredients' Targets²⁶, NPACT²⁰, TCMID²⁷, TCMSP²⁸, CancerHSP²⁹, Phytochemica³⁰, NPCARE³¹ or, NPASS³² in providing the entry of the compounds exhibit anticancer activity but not or least toxic to normal cell, which will be nevertheless facilitate novel anticancer drug discovery, mechanism study, and in the development of in-silico tools and techniques.

7. Conclusions

The compiled database as an open access central resource for cancer specific toxic natural products will provide opportunities for researchers to obtain various information required for the successful identification of pharmaceutically relevant substances for cancer. The bioactive natural products with anticancer therapeutic potential are abundantly reported, but majority of them are toxic to normal cells too; as a result, all those novel natural product molecules failed to proceed towards further detailed research or to reach into clinical trial and pharmaceutical drug development and drug approval.

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9. Disclosure

The authors report no conflicts of interest in this work.

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