

BLACK TURMERIC DATABASE: A DATABASE OF NATURAL COMPOUNDS FROM *CURCUMA CAESIA* ROXB.MUKUNTHAN KS¹, BALAJI B^{2*}, PATEL TN³¹Department of Biotechnology, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, Karnataka, India.²Department of School of Information Sciences, Manipal Academy of Higher Education, Manipal, Karnataka, India. ³Department of Medical Biotechnology, Vellore Institute of Technology, Vellore, Tamil Nadu, India.

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Received: 11 December 2017, Revised and Accepted: 17 January 2018

ABSTRACT

Objective: Most species have their trademark metabolites or a class of chemicals that are generally disseminated inside the genus variety. Secondary metabolites from the black turmeric are predominantly camphor, terpenes, lactones, alkaloids, and phenols classification. A database was constructed with the predicted absorption, distribution, metabolism, elimination, and toxicity, druglikeliness, and physiochemical properties of the exclusive black turmeric 103 compounds.

Methods: The interface has been designed using Microsoft Structured Query Language platform, keeping in mind the ease of use for a researcher. To support this, the entire set of chemicals and their properties was uploaded in database. Database is used as it is very efficient and supports multiple users at the same time.

Results: Black turmeric database gives complete data of compounds by means of 4 segments. Physiochemical, pharmacodynamics, pharmacokinetics, druglikeliness, and molecular information are displayed with chemical structure.

Conclusion: We solidly believe that the information from this database are the sources to infer novel pharmaceutical chemical compounds for medication.

Keywords: Black turmeric, Natural products, Absorption, distribution, metabolism, elimination and toxicity and Microsoft Structured Query Language.

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INTRODUCTION

Nature, the most productive source of chemical and biological qualities is the most encouraging repository of bioactive chemical compounds. Especially, the green source on the earth's surface offers an excellent source for exploration of novel drug molecules. Such new biologically active metabolites give material and key structures to the improvement of new items in chemical, pharmaceutical, food, cosmetic, and agrochemical sectors. Current drug research and development focuses on screening therapeutic compounds from nature for anticancer, antifungal, antitubercular, antiparasitic, antibacterial, and anti-inflammatory as well as other biological activities [1-9]. High throughput screening of plant small chemical molecules for a given drug target can be accomplished, if just the metabolites are accessible in a database [10]. Making a database of metabolite items and imparting it to drug discovery group will comprehend fundamental mechanism of the metabolites and may decrease the timeline in discovery stages of drug [11]. An openly available database that gives exhaustive data about these compounds is consequently useful to the applicable drug discovery groups [12].

Curcuma caesia (black turmeric/black zedoary), an endangering perennial herb of the family *Zingiberaceae*, is indigenous to India. Black turmeric is used as a spice, food preservative, and coloring material commonly in the Indian subcontinent. Black turmeric is the latest in spice family which are chemically being analyzed, with few reports published describing 100 plus secondary metabolites from this plant, and they will remain as a source for new bioactive compounds. This database is centered around biologically active compounds that aim the pharmaceutical market, alongside the physiochemical properties.

Secondary metabolites from black turmeric are predominantly camphor, terpenes, lactones, alkaloids, and phenols classification. Most species have their trademark metabolites or a class of chemicals that are generally disseminated inside the genus variety. The user interface has been designed keeping in mind the ease of the use for a researcher. The database has been designed using Microsoft Structured Query Language (SQL) platform. To support this, we have uploaded the entire set of chemicals and their properties on a database. Database is used as it is very efficient and supports multiple users at the same time. Moreover, the list of chemicals can be added timely. Previously, we have performed screening for plant metabolites from *C. caesia*. By building database, we can encourage the virtual screening process for the lead molecule identification. We decidedly assume that the constituents from this database are the sources to novel pharmaceutical compounds.

METHODS**Data collection**

In this present study, 103 chemical structures of *C. caesia* collected from experiment and literature [13-20] were drawn using ACD/Chemsketch 12 Version (ACD/Labs, 2010). The chemical structures were tested for its absorption, distribution, metabolism, elimination, and toxicity (ADMET) profile and druglikeliness through PreADMET (<http://preadmet.bmdrc.org>) open source tool [21]. Compounds in database are annotated by molecular property. Chemsketch (ACD/Labs, 2010) was employed to calculate physiochemical properties of the two-dimensional (2D) structures. Molecular properties essential for every stage of drug development were predicted using Medchem Designer (MedChem Designer v. 2.0, Simulations Plus, Inc.: Lancaster, CA, USA).

Database implementation

The data were stored in a Microsoft SQL server in a windows operating system. The dataflow is shown in Fig. 1.

Database interface

The database interface is implemented using ASP. This database is searchable by compound numbers from 1 to 103. In a query, a user can specify a number in search field. No wild characters were supported in the search field.

RESULTS

The database is extraordinary in giving complete data of compounds from *C. caesia* by means of 4 noteworthy segments. The main navigation menus of the database are predicted ADMET, druglikeness, physiochemical properties, and molecular properties. The ADMET part of the database section shows the compound's predicted adsorption for human intestinal absorption %, human epithelial colorectal adenocarcinoma cells (Caco-2), Madin-Darby canine kidney cells, distribution for skin, plasma protein binding and blood-brain barrier, metabolism with inhibition and substrate of liver enzymes cytochrome P450 2C19, cytochrome P450 2C9, cytochrome P450 2D6, and cytochrome P450 3A4 inhibition and substrate, mutagenicity (Ames test), and toxicity (mouse and rat). The data encompass qualitative and quantitative data. Druglikeness is then followed with compounds predicted by qualitative data such as lead like rule, rule of five, modern drug data report like rule, World Drug Index like rule, and Comprehensive Medicinal Chemistry like rule.

The physiochemical properties of chemical structure like its name in simplified molecular-input line-entry specification (SMILES), InChI followed by molecular formula, formula weight, composition, molar refractivity, molar volume, parachor, index of refraction, surface tension, density, dielectric constant, polarizability, monoisotopic mass, nominal mass, average mass, M+, M-, [M+H]⁺, [M+H]⁻, [M-H]⁺, and [M-H]⁻. The pre-computed molecular properties such as S+logP, S+logD, MlogP, Mwt, HBDH, MNO, topological polar surface area, and rule of five were predicted using MedChem Designer. Entering the chemical number (1-103) with the search bar and clicking on the tab will display the information about the chemical molecule with the assigned structures. The sample interface is shown in Fig. 2.

DISCUSSION

The chemical information displayed can be utilized for cheminformatics research such as pharmacophore inquiry, molecular docking, and quantitative structure-activity relationship analysis. It also depicts the array of secondary metabolites accessible in *C. caesia* and the need to protect the imperiling plant species. This database will support the identification of new leads for targeting prominent disease-causing proteins. The database also implements the predicted pharmacokinetics information for the chemical features in the compounds. Until date, there is no comprehensive database for the spice. Hence, this database can be utilized as an alternative source of information for new lead candidates. The chemical structures are available from database searching to theoretical chemists for access using their computer. The variations in chemical structures and their properties differ considerably could also help scientist draw parallel conclusions. Using exact match searches, similarity searches, and substructure searches, set of compounds can be eliminated with properties that were considered to be undesirable for drug. The addition of more data on molecular interactions with advanced interactive visualizer, new structure information in protein data bank, MOL, and SMILES format, which can be downloaded for molecular visualization and addition of chemical descriptors, will be done periodically. The purpose of this study is to make the database available on the World Wide Web for free access by researchers interested in the field of cheminformatics.

CONCLUSION

If there is a large and detailed database about the drugability of the *C. caesia* compounds or natural products from different origin,

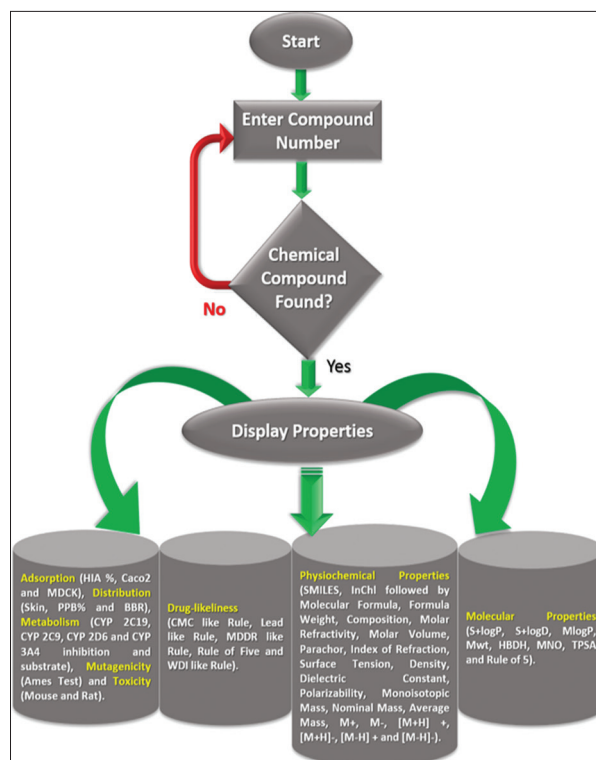


Fig. 1: Dataflow of black turmeric database

Medchem	
S+logP	2.834
S+logD	1.869
MlogP	2.498
MWt	281.441
HBDH	2
MNO	3
TPSA	43.7

Physicochemical Properties		Absorption	
SMILES	CC(CCCCCO)CC2=CC=CC=C(C)C2	Name	Pumiliotoxin
InChI	1.C17H18INO2-4-1487-4-5-10-19(11-15-12-17(2,20)16-8-6-9-18(10)13-15)11,14,16,19-20H,3-10,12-13H2,1-2H3,8-15-11-	HIA%	Good Absorption
Molecular Formula	C17H18INO2	Caco2	Moderate absorption
Formula Weight	281.4354	MDCK	Moderate absorption
Composition	C(72.55%),H(11.10%),N(4.98%),O(11.37%)	Distribution	
Molar Refractivity	83.27 ps 0.4 cm ³	Skin	-1869
Molar Volume	267.2 ps 0.0 cm ³	PPB	Poor
Parachor	688.4 ps 0.0 cm ³	BBR	Good
Index of Refraction	1.555 ps 0.03	Metabolism	
Surface Tension	44.0 ps 5.0 dyn/cm	CYP 2C1	No inhibition
Density	1.05 ps 0.1 g/cm ³	CYP 2D6	No inhibition
Dielectric Constant	Not available	CYP 2C9	Inhibitor
Polarizability	33.01 ps 0.5 10 ⁻²⁴ cm ³	CYP 2D6	Substrate
Monoisotopic Mass	281.235479 Da	CYP3A4	No inhibition
Nominal Mass	281 Da	CYP 3A4	Weakly
Average Mass	281.4355 Da	Toxicity	
M+	281.234931 Da	Ames	Non-Mutagen
M-	281.246028 Da	Mouse	Negative
[M+H] ⁺	282.242756 Da	Rat	Negative
[M+H] ⁻	282.243853 Da	Druglikeness	
[M-H] ⁺	280.227106 Da	CMC like Rule	Qualified
[M-H] ⁻	280.228203 Da	Lead like Rule	Suitable if its binding affinity is greater than 0.1 microM
		MDDR like Rule	Mid-structure
		Rule of Five	Suitable
		WDI like Rule	In 90% cutoff

Fig. 2: Snapshot of black turmeric database

this might encourage researchers to select a more appropriate lead structure for the desired purpose. Hence, a database was developed and will be made available online, where one could quickly find the compounds from the selected spice *C. caesia*. The dataset and web interface will be updated regularly with inclusion of more information on subatomic level interaction, representation devices, and extra chemical descriptors. We also have planned to include datasets of other

black variety crops. Black turmeric database is a platform is publicly available at <http://blackspice.manipal.edu>.

ACKNOWLEDGMENTS

The authors thank Mr. Sathish Kamath M, Asst. Director-IT Information Systems Department, Manipal University, for his support for hosting the website.

CONFLICT OF INTERESTS

We declare that we have no conflict of interest.

AUTHORS CONTRIBUTION

M.K.S. and B.B. carried out the data collection and database construction. P.T.N. encouraged M.K.S. and B.B. to investigate and supervised the project work. M.K.S. and B.B. wrote the manuscript with support from P.T.N.

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