The computationally predicted drug-likeness, pharmacokinetics properties, medicinal chemistry parameters, and toxicity properties of *Cucurbita maxima* compounds. [version 1; peer review: 2 approved]

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Abstract

Natural compounds are increasingly becoming an important source of drug leads for computer-aided drug design approaches. *Cucurbita maxima* has been observed to have medicinal properties and can, therefore, be a potential source of novel drug leads. However, before compounds can be synthesized in the lab for tests, modern approaches require that the candidate compounds be screened for drug-likeness characteristics and toxicity, among others. In this work, the computational tools, SwissADME and DataWarrior were used to screen *C. maxima* compounds for their potential consideration as drug leads. A total of 130 compounds, downloaded from the LOTUS natural products database, were computationally analysed. The data set presented in this work will be useful to researchers searching for novel drug leads based on natural compounds.

Keywords

*Cucurbita maxima*, medicinal plants, druglikeness, natural products, pharmacoinformatics

This article is included in the Cheminformatics gateway.
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Author roles: Shoko R: Conceptualization, Data Curation, Investigation, Methodology, Writing – Original Draft Preparation

Competing interests: No competing interests were disclosed.

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**Introduction**

Natural products (NP), such as plants and their extracts, have been used to cure diseases in humans and livestock since ancient times (Daina et al., 2017; Greenwell & Rahman, 2015). In modern computer-aided drug design approaches, NPs are considered to be a significant foundation for drug discovery due to their diverse chemical components and their often-unique biomedical properties (Süntar, 2020). Among their unique properties, the NPs are often rich in stereogenic centres and occupy portions of the chemical space that is usually not covered by most synthetic drugs (Marxer et al., 2012).

*Cucurbita maxima* (commonly known as giant pumpkin) is rich in phenolics, tannins, flavonoids, alkaloids, saponins, terpenoids, carbohydrates and proteins (Salehi et al., 2019; Sorescu et al., 2020). For centuries, extracts from different parts of the plant have been used to treat various diseases such as intestinal infections, renal failure, hyperplasia, constipation, and parasite infestation (Menendez-Baceta et al., 2014; Kujawska & Pieroni, 2015; Mahomoodally et al., 2016; Mtemeli et al., 2021). Thus, CADD approaches can be applied to investigate the potential of some compounds from this plant to act as drug leads. Before synthesising a compound in the laboratory for testing, modern computational approaches require that the compounds be computationally screened for drug-likeness and potential toxicity.

The standard method to evaluate drug-likeness of a compound is to assess compliance to Lipinski's Rule of Five (Lipinski et al., 1997), which covers the molecular weight, numbers of hydrophilic groups and hydrophobicity. This data note presents a list of *C. maxima* natural compounds and their computationally calculated data on drug-likeness characteristics, pharmacokinetics, medicinal chemistry parameters and predicted toxicity. Toxicity predictions are important because substructures with known toxic, teratogenic or mutagenic properties negatively affects the usefulness of a designed drug. With data produced in this work, researchers can better predict which *C. maxima* compounds have a better chance of succeeding throughout all stages of clinical trials, through to drug approval.

**Materials and methods**

To create a library of *C. maxima* natural compounds, the term 'Cucurbita maxima' was entered into the search box of the Lotus Natural Compounds Database (https://lotus.naturalproducts.net/). The search returned 130 natural products. A file containing the 130 compounds in the structure-data file (SDF) format was downloaded and then fed into BIOVIA Discovery Studio v21.0.20298, RRID:SCR_015651 to get the molecular structures in the corresponding simplified molecular-input line-entry system (SMILE) format. The SMILES were then used to calculate the various properties of the compounds using the SwissADME (Daina et al., 2017) web tool and the DataWarrior v5.5.0 (Sander et al., 2015) software.

**Dataset validation and limitations**

An inherent limitation of computational prediction of drug-likeness is the lack of validated datasets of drugs and non-drugs. Therefore, the classification presented here is solely based on the similarity of structure of the compounds to known drugs. Also compounds from completely new classes are likely to be wrongly classified. Another important limitation of computationally predicted drug-likeness is that it does not predict the biological/pharmacological activity of a compound. Wet bench methods are required to validate the biological/pharmacological activity.

In summary, the dataset presented here will probably be most useful in lead discovery where they could be used for prioritizing compounds for synthesis or for purchasing from external suppliers.

**Data availability**

**Underlying data**

Harvard Dataverse: Underlying data for ‘The Computationally predicted drug-likeness, pharmacokinetics properties, medicinal chemistry parameters, and toxicity properties of Cucurbita maxima compounds’. https://doi.org/10.7910/DVN/4ISBW1 (Shoko, 2022).

This project contains the following underlying data:

- Data file 1. (Druglikeness Properties of C. maxima natural compounds.)
- Data file 2. (Medicinal Chemistry Properties of C. maxima natural compounds.)
- Data file 3. (Pharmacokinetics Properties of C. maxima compounds.)
- Data file 4. (Toxicity Properties of C. maxima compounds.)
Data are available under the terms of the CC0 1.0 Universal (CC0 1.0) Public Domain Dedication.

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This data not summaries the computationally predicted ADME and toxicity parameters of Cucurbita maxima. Author has used SwissADME and DataWarrior tools to generate the database. Introduction is well written but incorporation of some latest references is recommended. At some places, full form of the abbreviations are missing for e.g. CADD. I will suggest to incorporate ADME and toxicity parameters calculated using other tools than SwissADME as well. It will be helpful to understand the variability in the parameters calculated using various tools.

Is the rationale for creating the dataset(s) clearly described?
Yes

Are the protocols appropriate and is the work technically sound?
Yes

Are sufficient details of methods and materials provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Drug Discovery, Medicinal Chemistry, Computer-aided drug design, computational chemistry, RNA biology

I confirm that I have read this submission and believe that I have an appropriate level of
expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 21 February 2024

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Edgar López-López
Department of Chemistry and Graduate Program in Pharmacology, Center for Research and Advanced Studies of the National Polytechnic Institute, Mexico City, Mexico

Dear author,

I consider this "data note" to be interesting and transcendent. This work presents a dataset of properties of pharmaceutical interest of molecules present in Curcubita maxima, which could be of interest to those research groups that plan to isolate, synthesize, or acquire any of these molecules for subsequent trials. However, I consider that some minor comments should be resolved:

1. Introduction section: About the sentence "... occupy portions of the chemical space that is usually not covered by most synthetic drugs". I suggest adding most recent references that support it. I share with you examples that could be useful: (Saldívar-G et al, 2019)[Ref 1], (Sorokina et al, 2021) [Ref 2], (Medina-Franco et al, 2022) [Ref 3], (López-Pérez et al, 2023) [Ref 4]

2. Introduction section: The abbreviation "CADD" could be unclear for "non-expert readers", I suggest adding the explicit significance of this.

3. Please change "SMILE" to "SMILES".

4. I suggest citing this "technology evaluation" article that complements the original Data Warrior reference: (López-López et al, 2019) [Ref 5]

5. Please, add a reference that supports the sentence "Another important limitation of computationally predicted drug-likeness is that it does not predict the biological/pharmacological activity of a compound."

6. Scientific names (e.g. Curcubita maxima) must be written using italic style.

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**Is the rationale for creating the dataset(s) clearly described?**
Yes

**Are the protocols appropriate and is the work technically sound?**
Partly

**Are sufficient details of methods and materials provided to allow replication by others?**
Yes

**Are the datasets clearly presented in a useable and accessible format?**
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Cheminformatics, Natural products, Drug design, Drug development, Computer-aided drug design.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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