

Saudi anti-human cancer plants database (SACPD): A collection of plants with anti-human cancer activities

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Abstract

Several anticancer drugs have been developed from natural products such as plants. Successful experiments in inhibiting the growth of human cancer cell lines using Saudi plants were published over the last three decades. Up to date, there is no Saudi anti-cancer plants database as a comprehensive source for the interesting data generated from these experiments. Therefore, there was a need for creating a database to collect, organize, search and retrieve such data. As a result, the current paper describes the generation of the *Saudi anti-human cancer plants database* (SACPD). The database contains most of the reported information about the naturally growing Saudi anticancer plants. SACPD comprises the scientific and local names of 91 plant species that grow naturally in Saudi Arabia. These species belong to 38 different taxonomic families. In Addition, 18 species that represent 16 family of medicinal plants and are intensively sold in the local markets in Saudi Arabia were added to the database. The website provides interesting details, including plant part containing the anticancer bioactive compounds, plants locations and cancer/cell type against which they exhibit their anti-cancer activity. Our survey revealed that breast, liver and leukemia were the most studied cancer cell lines in Saudi Arabia with percentages of 27%, 19% and 15%, respectively. The current SACPD represents a nucleus around which more development efforts can expand to accommodate all future submissions about new Saudi plant species with anticancer activities. SACPD will provide an excellent starting point for researchers and pharmaceutical companies who are interested in developing new anticancer drugs. SACPD is available online at <https://teeqrani1.wixsite.com/sapd>

Introduction

Cancer is one of the main causes of morbidity and mortality in

both, developed and developing countries. About 8.8 million deaths were reported in 2015 worldwide (World Health Organization). In Saudi Arabia, 15653-cancer incident cases were reported to the Saudi Cancer Registry (SCR) between January 01 and December 31, 2013. A total of 7,359 males (47.0%) and 8,294 females (53.0%) were affected by cancer. Breast cancer was the most common cancer among females whereas colorectal cancer was the most common in males. These figures are frightening and reflect the immediate need for intensive research in order to reduce cancer cases and find effective treatments. As a result, many research institution and funding agencies have been investing heavily in searching for innovative and creative strategies for fighting such serious disease.

A variety of approaches for inhibition the uncontrolled division of cancerous cells has been tested. Examples include surgery, radiation therapy, chemotherapy and immunotherapy. Recently, utilization of plant extracts has been emerged as a promising tool for controlling cancerous cell division. World Health Organization reported that about 80% of Asians and Africans consume plant products as traditional medicines. The products derived from more than 3000 plant species have been used against cancer.¹ Information about these plant species can be found at Dr. Duke's Phytochemical and Ethnobotanical Databases (<https://phytochem.nal.usda.gov/phytochem/search>).

Compared to synthetic anticancer compounds, plant-derived anticancer compounds are considered natural, safer and have less unexpected side effects. As a result, screening plants for new and effective anticancer compounds have attracted many researchers and funding agencies worldwide. The anticancer active compounds in plants are continuously reviewed.²⁻⁵ Various plant species showed their promising and effective role in cancer treatment. Examples include; extracts from *Podophyllum peltatum* against lung and testicular cancer,⁶ compounds isolated from *Curcuma longa* against cancer growth in several organs such as skin and colon,⁷ betulin and betulinic acid from *Ziziphus nummularia*,⁸ andrographolide compound from *Andrographis paniculata* against several kinds of cancer including leukemia, breast and colon.⁹ More recently, additional lists of anticancer medicinal plant species have been reported. Examples include *Cephalotaxus harringtonia*,¹⁰ *Euphorbia peplus*,¹¹ *Phyllanthus emblica*,¹² *Euphorbia hirta*,¹³ *Aristolochia bracteolata*,¹⁴ *Cichorium intybus*¹⁵ and *Euphorbia condylocarpa*.¹⁶ Interestingly, it has been reported that the combined application of plant-derived anticancer compounds and synthetic anticancer drugs can significantly improve the efficacy of chemotherapy.¹⁷

In Saudi Arabia, a large number of reports about the anticancer activities of many various extracts of different plants from different taxonomic groups has been published in national and international journals. Unfortunately such data are scattered and may be hard to find either because the absence of a recent and a comprehensive review of the subject or due to the nature of the journals in which the data were published. As a result, the use of such important data for more beneficial downstream applications has been limited. Therefore, the aim of this study was to build a database for Saudi

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anti-human cancer plants. The database provides important information about the number of the most studied anticancer plants and the type of human cancer cell lines that showed growth inhibited in response to these plants. Up to our knowledge, the SACPD database is the first database that covers details about Saudi anti-human cancer plants. The Saudi Herbal Plant Information System (SHPIS) is the only online database that gives a description of several herbal plants found in Saudi Arabia. These herbal plants used traditionally as a cure for many diseases excluding cancer.

Research methods

A systematic review was performed using Google Scholar web search engine. Keywords used for this search were 'Saudi', 'medicinal plants', 'cancer', 'cytotoxicity'. 100 pages and 2360 results were reviewed. The Google Scholar search engine was selected for its ability to search the full text of articles. The other search engines such as PubMed and Web of Science are limited to abstract searching. Species and family name's spelling were checked using <http://www.ipni.org> website.

The database was designed and created by the author. The website is hosted by Wix.com, a cloud-based web development platform.

Results and Discussion

Database architecture and implementation

The home page of the database provides a list of Saudi anticancer plants. The list contains the basic information such as plant's scientific and local name, plant's part, location, cell line type and references. Each reference was uploaded as a pdf file attached to the list. Users can search for a specific plant's name using the search box. The plants were alphabetically indexed based on species names. Another list of traditional medicinal plants that are commonly sold in the local markets in Saudi Arabia was created into a separate page. This list contains the basic information about medicinal plants, which are available commercially, and has its possible anticancer activities. The SACPD database allows users to add new submissions of new Saudi anticancer plants using an online submission

box or by a direct electronic mail contact. Statistics of some extracted information of the search were also provided.

Analysis of SACPD data

The database consists of two lists of anticancer plants. The first list provides users with information about Saudi anti-human cancer plants that grow naturally in Saudi Arabia. The second list provides information about traditional medicinal plants with potential anticancer activities. Traditionally, these medicinal plants have been used for decades as a treatment of several diseases, including cancer and can be found in the Saudi local markets.

Anticancer plants found naturally in Saudi Arabia

In the first list, data revealed that 91 species belonging to 38 families (Figure 1) of Saudi plants showed significant anticancer activities against human cell lines. Figure 1 shows that Asteraceae, Apocynaceae, Fabaceae, Boraginaceae and Brassicaceae were the most studied Saudi anticancer plant families with percentages of 25, 10, 7, 3 and 3 respectively. *Rhazya stricta* was reported four times as a Saudi anti-human cancer plant.¹⁸⁻²¹ More details regarding *Rhazya stricta* can be found in the SACPD database. Internationally, *Rhazya stricta* from different countries showed an inhibition effect against human cancer cells. Several studies described anticancer activities of *Rhazya stricta*.^{22,23} A review prepared by²⁴ presents more information about the medicinal importance of *Rhazya stricta*. Table 1²⁵⁻⁴⁷ shows the plant species which were studied by two or more researchers. *Achillea fragrantissima* and *Artemisia sieberi* were reported three times, by three different articles for their anticancer effect. *Caralluma quadrangular*, *Citrullus colocynthis*, *Haplophyllum tuberculatum*, *Lactuca serriola*, *Pulicaria crispera*, *Rosa damascena trigintipetala*, *Rumex vesicarius*, *Santolina chamaecyparissus*, *Solanum glabratum*, *Verbesina encelioides* were reported twice by two different articles for each plant (All references are available on the database).

Breast cancer was the most studied cancer cell lines among others with a percentage of 27%. This was not surprising as breast cancer is the most common cancer among females as mentioned previously. Similarly, breast cancer is considered as the most common cancer in women worldwide, according to World Cancer Research Fund International. Figure 2 shows the percentages of all cancer cell lines indicated in the SACPD database.

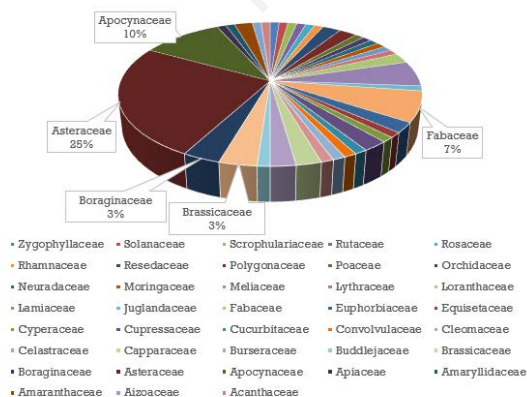


Figure 1. A pie chart of Saudi anticancer plant families as indicated in the SACPD database.

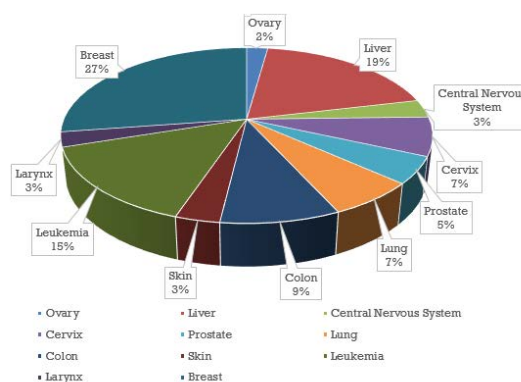


Figure 2. A pie chart of the most studied cancer cell lines as appeared in the SACPD database.

Anticancer plants sold in markets in Saudi Arabia

In the second list, data showed that 18 species of 16 families were investigated for their possible anticancer activities. The plant families of Apiaceae and Moringaceae were the most studied ones. Among all the species (Table 2),⁴⁸⁻⁶⁰ *Nigella sativa* was reported five times for its ability to inhibit five cancer cell lines, mostly breast (MCF7). Several *in vitro* and *in vivo* studies were conducted on *Nigella sativa* and reported its medical importance as an anti-cancer agent. A review by²⁵ investigated experimental results related to the capability of *N. sativa* in inhibition of cancer. The medical significance of this plant is derived from its intensive use in traditional medicine, which may be rooted back to the prophetic medicine (Ibn Maa'jah 3457; Shaykh Al-Albaani). Chemical anal-

ysis of different organs of the plants revealed the presence of many biologically active compounds such as anthranoids, hydroxyanthracene glycosides. Similarly, *Nigella sativa* also contains compounds of anticancer activities against most kinds of cancer.²⁶ It contains the thymoquinone (a strong antioxidant) and its derivatives such as thymohydroquinone, dithymoquinone, and thymol,²⁷ antimutagenic and anticarcinogenic.^{26,28,29} The seeds also contain α -hederin, which has strong activity against tumour.³⁰

Limitations and future development

Two limitations appeared during the preparation of this sys-

Table 1. Saudi anti-human cancer plants reported by two or more researchers.

Plant	Part	Cancer/Cells	Reference
<i>Achillea fragrantissima</i>	Leaves, flowers	Liver (HEPG2)	(31)
<i>Achillea fragrantissima</i>	Leaves	Leukemia (K562 and Jurkat)	(32)
<i>Achillea fragrantissima</i>	Aerial parts	Leukemia (CCRF-CEM and HL-60)	(19)
<i>Artemisia sieberi</i>	Leaves, flowers	Breast (MCF7)	(31)
<i>Artemisia sieberi</i>	Leaves	Breast (MCF7) Cervix (HeLa)	(33)
<i>Artemisia sieberi</i>	Aerial parts	Liver (HEPG2)	(34)
<i>Caralluma quadrangula</i>	Aerial parts	Breast (MCF7)	(35)
<i>Caralluma quadrangula</i>	Aerial parts	Breast (MCF7)	(36)
<i>Citrullus colocynthis</i>	Fruit	Larynx (HEp2)	(37)
<i>Citrullus colocynthis</i>	Aerial parts	Leukemia (CCRF-CEM and HL-60)	(19)
<i>Haplophyllum tuberculatum</i>	Aerial parts	Leukemia (CCRF-CEM and HL-60)	(19)
<i>Haplophyllum tuberculatum</i>	Not specified	Skin - Melanoma	(38)
<i>Lactuca serriola</i>	Aerial parts	Breast (MCF7) Liver (HEPG2) Lung (A549)	(39)
<i>Lactuca serriola</i>	Aerial parts	Liver (HEPG2)	(40)
<i>Pulicaria crispa</i>	Shoot system	Breast (MCF7) Liver (HEPG2)	(31)
<i>Pulicaria crispa</i>	Aerial parts	Leukemia (CCRF-CEM and HL-60)	(19)
<i>Rhazya stricta</i>	Aerial parts	Leukemia (CCRF-CEM and HL-60)	(19)
<i>Rhazya stricta</i>	Not specified	Breast (MCF7 and MDA-MB-231)	(18)
<i>Rhazya stricta</i>	Leaves	Colon (CACO) Liver (HEPG2)	(41)
<i>Rhazya stricta</i>	Stems	Stem Cell (NT2)	(21)
<i>Rosa damascena trigintipetala</i>	Roses	Liver (HEPG2)	(42)
<i>Rosa damascena trigintipetala</i>	Roses	Liver (HEPG2) Breast (MCF7)	(43)
<i>Rumex vesicarius</i>	Aerial parts	Leukemia (CCRF-CEM and HL-60)	(19)
<i>Rumex vesicarius</i>	Flowers	Breast (MCF7) Lung (NCI-H460) Central Nervous System (SF-268)	(44)
<i>Santolina chamaecyparissus</i>	Aerial parts	Liver (HEPG2)	(45)
<i>Santolina chamaecyparissus</i>	Aerial parts	Liver (HEPG2)	(40)
<i>Withania somnifera</i>	Fruits	Breast (MCF7) Liver (HEPG2) Colon (Colo20 and HCT-116) Leukemia (Jurkat)	(46)
<i>Withania somnifera</i>	Leaves	Breast (MCF7) Liver (HEPG2) Colon (HCT-116)	(47)

Table 2. Traditional medicinal plants sold in the local markets in Saudi Arabia and reported by two or more researchers.

Plant	Part	Cancer/Cells	Reference
<i>Lepidium sativum</i>	Garden Cress	Breast (MCF7)	(48)
<i>Lepidium sativum</i>	Garden Cress	Breast (MCF7)	(49)
<i>Nigella sativa</i>	Black Seed	Breast (MCF7) Liver (HEPG2)	(50)
<i>Nigella sativa</i>	Black Seed	Retina (911)	(52)
<i>Nigella sativa</i>	Black Seed	Cervix (Siha and C33A)	(53)
<i>Nigella sativa</i>	Black Seed	Lung (A549)	(54)
<i>Nigella sativa</i>	Black Seed	Breast (MCF7)	(55)
<i>Petroselinum sativum</i>	Parsley	Breast (MCF7)	(56)
<i>Petroselinum sativum</i>	Parsley	Liver (HEPG2)	(57)
<i>Trigonella foenum graecum</i>	Fenugreek	Breast (MCF7) Larynx (HEp2) Cervix (WISH)	(51)
<i>Trigonella foenum graecum</i>	Fenugreek	Breast (MCF7)	(58)
<i>Zingiber officinale</i>	Ginger	Breast (MCF7)	(59)
<i>Zingiber officinale</i>	Ginger	Colon (HCT-116)	(60)

tematic review. First, many articles related to Saudi anticancer plants were not available because of copyright issues. Second, it is expected that search engines have a limited capability of covering all the key words used or the search and some data will be missing. In order to fill these two gaps, the SACPD database provides a submission box and a direct contact for adding new or missing data. Furthermore, a regular search for Saudi anti-human cancer plants will be done to ensure that the database is updated. Despite these limitations, the total number of plant species indicated by the database was 109. It is a satisfied starting point for researchers to investigate the current list's plants or deciding to study other plants that were not mentioned in the database.

Conclusions

According to the Food and Drug Administration (FDA), there are five steps of the drug development process. First, a discovery of promising drugs by laboratory work. Second, preclinical research includes testing the cytotoxicity of these drugs on animals (*in vivo*) or on cell lines (*in vitro*). Third, clinical research in which drugs are tested on people. Fourth, FDA review for making a decision to approve the drug. Fifth, FDA Post-Market Safety Monitoring. In this study, most of the reviewed articles gave general information about the cytotoxicity of the plant extracts without identification and characterization of the active compounds behind the anticancer activity of these extracts. Testing these promising Saudi plants-derived anticancer compounds on animals and people is still the missing step noticed in most of the reviewed articles. It is the pharmaceutical companies' mission to take an action towards further studying and developing of these possible drugs. SACPD database collected all promising Saudi anticancer plants into one place. This will save time, effort and money for research centres and pharmaceutical companies who are interested in developing new drugs in the field of natural anticancer products.

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