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COLLECTION AND DATA-MINING OF BIOACTIVE COMPOUNDS WITH CANCER TREATMENT PROPERTIES IN THE PLANTS OF FABACEAE FAMILY

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Key words:

Medicinal Plants, Phytochemical Compound, Anticancer, Antitumor and Cancer Preventive Activities.

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ABSTRACT: Medicinal plants therapeutic agents are a big source of information for a wide variety of chemical constituents which could be developed as new drugs. The present study focused on anticancer, antitumor anticarcinogenic and cancer preventive activities of bioactive compounds found in plants belonging to Fabaceae family. The bioactive compounds and their scientific details were mining from publically available phytochemical databases (Dr. Duke's phytochemistry and ethnobotanical database and USDA phytochemical database). Fabaceae family is one of the largest family which includes 18,860 plant species, of them, 12 plant species were identified to posses 106 bioactive compounds related to cancer treatment. The plant species such as *Acacia nilotica, Arachis hypogaea, Cajanus cajan, Crotalaria juncea, Glycine max, Mimosa pudica, Pisum sativum, Psoralea esculenta, Tamarindus indica, Trifolium pratense, Trigonella foenum-graecum* and *Vigna subterranean* possess bioactive compounds leading to cancer treatment. The important and mostly studied phytochemical compounds are Beta carotene, Alpha tocopherol, Alanine, Genestein, Caffeic acid, Tannin, Alpha carotene, Ascorbic acid, Limonene, Daidzein, Rutin and Niacin.

INTRODUCTION: Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. It has become a big threat to human beings globally. The high mortality rate among cancer patients is an indication of the limited efficiency of the current therapies including radiation therapy, chemotherapy, immunotherapy and surgery.

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In recent years, focus on plant research by scientists and pharmacologists has increased all over the world and a large body of evidence has been accumulated to highlight the immense potential of medicinal plants used in various traditional systems of medicine [1, 2, 3]. Plants-derived compounds such as Beta carotene, Alpha-tocopherol, Alanine, fibre, Caffeic acid, Tannin, Kaempferol, Ascorbic acid, Limonene, Daidzein, Rutin, and niacin have played an important role in the development of several clinically useful anticancer agents [4]. Despite this encouraging preamble and the abundant literature describing the molecular mechanisms triggered by phytochemicals to inhibit cell growth and induce apoptosis in cancer cells, only a few of them entered clinical trials. So, the present study focuses

on bioactive compounds found in the Fabaceae family which leads to cancer treatment. Further, the present study will explain the putative mechanism(s) of action of largely studied phytoresources from *in vitro* and i*n vivo* studies, and the current status of their clinical applications in view of their realistic adoption as single chemotherapeutic agents or as chemosensitizers, in association with canonical and novel anticancer drugs.

MATERIALS AND METHODS:

Data-mining of bioactive phytochemicals:

In the present study, the bioactive phytochemicals which are having potential of cancer treatment and cancer prevention were manually mining from publically available phytochemical databases (Dr. Duke's phytochemistry and ethnobotanical database (www.ars-grin.gov/duke).

Collection and mining of literatures of bioactive compounds as therapeutic agents:

The literatures related to anticancer, antitumor cancer preventive activities of phytoresources were collected from publically available online sources. The full texts of peer-reviewed scientific publications in a variety of journal were manually mining from the online sources such as Google scholar (http://scholar.google.co.in/) and pubmed (http://www.ncbi.nlm.nih.gov/pubmed). The said journal was selected to capture the greatest quantity of high-quality data in a cost, and time-effective manner. From each publication, details of the compounds tested, the assays performed and any target information for these assays were abstracted.

RESULTS AND DISCUSSION:

In Fabaceae family, there are 12 plant species were identified as lead for cancer drugs. They are such as *Acacia nilotica, Arachis hypogaea, Cajanus cajan, Crotalaria juncea, Glycine max, Mimosa pudica, Pisum sativum, Psoralea esculenta, Tamarindus indica, Trifolium pratense, Trigonella foenum graecum* and *Vigna subterranea*. These plant species possessed 106 bioactive compounds related to anticancer, antitumor anticarcinogenic and cancer preventive agents. Among these phytochemical compounds, 23 phytochemical compounds were found to be possess anticancer activity, 49 phytochemical compounds possess antitumor activity, 15 phytochemical compounds possess Anticarcinogenic activity and 79 phytochemical compounds possess cancer preventive activity (**Table 1**).

TABLE 1: LIST OF PHYTOCHEMICAL COMPOUNDS PRESENT IN 12 PLANT SPECIES AND THEIR ANTICANCER, ANTITUMOR ANTICARCINOGENIC AND CANCER PREVENTIVE ACTIVITIES

S. No	Anticancer activity	Antitumor activity	Anticarcinogenic activity	Cancer preventive activity
1	Alpha carotene	Alpha-amyrin	(+) Catechin	(+) Catechin
2	Alpha-terpineol	Alpha-tocopherol	Ascorbic acid	4-hydroxycinnamic acid
3	Alpha-tocopherol	Beta-carotene	Biochannin a	5-hydroxytryptamine
4	Beta-carotene	Betulin	Caffeic acid	Alanine
5	Caffeic acid	Caffeic acid	Chlorogenic acid	Alpha linoleic acid
6	Chlorophyll	Canavanine	Cis-aconitic acid	Alpha-tocopherol
7	Daidzein	Carpaine	Ellagic acid	Arachidonic acid
8	Elemene	Chlorogenic acid	Ferulic acid	Ascorbic acid
9	Gallic acid	Chlorogenic acid	Fiber	Beta sitosterol
10	Gamma tocopherol	Citric acid	Luteolin	Beta-carotene
11	Gossypol	Coumarine	Mucilage	Biochannin a
12	Inositol-hexaphosphate	Cysteine	Oleic acid	Caffeic acid
13	Isoquercitrin	Delta-tocopherol	Phloroglucinol	Chlorogenic acid
14	Kaempferol	Dioscin	Quercetin	Chlorophyll
15	Lectin	Ellagic acid	Riboflavin	Chrysoeriol
16	Lignin	Ergosterol		Cinnamaldehyde
17	Limonene	Erucic-acid		Coumarine
18	Naringenin	Eugenol		Cysteine
19	Phytic acid	Ferulic acid		Daidzein
20	Rutin	Fiber		Daidzin
21	Tannin	Fumaric acid		Delphinidin
22	Vanillic acid	Gallic acid		Ellagic acid

23	Vicenin 2	Gamma tocopherol		Esculetin
24		Geraniol		Ferulic acid
25		Gossypol		Fiber
26		Hydroquinone		Formononetin
27		Isoliquiritigenin		Gallic acid
28		Isoquercitrin		Genisteine
29		Kaempferol		Geraniol
30		Lignin		Glutathione
31		Limonene		Glycine
32		Lupeol		Glycitein
33		Luteolin		Indole - 3 acetic acid
34		Malic acid		Isochlorogenic acid
35		Naringenin		Isoliquiritigenin
36		P-Coumaric acid		Isoquercitrin
37		Phytic acid		Isorhamnetin
38		Quercetin		Isovitexin
39		Quercitrin		Kaempferol
40		Rutin		Limonene
41		Salicyclic acid		Linoleic acid
42		Selenium		Luteolin
43		Senecionine		Methionine
44		Seneciphylline		Methyl salicylate
45		Squalene		Mucilage
46		Tannin		Mufa
47		Tigogenin		Myricetin
48		Tocopherol		Myristic acid
49		Vanillic acid		Naringenin
50				Niacin
51				Nicotinamide
52				Oleic acid
53				Orientin
54				P cresol
55				P hydroxyl benzoic acid
56				Pantothenic acid
57				P-Coumaric acid
58				Pectin
59				Pelargonidin
60				Phenol
61				Phloroglucinol
62				Phytic acid
63				Quercetin
64				Quercitrin
65				Riboflavin
66				Rutin
67				Safrole
68				Salicyclic acid
69				Selenium
70				Serine
71				Sinapic acid
72				Squalene
73				Stigmasterol
74				Tannin
75				Tocopherol
76				Tyrosine
77				Vanillic acid
78				Vitexin
79				Vitexin – 2 O rhamnoside
Total	23	49	15	79

1. *Acacia nilotica* L:

Acacia nilotica is a large tree which is commonly called as Babul. In this plant, totally 19 cancer treatment bioactive compounds were identified in different parts (**Table 3**). Among them, 5 (26.32%) phytochemical compounds possessed anticancer activity, 13 (68.42%) phytochemical compounds possess antitumor activity, 10 (52.63%) phytochemical compound possess anticarcinogenic activity and 14 (73.68%) compounds possess cancer preventive activity.

Besides, 5 phytochemical compounds possess 3 combined activities such as anticancer, antitumor and cancer preventive activities or antitumor anticarcinogenic and cancer preventive activities. Similarly, 3 phytochemical compounds possess two activities such as cancer preventive and antitumor activities and Lignin have anticancer and antitumor activities (**Table 2** and **Fig. 1**). The anticancer activity of this plant was studied by using various models by several authors. Gamma-sitosterol of *A. nilotica* exhibited potential anticancer activity through the growth inhibition, cell cycle arrest and the apoptosis on MCF-7 and A549 cells [5]. The aerial parts of methanolic extract of Acacia nilotica have anticancer activity against Dalton's ascetic lymphoma induced solid and ascetic tumor model [6].

TABLE 2: PHYTORESOURCES HAVING ANTICANCER, ANTITUMOR ANTICARCINOGENIC, AND CANCER PREVENTIVE ACTIVITIES

S. No	Plant Species Name	Anticancer activity		Antitumor activity		Anticarcinogenic activity		Cancer preventive activity		Total
		No of Compounds	%	No of Compounds	%	No of Compounds	%	No of Compounds	%	
1	*Acacia nilotica*	5	26.32	13	68.42	10	52.63	14	73.68	19
2	*Arachis hypogaea*	8	21.62	15	40.54	3	8.11	35	94.59	37
3	*Cajanus cajan*	1	5.26	4	21.05	-	-	17	89.47	19
4	*Crotalaria juncea*	-	-	3	60	-	-	3	60	5
5	*Glycine max*	16	25.39	33	52.38	4	6.35	49	77.78	63
6	*Mimosa pudica*	2	25	3	37.5	-	-	8	100	8
7	*Pisum sativum*	5	11.36	17	38.64	2	4.54	39	88.63	44
8	*Psoralea esculenta*	1	12.5	1	12.5	-	-	7	87.5	8
9	*Tamarindus indica*	4	14.81	7	25.93	-	-	24	88.89	27
10	*Trifolium pratense*	4	15.38	10	38.46	2	7.69	25	96.15	26
11	*Trigonella foenum graecum*	6	20.69	13	44.83	1	3.45	23	79.31	29
12	*Vigna subterranea*	1	20	1	20	-	-	4	80	5

2. *Arachis hypogaea L:*

Arachis hypogaea is commonly known as ground nut. It is an annual herbaceous plant. It has totally 37 phytochemical compounds in different parts such as leaf and seed (**Table 3**). Among them, 8 (21.62%) phytochemical compounds possess anticancer activity, 15 (40.54%) compounds possess antitumor activity, 3 (8.11%) compounds possess anticarcinogenic activity and 35 (94.59%) compounds possess cancer preventive activity. Besides, 5 compounds were identified to possess 3 activities such as anticancer, antitumor and cancer preventive activities in each of 5 compounds. Compounds like Chlorogenic acid and Ferulic acid possessed antitumor anticarcinogenic and cancer preventive activities (**Table 2** and **Fig. 1**). Alike, some other 5 phytochemical compounds possess antitumor and cancer preventive activities. Resveratrol isolated from *A. hypogaea* exhibited anticancer activity against mouse xenograft models of human neuroblastoma and human colorectal cancer cells [7].

3. *Cajanus cajan L:*

Cajanus cajan is commonly called Pigeon pea. It is a perennial shrub. There were 19 phytochemical compounds reported to have the ability of cancer treatment (**Table 3**). They found in leaf, fruit and

seed of this plant. Among them, 89.47% (17) of compounds were reported that they possess cancer preventive activity. Four (21.05%) of them were reported as antitumor agents (**Table 2** and **Fig. 1**). Apart from, Beta carotene is a single compound that possesses 3 activities such as anticancer, antitumor and cancer preventive activities. Root of *Cajanus cajan* plant arrested the cell cycle in the G2/m phase and induced apoptosis via a relative oxygen species (ROS) mediated mitochondria-dependent pathway [8].

4. *Crotalaria juncea L:*

Crotalaria juncea is commonly called as Sun hemp. It is an herb. It has 5 cancer treatment compounds (**Table 3).** It includes 3 antitumour and 2 cancer preventive chemical compounds (**Table 2** and **Fig.1**). Leaf extracts of *C. juncea* exhibited anticancer activity on human cervical cancer cell line. It might be due to the presence of the bioactive compounds [9].

5. *Glycine max L:*

Glycine max is commonly called Soyabean. It is a bushy herbaceous plant. Among the 12 plant species under study, *G. max* plant possesses 63 cancer treatment compounds (**Table 3**). Interestingly, 49 compounds were reported as cancer preventive agents. Similarly, 33, 16 and 4 compounds were used as antitumour, anticancer and anticarcinogenic drugs respectively. Some bioactive compounds found in this plant exhibited two or more activities (**Table 2** and **Fig.1).** For example, Caffeic acid possesses 4 activities *viz.*, anticancer, antitumor anticarcinogenic and cancer preventive activities. Bioactive compound aglycones isolated from ethylacetate extract of fermented *G. max* have antiproliferation activity against osteoblast cell line [10].

6. *Mimosa pudica L:*

Mimosa pudica is a pantropical weed which is commonly called as sensitive plant. It is a creeping annual or perennial herb. It contains eight phytochemical compounds with cancer treatment property. All these compounds possess cancer preventive activities. Among them, 3 were antitumour and 2 were anticancer agents (**Table 2** & 3 and **Fig.1**). Flavanoids isolated from *M. pudica* has the high cytotoxic effect against MCF-7 human breast cancer cell line [11]. ITME (2011) reported that isolated 6 -glycosylflavone from *Mimosa pudica* possesses antitumor and antiproliferation activity on MCF-7 breast cancer cell line [12]. The pure compound L-Mimosine and hydroalcoholic extract of *Mimosa pudica* has antiproliferation activity on Lymphoma Daudi cells [13]. The methanolic extract of *M. pudica* aerial part had cytotoxic activity [14].

7. *Pisum sativum L*:

Pisum sativum is commonly called as Pea. It is an herbaceous plant. Root, fruit and seed of *P. sativum* has 44 phytochemical compounds with cancer treatment properties (**Table 3).** Among them, 39 compounds, 17 compounds, 5 compounds, and 2 compounds were reported as cancer preventive, antitumour, anticancer and anticarcinogenic agents (**Table 2** and **Fig. 1**). Methanolic extract of *P. sativum* showed anticancer activity against CaSki cells with IC_{50} value of 14.8 [15]. Asperagenase enzyme isolated from *P. sativum* has a cytotoxic effect against L20B Tumor cell line [16].

8. Psoralea esculenta L:

Psoralea esculenta is commonly called Indian turnip. It is an herbaceous perennial plant. It has 8 phytochemical compounds with cancer treatment properties (**Table 3**). Beta carotene possesses anticancer activity and other 7 compounds of this plant possess cancer preventive activity. Although, this plant bears bioactive phytochemicals with anticancer, antitumor anticarcinogenic and cancer preventive activities compounds, there was no scientific reports available regarding its cancer treatment property.

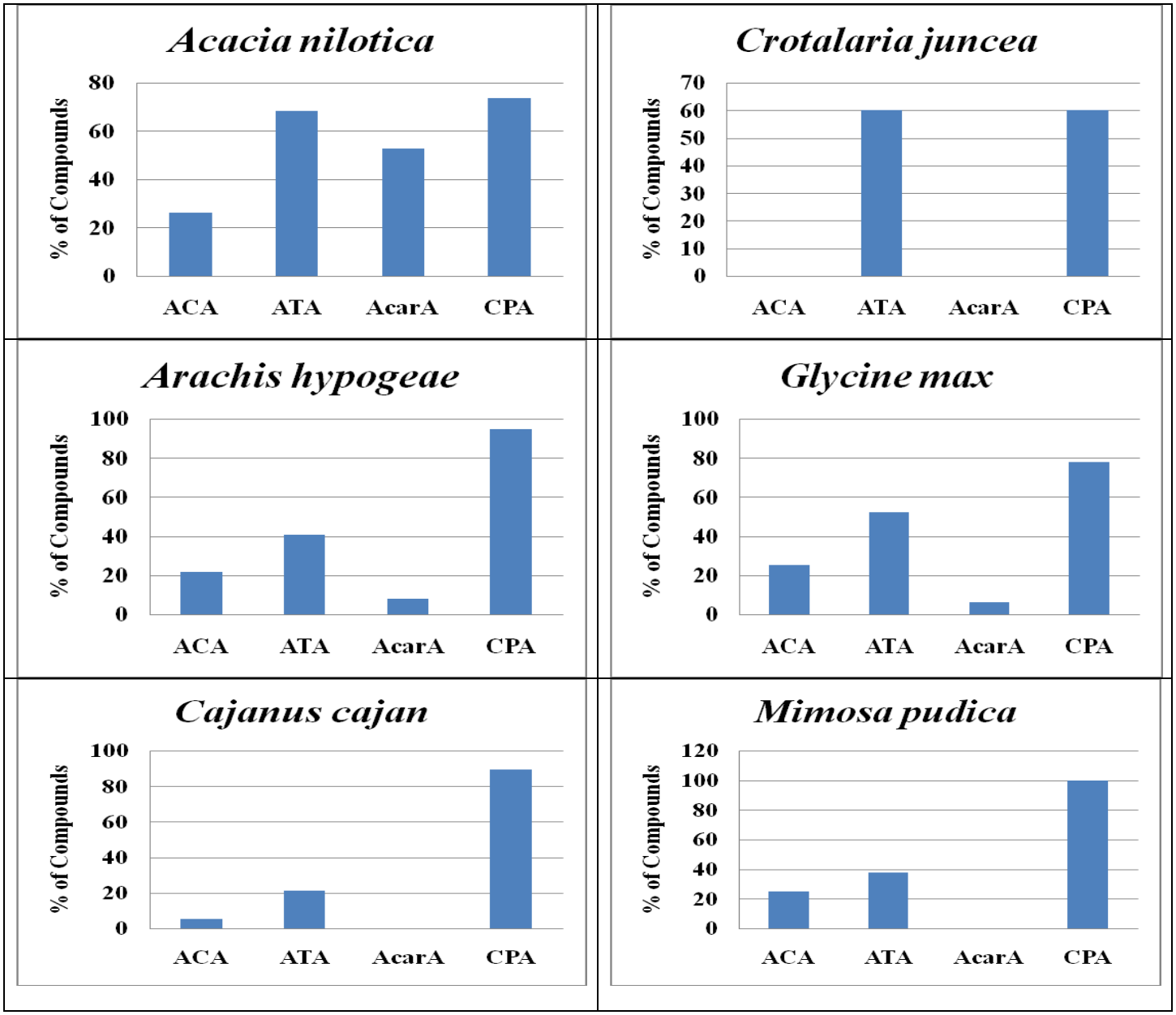
9. *Tamarindus indica L:*

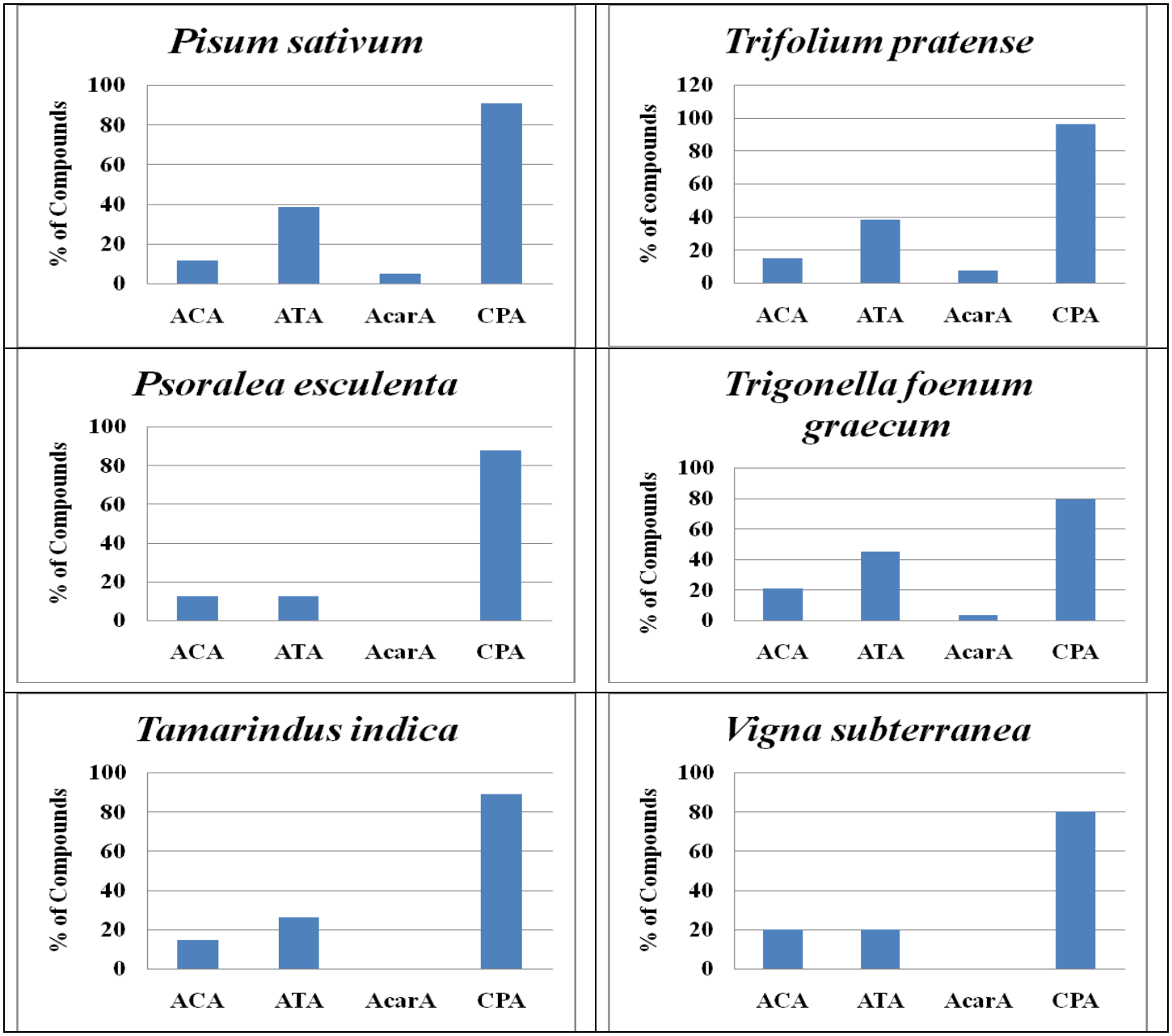
Tamarindus indica is commonly called Tamarind. It is a leguminous tree. It contains 27 phytochemical compounds in different parts like leaf, fruit, flower, and seed (**Table 3**). Among them, 4 (14.81%) phytochemical compounds possess anticancer activity, 7 (25.93%) phytochemical compounds possess antitumor activity, and 24 (88.89%) phytochemical compounds possess cancer preventive activity (**Table 2** and **Fig. 1).** Limonene and tannin have anticancer, antitumor and cancer preventive

activities, geraniol possesses antitumor and cancer preventive activities. PST001 isolated from the *T. indica* could suppress DLA and EAC cell growth and reduce the cell survival by reducing apoptosis of tumor cells [17]. Polyphenolic compounds (2-hydroxy-dihydroxyaceophenone, (-) epicatechin, tannin, anthocyanidine and oligomeric proanthocyanidins) isolated from *T. indica* seeds have cancer related signal pathway blockage effect [18].

10. *Trifolium pratense L:*

Trifolium pratense is commonly called Red Clover or Cow Grass. It is a perennial sometimes biennial herb. It has 26 phytochemical compounds with cancer treatment properties and they were found in different parts like leaf, seed, flower, inflorescence, shoot, and stem (**Table 3**). Twenty five compounds of this plant possess cancer preventive activity and 10 possess antitumor activities (**Table 2** and **Fig. 1**). Alpha tocopherol and beta carotene of this plant have anticancer, antitumor and cancer preventive activities. Chlorogenic acid possess antitumor anticarcinogenic and cancer preventive activities. Biochannin-a isolated from *T. pratense* inhibited carcinogen activity in hamster embryo cell culture [19].





ACA: Anticancer Activity; **ATA**: Antitumor Activity; **ACAR A:** Anticarcinogenic Activity; **CPA:** Cancer Preventive Activity

FIG. 1: PHYTORESOURCES HAVING ANTICANCER, ANTITUMOR ANTICARCINOGENIC, AND CANCER PREVENTIVE ACTIVITIES

TABLE 3: PERCENT DISTRIBUTION OF CANCER TREATMENT PHYTOCHEMICAL COMPOUNDS IN 12 PLANT SPECIES OF FAMILY FABACEAE

S. No	Plant Species name	Total No of Compounds	Percentage (%)
1	*A. nilotica*	19	17.92
2	*Arachis hypogaea*	37	34.90
3	*Cajanus cajan*	19	17.92
4	*Crotalaria juncea*	5	4.72
5	*Glycine max*	63	59.43
6	*Mimosa pudica*	8	7.55
7	*Pisum sativum*	44	41.51
8	*Psoralea esculenta*	8	7.55
9	*Tamarindus indica*	27	25.47
10	*Trifolium pratense*	26	24.52
11	*Trigonella foenum graecum*	29	27.35
12	*Vigna subterranea*	5	4.72

11. *Trigonella foenum-graecum L.:*

Trigonella foenum-graecum is commonly called Fenugreek. It is an annual herb. It contains 29 bioactive compounds with cancer treatment properties (**Table 3**). Six compounds of this plant possess anticancer activity, 13 possess antitumor activity and 23 phytochemical compounds of it possess cancer preventive activities. Lignin possesses 3 activities such as antitumor anticarcinogenic and cancer preventive activities. Fenugreek (*T. foenum graecum*) extracts exhibited cytotoxic effect on many type of cancers [20].

12. *Vigna subterranea L.:*

Vigna subterranea commonly called Ground Bean. It is an annual, creeping lugume with glabrous, trifoliate leaves. It has 5 phytochemical compounds with anticancer activities (**Table 3).** *V. subterranean* showed preventive effect on lung cancer and liver cancer induced by morphine and sodium nitrite [21]. Several animal studies of chemical induced carcinogenesis demonstrated that phytochemicals are able to inhibit cancer development (pre-initiation) and also able to cure cancer [22, 23, 24]. Due to the variety of their physiological roles in plant tissues in regulating enzymes involved in cell metabolism and in mechanisms of defence against foreign agents (radiations, viruses, parasites), phytochemicals have been associated to pleiotropic effects in animal cells. Phytochemicals attracted scientists' interests since the demonstration that their biological targets in mammalian cells were the same involved in inflammatory processes and oncogenic transformation, such alterations of cell cycle control, apoptosis evasion, angiogenesis and metastases.

In addition, a large number of epidemiological studies suggested that a daily intake of phytochemicals can reduce the incidence of several types of cancers [25].

CONCLUSION: In the present study, the anticancer activities of a group of phytochemicals representing good candidates for chemopreventive and chemotherapeutic applications have been reviewed. They have been selected from the available literatures. All compounds given in this paper are commonly found in the edible plants. They are cultivated by the farmers and some them naturally grow. All of them are available in the Indian vegetative environment. Well documented the presence of anticancer activities of these plants was supported by various experimental models, namely cell cultures and animal models of induced carcinogenicity. These molecules are largely cited in the current literatures and their activities are often associated with the term chemoprevention. The results of the present study may provide a foundation for designing new drug to ascertain the full chemopreventive and chemotherapeutic efficacy of phytochemicals.

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