



ISSN (E): 2277- 7695

ISSN (P): 2349-8242

NAAS Rating: 5.03

TPI 2020; 9(8): 52-60

© 2020 TPI

www.thepharmajournal.com

Received: 28-05-2020

Accepted: 25-07-2020

Rani Sebastian

Assistant Professor, College of
Pharmaceutical Sciences,
Government Medical College
Kottayam, Tamil Nadu, India

Dr. B Jaykar

Principal, Vinayaka Mission's
College of Pharmacy, Salem,
Tamil Nadu, India

Dr. V Gomathi

Professor, Vinayaka Mission's
College of Pharmacy, Salem,
Tamil Nadu, India

Current status of anticancer research in fabaceae family

Rani Sebastian, Dr. B Jaykar and Dr. V Gomathi

Abstract

Cancer is a general term used for a large group of diseases, whose causes, characteristics and occurrence can vary greatly. Treatment of cancer is almost successful with chemotherapeutic agents but different treatment modalities have severe side effects. Plants possess many phytochemicals and these phytochemicals have a significant role in the prevention and treatment of cancer. The family Fabaceae includes a number of important agriculture and food plants. Traditionally the herbs of Fabaceae family have been used in the treatment of a number of diseases. Various phytochemicals present in Fabaceae family includes isoflavones, lectins, saponins and phenolic compounds. These phytochemicals act as antioxidants and can be used in the treatment and prevention of various oxidative stress diseases like cancer and cardiovascular problems. This review emphasizes on various plants present in Fabaceae family and their anticancer potential.

Keywords: Fabaceae, anticancer potential, isoflavones, phenolic compounds, apoptosis

Introduction

Cancer is one of the most life-threatening diseases and possess many health hazards in both developed and developing countries, characterized by irregular proliferation of cells [1]. Many biological changes can be seen when a normal cell progresses to cancerous one. Smoking, dietary imbalances, hormones and chronic infections leading to chronic inflammation accounts high casuals for cancer disease. Even though many treatments are available for cancer therapy still cancer is the 2nd leading cause of death in the globe. There are different treatment modalities for cancer like surgery, radiotherapy, immunotherapy, chemotherapy and stem cell transplantation. Treatment of Cancer is somewhat successful with chemo preventive agents but these treatment modalities are often accompanied by severe side effects [2,3]. In view of serious side effects of chemotherapy and radiation treatment for cancer, there should be immediate search for alternative and safer methods of treatment [4].

Use of phytochemicals in cancer therapy

Medicinal herbs serve as nature's gift to humans to help them pursue better health. Plants and their phytoconstituents are in medicinal practices since ancient times. The search for cancer drugs from natural sources started with discovery of Podophyllotoxin in late 1960s, further lead to discoveries of vincristine, vinblastine, camptothecin and taxol. Several medicinal plant species and their phytochemicals inhibit the progression and development of cancer [5]. It has been researched that plant kingdom comprised of approximately 250 000 plant species and only around 10% have been studied for treatment of different diseases. Phytochemicals and their derived analogues are present in different parts of the plant, e.g., flower, flower stigmas, pericarp, sprouts, fruits, seeds, roots, rhizomes, stem, leaf, embryo, bark and perform several pharmacological functions. Several plant products such as alkaloids, flavonoids, lignans, saponins, terpenes, taxanes, vitamins, minerals, glycosides, gums, oils, biomolecules and other primary and secondary metabolites play significant roles in either inhibiting cancer cell activating proteins, enzymes and signalling pathways or by activating DNA repair mechanism or by inducing antioxidant action. Thus, these Phyto molecules exhibit strong anticancer effects in terms of their efficacy on the above-mentioned proteins, enzymes and signalling pathways [6,7].

Steps involved in anticancer drug development from medicinal plants

The ability of medicinal herbs as therapeutic agents depends upon the quality and quantity of active phytochemicals in them, which vary with age, climate and season from species to species.

Corresponding Author:

Rani Sebastian

Assistant Professor, College of
Pharmaceutical Sciences,
Government Medical College
Kottayam, Tamil Nadu, India

Pharmacological functions and their level vary with plant parts. These bioactive Phyto molecules can also be used in anticancer therapeutics, but they still demand further research. The purification of active Phyto molecules may involve various strategies such as combinatorial chemistry, isolation assays, and bioassay-guided fractionation. Bioassay guided fractionation with various analytical techniques could be used to separate various bioactive compounds from the mixture of compounds. The process begins with the natural extracts test (from dry/wet plant material) with confirmed biological activity. Then, suitable matrices are used for the fractionation of active extracts, tested for bioactivity and various analytical techniques such as TLC, HPLC, FTIR, Mass spectroscopy

and NMR *etc.* must be used for the separation of active fractions. For separation different solvents should be used. Superdex, Silica or any other suitable matrix can be used for fractionation. There are so many dyeing agents used for the detection of natural compounds in medicinal plants. After purification of these Phyto molecules they must be examined for *in-vitro* or *in-vivo* anticancer effects. If a better anticancer property is achieved by the molecule then other aspects like pharmacokinetics, pharmacodynamics, immunogenicity, metabolic fate, biosafety, side effects, drug interactions and dose determination must be researched for future drug designing. Detailed scheme for anticancer drug development from plants is shown in Figure 1 [8].

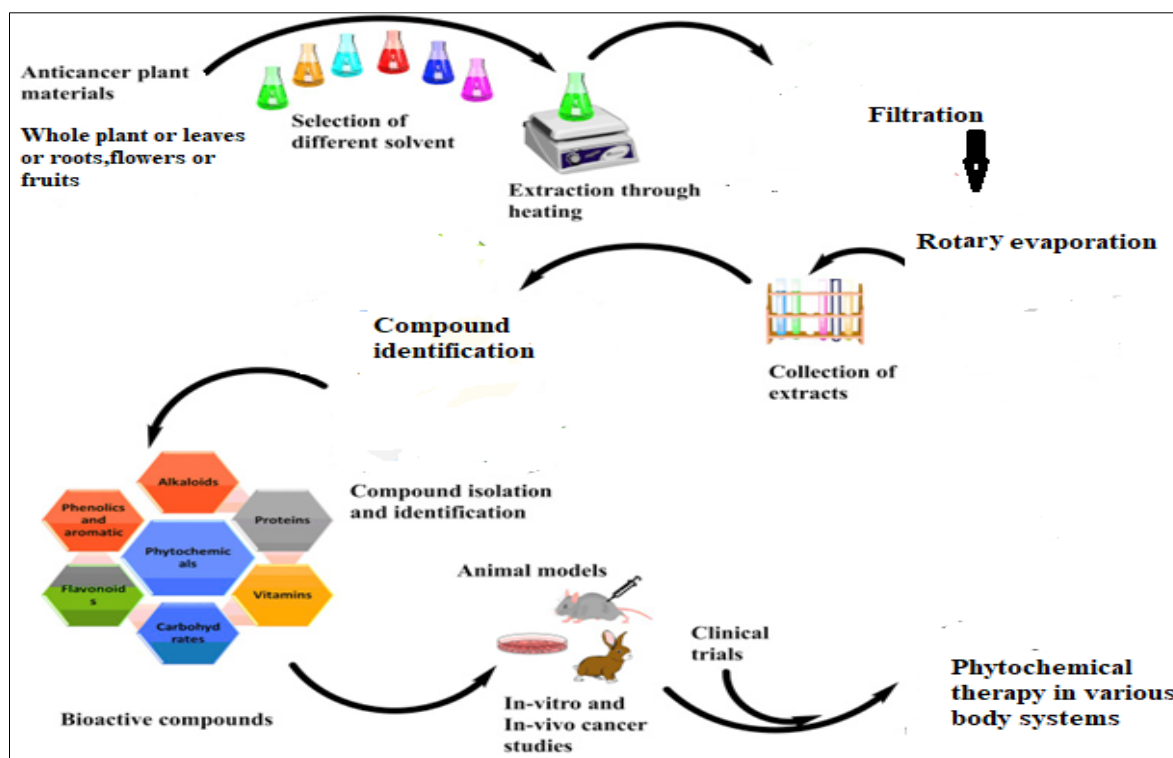


Fig 1: Scheme for development of plant derived anticancer agent.

Medicinal plants have a pivotal role in the expansion of modern medicine and continue to be widely used in their native form. The anticancer characteristics of a number of plants are still being actively researched and some have shown promising results. Indian herbs belonging to apocyanaceae, asteraceae, solanaceae, fabaceae and zingiberaceae family are rich in anticancer principles. This review article gives a detailed study of plants belongs to Fabaceae family which contains anticancer principles.

Fabaceae family

The Fabaceae or Leguminosae, commonly known as the legume, pea, or bean family, are a large and economically important family of flowering plants. It includes trees, shrubs, and perennial or annual herbaceous plants, which are easily recognized by their fruit (legume) and their compound, stipulate leaves. Many legumes have characteristic flowers and fruits. The family is widely distributed, and is the third-largest land plant family in number of species, behind only the Orchidaceae and Asteraceae, with about 751 genera and about 19,000 known species [9].

Some of the most important commercial species include soybeans (*Glycine max*), garden peas (*Pisum sativum*),

lentils (*Lens culinaris*), and chick pea (*Cicer arietinum*) [9]. The nutritional values of legume are low fat, high protein, dietary fibre, and various micronutrients and phytochemical substances which exhibit the medicinal properties, especially anticancer property [10].

Phytochemicals from Fabaceae family

Several studies found that a diet high in whole grains including legumes may reduce the risk of cancer such as breast cancer, colorectal cancer and endometrial cancer. Various phytoconstituents in legumes have been reported their anticancer activities.

Isoflavones

The most abundant isoflavones in the legume sprouts were found as genistein followed by daidzein. Studied are conducted on the growth inhibitory properties of isoflavones extract of legume sprout from India on breast cancer MCF-7 and reported that isoflavones worked as phytoestrogens and could inhibit tumorigenesis both *in vitro* and *in vivo* studies. Their mechanisms were DNA repair, induction of apoptosis, cell proliferation, migration, and invasion.

Lectins

There are the most abundant lectin proteins in several legume tree barks, and they have great potential as antitumor and anticancer properties. Several studies have suggested the cytotoxicity or tumour inhibition mechanisms of lectins to various tumour cell lines such as skin, liver, bile duct, and bone cell lines [10].

Saponins

A number of legumes contain saponins such as soybean, chickpea, peanut, and lentil, which have reported to exhibit anticancer activities. Several studies suggest that legume saponins may possess anticancer activities in melanoma cell, colon cancer, and cervical cancer. The mechanism of suppressing the metastatic of cancer was by using

sialyltransferase inhibition activity of saponin on the cell surface. The other mechanism was saponin regulation of the apoptosis pathway enzymes, leading to programmed cell death of cancer cells.

Phenolic compounds

It has been recognized that phenolic compounds act as antioxidants and were found high amount in peas. There is a direct link between association of antioxidant properties of plant phenolic compounds and their effects in the prevention of various oxidative stress diseases like cancer or cardiovascular diseases [11].

Plants belonging to Fabaceae family which contains anticancer principles

| Plant name | Part used | Phytochemicals | Specific cancer suppressed | Literature cited |
|--------------------------------------|-----------|--|--|------------------|
| <i>Vigna unguiculata</i> | Seeds | Trypsin chymotrypsin inhibitor | Human breast cancer invitro | 12 |
| <i>Vicia faba</i> | seeds | Field beans protease inhibitor | Skin cancer (invitro and <i>in vivo</i>) | 13 |
| Glycine max | seeds | Bowman – birk inhibitors | Colorectal, prostate and colon cancer | 14 |
| <i>Bauhinia variegata</i> | Flower | Kaempferol galactoside | Breast, lung and liver cancer | 15 |
| <i>Cicer arietinum</i> | seeds | Bowman - Birk type protease | Breast and prostate cancer | 16 |
| <i>Enterolobium contortisiliquum</i> | Seeds | <i>Enterolobium contortisiliquum</i> trypsin inhibitor | Gastric and breast cancer (Both <i>in vitro</i> and <i>in vivo</i>) | 17 |
| <i>Lens culinaris</i> | seeds | Lentil (<i>Lens culinaris</i> trypsin inhibitor) | Human colon cancer (Both <i>in vitro</i> and <i>in vivo</i>) | 18 |
| <i>Pisum sativum</i> | pea | Protease inhibitors, rTI1B, rTI2B | Human colorectal and colon cancer (<i>In vitro</i>) | 19 |
| <i>Phaseolus vulgaris</i> | seeds | Tepary bean protease inhibitor | Leukaemia L1210 and lymphoma MBL2 (<i>In vitro</i>) | 20 |
| <i>Butea monosperma</i> | flower | Butrin, (7,3',4'-trihydroxyflavanone-7,3'-diglucoside) | Liver cancer (<i>In vitro</i> and <i>in vivo</i>) | 21 |

Vigna unguiculata

Genus: *Vigna*

Species: *Unguiculata*



Common names [22]

Cowpea, Vellapayar

Phytoconstituents

Many Phyto -constituents were identified from different parts of *Vigna unguiculata*. The whole leaves and seeds have been reported to contain secondary metabolites like flavonoids, alkaloids, tannins, sterols, reducing sugar, terpenoids and phenolic acids, such as p-hydroxybenzoic acid, protocatechuic acid, 2,4-dimethoxybenzoic acid, and cinnamic acid derivatives, such as p-coumaric acid, caffeic acid, cinnamic acid and ferulic acid. *Vigna unguiculata* was considered as a suitable source for production of L - asparaginase [23].

Anticancer activity

L-asparaginase is used to treat acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML), and non-Hodgkin's lymphoma. It is given by injection into a vein, muscle, or under the skin. The rationale behind asparaginase is that it takes advantage of the fact that acute lymphoblastic leukaemia cells and some other suspected tumour cells are unable to synthesize the non-essential amino acid asparagine, whereas normal cells are able to make their own asparagine; thus leukemic cells require high amount of asparagine. These leukemic cells depend on circulating asparagine. Asparaginase, however, catalyses the conversion of L-asparagine to aspartic acid and ammonia. This deprives the leukemic cell of circulating asparagine, which leads to cell death [24].

Moharib *et al.* (2018) evaluated Cytotoxic activity of L-asparaginase *in vitro* using four carcinoma cell lines. L-asparaginase was highly effective in growth inhibition against HEPG2 and HCT-116 but lower against HELA and MCF7 carcinoma cell lines. The data show that L-asparaginase has a higher cytotoxic activity against HEPG2 and HCT116, revealed higher percentage of cell death, indicating antitumor properties, and demonstrate direct effect on cancer cell proliferation of HEPG2 and HCT116. Therefore, *Vigna unguiculata* was considered to be a suitable source for production of L-asparaginase. Purified L-asparaginase obtained from *Vigna unguiculata* could be employed in drug chemotherapy and treatment of cancer [25].

Vicia fabaGenus: *Vicia*Species: *Vicia faba***Common names**Broadbean, fava-bean, horse bean ²⁶**Phytoconstituents**

The protein content of Faba bean seeds ranges from 200 g·kg⁻¹ to 410 g·kg⁻¹, which depends on the variety. Faba bean seeds contain 510 g·kg⁻¹ to 680 g·kg⁻¹ of carbohydrates in total, the major proportion of which is constituted by starch (410–530 g·kg⁻¹). Lipids are contained at 12–40 g·kg⁻¹. Dietary fibre ranges between 150 g·kg⁻¹ and 300 g·kg⁻¹, which depends on the seed variety, hemicellulose being the major component. Micronutrients include vitamin C, Folate, carotenoids, tocopherols and poly phenols etc. Flavonoid compounds found in Faba beans, include flavanol monomers (such as gallic acid, epigallocatechin and catechin), proanthocyanidins, flavanols (glycosylated derivatives of myricetin, quercetin and kaempferol), flavanonols, isoflavones (genistein and daidzein) and flavanones. Moreover, other phenolic compounds were found in Faba beans, including phenolic acids (caffeic acid, ferulic acid, p-coumaric acid and syringic acid) ^[27].

Anticancer activity

Protease inhibitors are now treated as very important signalling molecules in many biological activities such as inflammation, apoptosis, blood clotting and hormone processing. In recent years, PIs have been examined extensively as therapeutic agents, primarily to deal with various human cancers. Among all types of PIs, Bowman-Birk inhibitors (BBI) have been studied extensively in the treatment of many diseases, especially in the field of cancer prevention. So far, crops such as beans, potatoes, barley, squash, millet, wheat, buckwheat, groundnut, chickpea, pigeon pea, corn, and pineapple have been identified as good sources of PIs ^[28].

Fernandes and Banerji (1995) tested the ability of the Faba bean protease inhibitor (FBPI), when administered by gavage, to subdue benzopyrene (BP)-induced neoplasia of the forestomach of mice.

Skin carcinogenesis can be effectively suppressed by topical treatment with a FBPI as reported by Fernandes and Banerji (1996) and plasmin inhibitory activity of FBPI can help to stop pulmonary metastasis of B16F10 melanoma cells systemically injected into BDF1 mice. Banerji *et al.* (1998) investigated the ability of FBPI to stop ethyl nitroso urea (ENU)-induced tumours of the nervous system of Sprague-Dawley rats ^[29].

Glycine maxGenus: *Glycine*Species: *Glycine max***Common name**Soya bean ^[30]**Phytoconstituents**

Soybean contains 35–40% protein and roughly 19% oil. Triglycerides are the major component in the oil. Soy oil is characterized by relatively large amounts of the polyunsaturated fatty acids (PUFA) i.e., 55% linoleic acid (essential fatty acid) and 8% α -linolenic acid. The oil also contains saturated fatty acid - Palmitic acid, Stearic acid and unsaturated fatty acid - Oleic acid. Soybean oil also contains tocopherols, which are excellent natural antioxidants. Soybean oil contains α -tocopherol, β -tocopherol, γ -tocopherol, and δ -tocopherol in trace amount (mg/kg). Soybean oil contains about 300 to 400 mg of plant sterols per 100 g. Soybean oil contains 1–3% phospholipids. Soybean is a better source of B-vitamins compared to cereals, although it lacks B12 and vitamin C. The soybean is most abundant source of isoflavones (up to 3 mg/g dry weight) in the nature. Soybean contains three types of isoflavone aglycone viz., daidzein, genistein and glycitein. Soybean also contains 2% soy saponins (triterpene glycosides) ^[31].

Anticancer activity

One protease inhibitor, the soybean-derived Bowman-Birk inhibitor (BBI) is particularly effective in suppressing carcinogenesis. BBI is a protein of a molecular weight of 8000 with a well-characterized ability to inhibit trypsin and chymotrypsin. BBI has been extensively studied, both as purified BBI and as an extract of soybeans enriched in BBI called BBI concentrate (BBIC). Purified BBI and BBIC have comparable suppressive effects on the carcinogenic process in a variety of *in vivo* and *in vitro* systems. BBI appears to be a universal cancer preventive agent. Purified BBI and BBIC suppress carcinogenesis in several organ systems and tissue types [eg. colon, liver, lung, oesophagus, cheek pouch (oral epithelium), and cells of hematopoietic origin] and in cells of epithelial and connective tissue origin. BBIC is a promising cancer chemo preventive agent in humans. It is believed that BBIC will be able to prevent human cancer without toxicity ^[32, 33].

Bauhinia variegataGenus: *Bauhinia*Species: *Bauhinia variegata*

**Common name**

Orchid tree, mountain ebony ^[34]

Phytoconstituents

Different extracts of *Bauhinia variegata* contains tannins, phenolic compounds, phytosterols, triterpenoids, saponins, alkaloids and flavonoids ^[34].

The chemical constituents isolated so far from the plant are β -sitosterol, kaempferol-3-glucoside, quercetin, rutin, quercitrin, apigenin, apigenin-7-O-glucoside, heptatriacontan-12, 13-diol and dotetracontan-15-en-9-ol ^[35].

Anticancer activity

Kaempferol represents one of the most encountered aglycone flavonoids in the form of glycoside. It is a tetrahydroxy flavone which contains four hydroxy groups and it is a yellow compound. Kaempferol is found in various plant parts, such as seeds, leaves, fruits, flowers, and even vegetables ^[36].

Kaempferol is a natural flavanol, a class of flavonoid, found in many fruits, vegetables and herbs, including grapes, tomatoes, broccoli, tea, and ginkgo biloba leaves. This biologically active compound exhibits many pharmacological activities including antioxidant, anti-inflammatory, antimicrobial, antidiabetic, and anticancer activities ^[37].

The anticancer activity of kaempferol has been reported in cancer cells from different organs including breast, ovarian, gastric, lung, pancreatic cancer, and blood cancers. Kaempferol interferes with many signalling pathways required for the survival of cancer cells. In breast cancer cells, kaempferol induces apoptosis through an extracellular signal regulated kinase (ERK) dependent mechanism. Kaempferol can also induce apoptosis in breast and ovarian cancer cells through activation of p53 and suppression of cell cycle genes. In addition to decreasing ERK activity, kaempferol also increases ROS production in human glioma cells leading to induction of apoptosis. Glioblastoma cells were also rendered more sensitive to doxorubicin upon cotreatment with kaempferol. Similarly, kaempferol increases sensitivity of glioma cell to TRAIL (TNF related apoptosis inducing ligand)-induced apoptosis through reduction of Akt activity and survivin protein. Kaempferol was shown to be as potent as 5-FU in promoting apoptosis in pancreatic cancer cells, and when combined with 5-FU, has an additive effect on cell death. Kaempferol as a phytoestrogen has been studied as potential targets for hormone-dependent cancers such as breast and prostate. However, kaempferol was effective in both hormone dependent and independent breast and prostate cancers ^[15].

Sonam Pandey *et al.* (2017) evaluated the antitumor potential of *Bauhinia variegata* against B16F10 melanoma tumour model in C57BL mice. The *B. variegata* leaf, stem bark and flower extracts were studied on the inhibition of B16F10

melanoma tumour bearing mice. The activity of *B. variegata* was found in following order floral bud > leaf extract > stem bark extract. The antitumor activity of *B. variegata* in mice may be attributed to the presence of polar phytoconstituents such as alkaloids, flavonoids, tannins, terpenoids, and glycosides present in the crude extract of *B. variegata*. The hydro methanolic extract of *B. variegata* was found to be an effective and potent antitumor agent against human melanoma so it may provide a drug of preference to the world ^[38].

Cicer arietinum

Genus: Cicer

Species: Cicer arietinum

Common name

Bengal gram, Chickpea ^[39]

**Chemical constituents**

The preliminary phytochemical screening of *Cicer arietinum* seeds revealed the presence of carbohydrates, proteins, amino acids, fixed oils, phytosterols, alkaloids, Phenolic compounds, tannins, flavonoids, glycosides and saponins ^[40].

Anticancer effect

Cytotoxic activity of C-25 protein isolated from *Cicer arietinum* was studied on oral cancer cells and normal cells. It reduced the cell proliferation of human oral carcinoma cells with IC₅₀ of 37.5 μ g/ml and no toxic effect was found on normal human peripheral blood mononuclear cells even at higher concentration of 600 μ g/ml.

Results of the cytotoxicity evaluation of isoflavones isolated from *Cicer arietinum* against MCF-7 breast cancer cell line showed a dose dependent inhibition of cell growth.

Protease inhibitor concentrates (PICs) were isolated from various leguminous sources (including soybean) and characterized. The effects of PICs on the proliferation of breast and prostate cancer cells were investigated *in vitro*. Chickpea PIC significantly inhibited the viability of MDA-MB-231 breast cancer and PC-3 and LNCaP prostate cancer cells at all concentrations ^[41, 16].

Enterolobium contortisiliquum**Common name**

Ear pod Tree ^[42].

Genus: Enterolobium

Species: E. contortisiliquum



Phytoconstituents

Phytochemical screening of *E. contortisiliquum* pericarps revealed the presence of various classes of biologically active compounds (saponins, triterpenes and/ or sterols, fatty acids, carbohydrates, proteins and phenolic compounds). Among them α -amyrin (31.75%), 4-methyl-2,6-di-tert-butylphenol (21.55%) and β -amyrin (10.19%) represented as predominant compounds. The saturated and unsaturated fatty acids represented 43.10 % & 56.90 % respectively, where palmitic acid constitute 23.68% and linoleic acid constitute 53.80% of total identified fatty acids.

Sixteen amino acids have been identified in protein fraction (PF). One bisdesmosidic and two monodesmosidic triterpene saponins of acacic acid were identified by ESI-MS for the first time. Gallic, protocatechuic, syringic, p-coumaric acids, pyrogallol, quercetin-7-O-rutinoside, catechin, isovitexin and quercetin were isolated from phenolic fraction [43].

Anticancer activity

Enterolobium contortisiliquum trypsin inhibitor (EcTI), showed no effect on the proliferation of gastric cancer cells or fibroblasts but inhibited the adhesion, migration, and cell invasion of gastric cancer cells; however, EcTI had no effect upon the adhesion of fibroblasts. EcTI was shown to decrease the expression and disrupt the cellular organization of molecules involved in the formation and maturation of invadopodia, such as integrin β 1, cortactin, neuronal Wiskott-Aldrich syndrome protein, membrane type 1 metalloprotease, and metalloproteinase-2. Moreover, gastric cancer cells treated with EcTI presented a significant decrease in intracellular phosphorylated Src and focal adhesion kinase, integrin-dependent cell signalling components. Together, these results indicate that EcTI inhibits the invasion of gastric cancer cells through alterations in integrin-dependent cell signalling pathways [43].

Lens culinaris

Genus: *Lens*

Species: *Lens culinaris*

Common name

Lentil [43]



Phytoconstituents

Lentils contain a plethora of bioactive phytochemicals such as extractable and insoluble-bound phenolics, carotenoids, tocopherols, saponins, phytic acid, and phytosterols. The major phenolic compounds found in lentils include subclasses of phenolic acids, flavan-3-ols, condensed tannins (proanthocyanidins), anthocyanidins, flavanols, stilbenes, flavones, and flavanones. Lentil was reported to have the highest total phenolic content (TPC) of 7.53 mg gallic acid equivalents (GAE)/g dry weight (DW) among 8 different types and varieties of pulses, as well as 2.21 mg catechin equivalents (CE)/g DW of total flavonoids content. Phytosterols, primarily β -sitosterol, campesterol, and stigmasterol, are integral natural components of plant cell membranes. Carotenoids and tocopherols are well-known lipophilic antioxidants that are synthesized in whole or part from the plasmid isoprenoids [44].

Anticancer activity

The recombinant BBI proteins derived from *Lens culinaris* proved to be active against trypsin and chymotrypsin. The effects of mature BBI on the growth of human colon adenocarcinoma HT29 and colonic fibroblast CCD-18 Co cells were evaluated. Lentil BBI was able to inhibit the growth of such cells at concentrations higher than 19 μ M, in a concentration-dependent manner; by contrast, the CCD18-Co cells were unaffected [18].

Pisum sativum

Genus: *Pisum*

Species: *P. sativum*



Common name

Pea

Phytoconstituents

The active phytochemical substances of *P. sativum* are asparaginase, flavonoids including apigenin, daidzein, genistein, and kaempferol, phenolic compounds including caffeic, catechin, coumaric acids, gentisic acids, ferulic, protocatechuic, and vanillic acids, pisatin and an allelopathic active substances, proanthocyanidin, saponins, and steroid phytohormone including brassinosteroid and tannins [10].

Anticancer activity

The extracts of *P. sativum* have been investigated and found to be pharmacologically active in inducing anticancer activity. Clemente *et al* compared the effect of Bowman-Birk trypsin-chymotrypsin inhibitor, a potential cancer chemo preventive agent, with the protease inhibitors, rT11B and rT12B, from *P.*

sativum seed. They studied the inhibitory activities on the growth of human colorectal adenocarcinoma HT-29. El-Aassar *et al* studied the *P. sativum* extracted lectins from Egypt and these lectins exhibited antiproliferative property to liver cancer cell line. Patel *et al* extracted lectin from leaves and buds of *P. sativum* from Saudi Arabia and studied cytotoxicity to many cancer cell lines such as MCF-7 (breast), HepG-2 (liver), HEP-2 (larynx), and HCT-116 (colon). Recently, Stanisavljevic *et al.* identified the number of phenolic compounds from pea seeds in different colours from Croatia. They reported the darker seed colour, the higher total phenolic content in the form of gallic acid, epigallocatechin, naringenin, and apigenin. The seed extracts also showed the cytotoxic effects on malignant cell lines, for example, LS174 (colon), MDA-MB-453 (breast), A594 (lung), and K562 (blood). In several review articles have mentioned the health benefits of *P. sativum* due to its concentration and properties of starch, protein, fibre, vitamins, minerals, and phytochemicals [10].

Phaseolus vulgaris

Genus: Phaseolus
Species: *P. vulgaris*



Common name

Common bean [45]

Phytoconstituents

Common beans (*Phaseolus vulgaris*) seeds have some bioactive components related with health benefits, such as alkaloids, anthocyanin, carbohydrate, catechin, fibres, flavonoids, phasine, phytic acid, quercetin, saponins, steroids, tannins and terpenoids and trypsin inhibitors [46].

Anticancer activity

Two trypsin inhibitors with molecular weight of 16 kDa were isolated from white cloud beans by Sun *et al* (2010). The inhibitors inhibited trypsin with an IC₅₀ of approximately 0.6µM. The inhibitor was devoid of inhibitory activity toward fungal growth, proliferation of lymphoma MBL2 cells and HIV -1 reverse transcriptase, But exerted activity toward L1210 leukemia cells [47].

Butea monosperma

Genus: Butea

Species: *B. monosperma*



Common names

Flame-of-the-forest, bastard teak, free fire.

Phytoconstituents

Flower: Triterpene, butein, butin, isobutrin, coreopsin, isocoreopsin (butin 7-glucoside), sulphurein, monospermoside (butein 3-β-D-glucoside) and isomonospermoside, chalcones, aurones, flavonoids (palasitrin, prunetin) and steroids.

Gum: Tannins, mucilaginous material, pyro catechin.

Seed: Oil (yellow, tasteless), proteolytic and lipolytic enzymes, plant proteinase and polypeptidase. (Similar to yeast trypsin). A nitrogenous acidic compound, along with palasonin is present in seeds. It also contains monospermoside (butein 3-β-D-glucoside) and isomonospermoside. From seed coat allophanic acid has been isolated and identified.

Bark: Kino-tannic acid, Gallic acid, pyrocatechin. The plant also contains palasitrin, and major glycosides as butrin, alanind, allophanic acid, butolic acid, cyanidin, histidine, lupenone, lupeol, (-)-medicarpin, miroestrol, palasimide and shellolic acid.

Stem: 3-α-hydroxyeuph-25-ene and 2,14-dihydroxy-11,12dimethyl-8-oxo-octadec-11-enylcyclohexane.

Stigmasterol-β-D-glucopyranoside and nonacosanoic acid [48].

Anticancer activity

Extracts of *B. monosperma* flowers exhibit potential anticancer activity due to its flavonoids such as butin, butein, butrin, isobutrin, palasitrin, coreopsin, isocoreopsin, sulphurein, monospermoside and isomonospermoside. The novel glucoside isocoreopsin of *Butea monosperma* showed a better free radical scavenging and anticancer activity.

Kamble (2015) *et al.* evaluated anticancer activity of hydroalcoholic flower extract of *Butea monosperma*. To determine *in-vitro* anticancer activity, different concentrations of crude extract were tested on MCF-7 breast cancer cell line by 3-(4,5-dimethyl thiazole-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The extract showed significant antiproliferative activity and a dose-dependent effect [49].

Banu Rekha J and Jayakar B (2011) evaluated ethanolic extract of leaves of *Butea monosperma* (Lam) Taub for its anticancer activity against Ehrlich Ascites Carcinoma (EAC) in Swiss albino mice. The anticancer activity of *Butea monosperma* (Lam) Taub was examined by determining the tumour volume, tumour cell count, viable tumour cell count, non-viable tumour cell count, mean survival time and increase in life span in experimental animal models. Ethanolic extract of *Butea monosperma* (Lam) Taub increased the life span of EAC treated mice and restored the haematological parameters as compared with the EAC bearing mice [50].

Boopathi *et al.* isolated three bioactive compounds, namely isocoreopsin, butrin and isobutrin from the n-butanol extract of *Butea monosperma* (NBE). The novel glucoside isocoreopsin of NBE showed a better free radical scavenging and anticancer activity. The compound isocoreopsin showed significantly greater efficacy in cell death on human colon and liver cancer cell lines (50 µg/mL in HT-29 and 100 µg/mL in HepG2) than butrin (100 µg/mL in HT-29 and 500 µg/mL in HepG2) and isobutrin (80 µg/mL in HT-29 and 150 µg/mL in HepG2). These results suggest that isocoreopsin, butrin and isobutrin are the important key compounds for the chemoprevention of colon cancer and isocoreopsin can be considered as a promising novel drug ^[51].

Conclusion

Cancer is a devastating disease and the current treatment modalities available for cancer treatment put patients in lots of struggle due to the undesirable side effects. Chemotherapeutic agents have limitations mainly due to their toxic effect on non-targeted tissues and further impair human health. Therefore, there is an increasing demand for plant derived anticancer agents. As demonstrated above, different phytochemicals in fabaceae family such as Flavanoids, lectins, saponins and phenolic compounds have significant anticancer potential. Therefore, these Phyto molecules are suitable candidates for the development of new anticancer agents. Some of these compounds are excellent lead molecules and by making suitable pharmaceutical interventions such as structural modification, alternative formulation and effective delivery systems, the pharmacological potential can be increased. The present study is an aid to identify and further develop newer anticancer agents from Fabaceae family.

References

- Izevbogie EB. Discovery of water-soluble anticancer agents from a vegetable found in Benin City, Nigeria. *Exp Boils Med* (Maywood). 2003; 228:293-298.
- Om Prakash, Amit Kumar, Pawan Kumar, Ajeet. Anticancer Potential of Plants and Natural Products: A Review. *American Journal of Pharmacological Sciences*. 2013, 104-115.
- Prakash O, Kumar A, Kumar P, Ajeet. Anticancer Potential of Plants and Natural Products. *American J Ph. cological Sci*. 2013; 1:104-115 .
- Ames BN, Gold LS. The cause and prevention of cancer. *Proceedings of the National Academy of Sciences USA*. 1995; 9:5258-65.
- Aung TN, Qu Z, Kortschak RD, Adelson. Understanding the effectiveness of natural compound mixtures in cancer through their molecular mode of action. *Int J Mol Sci*. 2017; 18:656.
- Thakore P, Mani RK, Kavitha SJ. A brief review of plants having anti-cancer property. *Int J Pharm Res Dev*. 2012; 3:129-136.
- Tariq A, Sadia S, Pan K, Ullah I, Mussarat S, Sun F. A systematic review on ethnomedicines of anti-cancer plants. *Phyto ther Res*. 2017; 31:202-264.
- Javed Iqbal, Banzeer, Ahsan Abbasi, Tariq Mahmmod, Sobia Kanwal, Barkat Ali. Plant-derived anticancer agents: A green anticancer approach. *Asian pacific journal of tropical biomedicine*. 2017, 1129-1150.
- Wojciechowski MF. *Astragalus* (Fabaceae): A molecular phylogenetic perspective. *Brittonia*. 2005; 57(4):382-396.
- Rungruangmaitree, Runchana, Wannee Jiraungkoorskul. Pea, *Pisum sativum*, and its anticancer activity. *Pharmacognosy Reviews*. 2017; 57:39.
- Dai J, Mumper RJ. Plant phenolics: Extraction, analysis and their antioxidant and anticancer properties. *Molecules*. 2010; 15:7313-52.
- Mehdad A, Brumana G, Souza A, Barbosa JA, Ventura AM. A Bowman-Birk inhibitor induces apoptosis in human breast adenocarcinoma through mitochondrial impairment and oxidative damage following proteasome 20S inhibition *Cell Death Dis*. 2016; 2:15067.
- Amin S, Barkatullah HK. Pharmacology of Xanthium species. A review. *J Phyto pharm*. 2016; 5:126-127.
- Srikanth S1, Chen Z1. Plant Protease Inhibitors in Therapeutics-Focus on Cancer Therapy. *Front Pharmacol*. 2016; 7:470.
- Tu LU, Pi J, Jin H, Cai JY, Deng SP. Synthesis, characterization and anticancer activity of kaempferol-zinc (II) complex. *Bioorg Med Chem Lett*. 2016; 26:2730-2734.
- Magee J, Owusu Apenten R, McCann MJ, Gill CI, Rowland. Chickpea (*Cicer arietinum*) and other plant-derived protease inhibitor concentrates inhibit breast and prostate cancer cell proliferation *in vitro* *Nutr Cancer*, 2012, 741-748.
- Nakahata AM, Mayer B, Rie C, de Paula, Karow M, Neth. The effects of a plant proteinase inhibitor from *Enterolobium contortisiliquum* on human tumour cell lines. *Biol Chem*, 2011; 392:327-336.
- Caccialupi LR, Ceci RA, Siciliano D, Pignone A, Clemente G. Sonnante Bowman-birk inhibitors in lentil: heterologous expression, functional characterisation and anti-proliferative properties in human colon cancer cells. *Food Chem*. 2010; 120:1058-1066.
- Alfonso Clemente, Jennifer M. Gee, Ian Johnson T, Donald A. Mackenzie Claire Domoney. Pea (*Pisum sativum* L.) Protease Inhibitors from the Bowman-Birk Class Influence the Growth of Human Colorectal Adenocarcinoma HT29 Cells *in Vitro*. *J Agric. Food Chem*. 2005, 53, 23, 8979-898.
- Sun J, Wang H, Tzi Bun Ng. Trypsin isoinhibitors with antiproliferative activity toward leukaemia cells from *Phaseolus vulgaris* cv 'white cloud bean *J Biomed Biotech*. 2010, 219793.
- Choedon T, Shukla SK, Kumar V. Chemo preventive and anticancer properties of the aqueous extract of flowers of *Butea monosperma*. *J Ethnopharmacol*. 2010; 129:208-213.
- Singh A, Dwivedi B, Raghav P, Singh R, Pant P, Padhi MM. Review on Standardization and Phytochemical of *Vigna unguiculata*. *IJPRS*. 2015; 4(2):506-516.
- Nafessa SKA, IME, Amna EH. Phytochemical screening and hypolipidemic activity of extracts from seeds and leaves of *Vigna unguiculata* growing in Sudan. *Journal of Pharmacognosy and Phytochemistry*, 2017; 6(3):488-491, 18.
- Broome JD. L-Asparaginase: Discovery and development as a tumour-inhibitory agent". *Cancer Treatment Reports*. 1981; 4:111-114.
- Sorial Moharib A. Anticancer Activity of L-Asparaginase Produced from *Vigna Unguiculata*. *World Scientific Research*. *Asian Online Journal Publishing Group*. 2018; 5(1):1-12.
- Sathya Prabhu D, Devi Rajeswari V. Nutritional and

- Biological properties of *Vicia faba*: A perspective review. International Food Research Journal. 2018; 25(4):1332-1340.
27. Imma Turco, Gianna Ferretti, Tiziana Bacchetti. Review of the health benefits of Faba bean (*Vicia faba* L.) polyphenols. Journal of Food and Nutrition Research. 2016; 55:283-293.
 28. Srikanth S, Chen Z. Plant Protease Inhibitors in Therapeutics-Focus on Cancer Therapy. Frontiers in pharmacology. 2016; 7:470.
 29. Banerji A, Fernandes A, Bane S. Treatment with field bean protease inhibitor can effectively repress ethyl nitrosourea (ENU)-induced neoplasms of the nervous system in Sprague-Dawley rats. Cancer Lett. 1998; 130:161-7.
 30. Newell CA, Hymowitz T. A taxonomic revision on the genus *Glycine* subgenus *Glycine* (Leguminosae). Brittonia. 1980; 32:63-69.
 31. Okwu DE, Orji BO. Phytochemical Composition and Nutritional Quality of *Glycine max* and *Vigna unguiculata* (L.) Walp. American Journal of Food Technology. 2007; 2:512-520.
 32. Kennedy AR. The Bowman-Birk inhibitor from soybeans as an anticarcinogenic agent. Am J Clin Nutr. 1998; 68:1406-1412.
 33. The Legume Phylogeny Working Group (LPWG). A new subfamily classification of the Leguminosae based on a taxonomically comprehensive phylogeny. Taxon. 2017; 66(1):44-77.
 34. Sudheer Kumar K, Seetaramswamy S, Ashok Babu K, Kishore Kumar P. Phyto pharmacognostical and isolation of chemical constituents from *Bauhinia variegata* leaf extract. Journal of Pharmacognosy and Phytochemistry. 2015; 4(1):189-191.
 35. Syeda Shahana, Anna Pratima Nikalj G. A Brief Review on *Bauhinia variegata*: Phytochemistry, Antidiabetic and Antioxidant potential. Am. J PharmTech Res. 2017; 7(1):187-193.
 36. Li H, Ji HS, Kang JH, Shin DH, Park HY, Choi MS. Soy Leaf Extract Containing Kaempferol Glycosides and Pheophorbides Improves Glucose Homeostasis by Enhancing Pancreatic β -Cell Function and Suppressing Hepatic Lipid Accumulation in db/db Mice. J Agric Food Chem. 2015; 63(32):7198-210.
 37. Muhammad Imran, Bahare Salehi, Javad Sharifi-Rad, Tanweer Aslam Gondal, Farhan Saeed, Ali Imran *et al.* Kaempferol: A Key Emphasis to Its Anticancer Potential. Molecules. 2019; 24(12):2277.
 38. Pandey S. *In vivo* antitumor potential of extracts from different parts of *Bauhinia variegata* Linn. against b16f10 melanoma tumour model in c57bl/6 mice. Appl Cancer Res. 2017; 37:33.
 39. Abbo S, Van-Oss RP, Gopher A. Plant domestication versus crop evolution: a conceptual framework for cereals and grain legumes. Trends in Plant Science. 2014; 19(6):351-360.
 40. Ali Esmail Al-Snafi. The medical Importance of *Cicer arietinum*: A review. IOSR Journal of Pharmacy. 2016; 6:29-40.
 41. Kumar S, Kapoor V, Gill K, Singh K, Das SN, Dey S. Antifungal and antiproliferative protein from *Cicer arietinum*: a bioactive compound against emerging pathogens. Biomed Res Int, 2014, 387203.
 42. Cláudia Alessandra Andrade de Paula, Vivien Jane Coulson-Thomas, Joana Gasperazzo Ferreira, Paloma Korehisa Maza, Erika Suzukia, Adriana Miti Nakahata *et al.* *Enterolobium contortisiliquum* Trypsin Inhibitor (EcTI), a Plant Proteinase Inhibitor, Decreases *in Vitro* Cell Adhesion and Invasion by Inhibition of Src Protein-Focal Adhesion Kinase (FAK) Signalling Pathways. The Journal of Biological Chemistry. 2012; 287:170-182.
 43. Matloub AA, Mohammed RS, Souda SS, Hallouty SM, Gomaa EZ, Hassan AA. Phytochemical and Biological Studies on *Enterolobium contortisiliquum* (Vell.) Morong Pericarps. J Mater. Environ. Sci. 2018; 9:2768-2778.
 44. Roy F, Boye JI, Simpson BK. Bioactive proteins and peptides in pulse crops: pea, chickpea, and lentil. Food Res Int. 2010; 43:432-442.
 45. Zhang B, Peng H, Deng Z, Tsao R. Phytochemicals of lentil (*Lens culinaris*) and their antioxidant and anti-inflammatory effects. J Food Bioact. 2018; 1:93-103.
 46. Gentry Howard Scott. Origin of the Common Bean, *Phaseolus vulgaris*. Economic Botany. New York: New York Botanical Garden Press. 1969; 23(1):55-69.
 47. Ocho-aninatchibri AL, Kouakou TH, Brou KD, Kouadio YJ, Gnakri D. Evaluation of bioactive components in seeds of *Phaseolus vulgaris* L. (Fabaceae) cultivated in Côte d'Ivoire. Journal of Applied Biosciences. 31:1928-1934.
 48. Ng TB, Cheung RCF, Wong JH, Ye XJ. Protease inhibitors of botanical origin. Functional plant science and biotechnology. 2012; 6:1-10.
 49. Kamble MA, Dhabarde DM, Ingole AR, Sant AP. Evaluation of *in vitro* anti-cancer activity of hydroalcoholic flower extract of *Butea monosperma* var. lutea. Int J Pharmacognosy. 2015; 2(4):186-89.
 50. Banu Rekha J, Jayakar B. Anti-cancer activity of ethanolic extract of Leaves of *Butea monosperma* (Lam) Taub. Journal of Current Pharma Research;2011;1: 106-110
 51. Boopathi Subramaniyan, Navaneethakrishnan Polachi, Ganeshan Mathann. Isocoreopsin: An active constituent of n-butanol extract of *Butea monosperma* flowers against colorectal cancer. Journal of Pharmaceutical Analysis. 2016; 6: 318-325.