Potential Anticancer Activity of Bioactive Compounds from *Ipomoea batatas*

Carmen R. Silva-Correa¹,*, Julio Hilario-Vargas², Victor E. Villarreal-La Torre¹, Abhel A. Calderón-Peña³, Anabel D. González-Siccha¹, Cinthya L. Aspajo-Villalaz², José L. Cruzado-Razo¹

**ABSTRACT**

*Ipomoea batatas* L. (Lam.) known as “sweet potato” is a plant species of great importance in the human diet due to the contribution of nutrients and also for its bioactive compounds that have various medicinal properties. The anticancer activity is one of the properties that attract the attention of researchers in the study of plant species. This review aims to make a critical compilation of current information on research that evaluated the antitumor and antiproliferative activity of *Ipomoea batatas*. The studies included in this review show a diversity of bioactive compounds present in *Ipomoea batatas* such as phenolic compounds, anthocyanins, flavonoids, coumarins and steroids; also isolated compounds such as pectin, peptides and glycoproteins that can be related to their biological activity. It is concluded that there are positive results about *Ipomoea batatas* and its anticancer activity evaluated through in vitro and in vivo tests. In humans, safety and efficacy trials are still lacking to support its future use and allow drug development. Further research evaluating the safety and efficacy of reported bioactive compounds in *Ipomoea batatas* is important for the development of this promising area.

**Key words:** Cancer, Sweet potato, Antiproliferative, Antitumoral.

**INTRODUCTION**

The enormous advances and efforts that have been made in the prevention and treatment of cancer in recent years have not been enough, since they have not achieved control of the disease. Cancer remains the leading cause of morbidity worldwide.¹

Evidence shows that the cause of cancer is multifactorial. Neoplastic cells change for a variety of reasons, including mutations that disrupt post- and co-transcriptional regulation of gene expression, natural selection, and genetic drift.²,³ Dietary patterns with a high glycomic index and high glycomic load are associated with moderate adverse effects on colorectal and probably bladder and kidney cancers. There is also a possible moderate positive association between glycomic load and endometrial cancer.⁴ Diets rich in saturated and trans-fatty acids (fatty dairy products and processed meats) and deficient in vitamins and minerals (low in vegetables and fruits) predispose to the development of prostate cancer through a series of mechanisms that stimulate cell proliferation cancer cells and the processes of angiogenesis.⁵

Myeloid neoplasms, a product of mutations, caused by prior exposure to chemotherapy and/or radiotherapy of primary hematologic malignancies, solid tumors and autoimmune diseases have been reported.⁶ Also, there is evidence that an alteration in the microbiome (viruses, bacteria, fungi, and parasites) can be a cause of neoplasia and is an informative biomarker.⁶

Today, various methods are used for cancer treatment, such as surgery, radiation therapy and chemotherapy.⁷ These methods have no selectivity and cause a high percentage of destruction of healthy cells and cancer cells.⁸ In addition, chemotherapy causes adverse side effects and drug resistance; so there is a current trend to search for new compounds as therapeutic agents.¹,¹⁰ Evidence suggests that the foods included in our diet usually contain high levels of bioactive compounds that help reduce the risk of developing degenerative diseases, such as cancer.¹¹,¹² Plant species are considered an important source of bioactive compounds that have various therapeutic properties.¹³ *Ipomoea batatas* L. (Lam.) known as “sweet potato”, is a dicot belonging to the Convolvulaceae family, which is cultivated in China, sub-Saharan Africa, Indonesia, Asia and South America.¹⁴,¹⁵ *Ipomoea batatas* are ranked as the seventh most important food crop after crops such as rice, wheat, potato, maize and cassava, due to their high yield, high adaptability and resistance.¹⁶,¹⁷

In this work, a critical compilation of the current information on the main bioactive compounds reported in *Ipomoea batatas* and their anticancer activity was carried out, discussing the possible underlying mechanisms. This review hopes to provide a perspective for future research on anticancer compounds from *Ipomoea batatas*.

**ANTICANCER EVALUATION OF SWEET POTATO**

Sweet potato (*Ipomoea batatas*) is one of the world’s most important food crops. Its leaves, stems, and tubers are consumed by an increasing number of people, especially in Asian countries,¹⁸ because it plays an important role as a source of energy and phytochemicals in human nutrition.¹⁹ *Ipomoea batatas* are characterized by the diversity of colors of the skin and roots that vary from white to yellow, orange and dark purple. The peels contain different...
bioactive compounds (such as phenolics, flavonoids, anthocyanins and carotenoids), which have a high nutritional value and great therapeutic importance, including antioxidants, antimutagenic, anti-inflammatory, antimicrobial and anticancer properties. Therefore, they are important for various health-promoting functions in humans. Extracts from different parts of Ipomoea batatas exhibit anticancer and antitumor properties by inhibiting proliferation and inducing apoptosis in cancer cells. Plant extracts are evaluated both in vitro on cancer cell lines and in vivo using different animal models. The main anticancer evaluation studies of Ipomoea batatas are described in Table 1.

**ANTICANCER MECHANISMS OF BIOACTIVE COMPOUNDS**

*Ipomoea batatas* have in their various parts (leaf, stalk, stem, skin and flesh) main compounds such as phenolic acids, flavonoids, and anthocyanins. Other phytochemicals, such as alkaloids, anthraquinones, oxalates and steroids, are reported in the leaves at concentrations of 345.7, 328.4, 1.66 and 0.375 mg/100 g dry weight, respectively and lesser amounts of phytic acid, cyanide, saponins and tannins.

These bioactive compounds exert anticancer effects independently or synergistically with other compounds through regulation of metabolic and signaling pathways, inhibition of enzymes vital for cancer progression, angiogenesis, microtubule assembly and induction of apoptosis. (Figure 1)

### Flavonoids

Flavonoids are a type of natural antioxidant substance capable of eliminating free superoxide radicals, thus showing anti-inflammatory properties and reducing the risk of cancer. The concentration of quercetin in leaves of *Ipomoea batatas* purple variety reports a concentration of 0.26 Μm. In vitro and in vivo studies showed that quercetin was capable of inhibiting cell viability when tested in leukemic cells, colon, and ovarian carcinoma cells, and especially human breast cancer cells. The leaves of *Ipomoea batatas* report the presence of hyperoside, quercetin-3-O-hexoside, luteolin-7-O-glucoside and kaempferol-3-O-glucoside. Quercetin, rutin and other dietary flavonoids inhibit carcinogenesis in animal models, inducing apoptosis in tumor cells and alternative cell death processes in epithelial cells, including autophagy and paraapoptosis. Quercetin inhibits metastasis due to suppression of extracellular matrix remodeling and reduces tumor promotion and progression events via suppressor matrix metalloproteinase. Quercetin increases the expression of proapoptotic proteins, including Bax and Bak; while the expression of Bcl-2 decreases. Bax causes apoptosis by directly modulating caspase-3 expression.

Flavonoids acting as pro-oxidants could suppress cancer cell proliferation by inhibiting epidermal growth factor receptor/mitogen-activated protein kinase (EGFR/MAPK), phosphatidylinositol 3-kinase 3-kinase, protein kinase B and nuclear factor kappa light chain enhancer of activated B cells.
### Table 1: Studies evaluating the anticancer activity of *Ipomoea batatas*.

<table>
<thead>
<tr>
<th>Plant part</th>
<th>Extract</th>
<th>Doses</th>
<th>Bioactive compounds</th>
<th>Experimental model</th>
<th>Results</th>
<th>Mechanisms</th>
<th>Conclusion</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Root, leaves</td>
<td>Aqueous and ethanolic</td>
<td>25, 50, 100, 200, 400, 800 and 1000 µg/mL</td>
<td>Phenolic compounds and flavonoids</td>
<td>Antiproliferative assay: NB4 Human Lymphoma Cell Line</td>
<td>IC₅₀: Water extract of vein 449.6 µg/mL, Root aqueous extract: 594.6 µg/mL, aqueous leaf extract: 697.8 µg/mL, ethanolic root extract: 791.9 µg/mL and ethanolic leaf extract: 1221.1 µg/mL.</td>
<td>Antioxidant activity is associated with the ability to inhibit tumor cell proliferation</td>
<td>Water extract of the vein showed strong antiproliferative activity</td>
<td>(25)</td>
</tr>
<tr>
<td>Acidified ethanolic of tuber peeled (SP) y no peeled (SNP)</td>
<td>1, 2, 3, 4, 5, and 6 mg/mL</td>
<td>Anthocyanins</td>
<td>Antiproliferative assay: MCF-7 (breast cancer), WiDr (colon adenocarcinoma), and SNU-1 (gastric cancer).</td>
<td>IC₅₀ at 72 h: MCF-7 (SP: 4.1 mg/mL, SNP: 3.4 mg/mL), SNU-1 (SP: 2.7 mg/mL, SNP: 3.6 mg/mL), WiDr (SP: 5.9 mg/mL, SNP: 4.6 mg/mL)</td>
<td>Anti-inflammatory mechanism: Suppresses the production of nitric oxide (NO) and some proinflammatory cytokines, such as NFκ-β, TNF-α and IL-6</td>
<td>The extracts of <em>Ipomoea batatas</em> purple variety showed anti-inflammatory and anticancer activities.</td>
<td>(26)</td>
<td></td>
</tr>
<tr>
<td>Leaves</td>
<td>Methanolic extract</td>
<td>8, 40, 200, 1,000 and 5,000 µg/mL</td>
<td>Polyphenolic components</td>
<td>Antiproliferative assay: Rat liver epithelial cell (WB-F344), Liver cancer cell (ATCC-HB-8065), Stomach cancer cell (SNU-C-1), Colon cancer cell (SNPC-1), Lung cancer cell (ATCC-CCL-185) and Uterus cancer cell (ATCC-CCL-2).</td>
<td>IC₅₀ (µg/mL) WB-F344: 1,035, SNU-1:244, SNU-C-1:854, ATCC-CCL-2: 950, ATCC-HB-8065: 2,125, ATCC-CCL-185: 2,494</td>
<td>Inhibition of tumor cell proliferation</td>
<td>IC₅₀ of stomach cancer cells was lower than that of normal rat liver epithelial cells</td>
<td>(27)</td>
</tr>
<tr>
<td>Tubers</td>
<td>Ethanol extract (n-hexane fraction) of sweet potato peel</td>
<td>100 µg/mL</td>
<td>Polyphenolic components</td>
<td>Antiproliferative assay: Colon 1-DLD-1, Colon 2-SW-620, Lung-A549, Breast-1-MCF-7, Breast-2-MDA-MB-231 and Head and neck-FaDu</td>
<td>Inhibitory activity 76.79%, 64.31%, 93.72%, 84.35% and 77.72% for Colon-1, Colon-2, breast, lung and head, and neck cancer cell lines, respectively</td>
<td>Antioxidant activity</td>
<td>The caspase-independent pathway is the major pathway for cell death in PC-3 cells, whereas LNCaP cell death was both caspase-dependent and caspase-independent. Caspase-3 and poly(ADP-ribose) polymerase are activated, increasing levels of cleaved caspase 3 and 9.</td>
<td>(28)</td>
</tr>
<tr>
<td>Leaves</td>
<td>16-amino-acid peptide</td>
<td>1,10 y 100 (pM,nM,µM)</td>
<td>Peptide</td>
<td>Antiproliferative assay: Panc-1 (pancreatic cancer)</td>
<td>Inhibition of tumor cell proliferation</td>
<td>Antioxidant activity and genomic DNA fragmentation</td>
<td>Cancer cell apoptosis</td>
<td>The chromatographic fraction IB F002c had greater anticancer potential</td>
</tr>
<tr>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>10-1000 µM</td>
<td>Polyphenolic components</td>
<td>Antiproliferative assay: stomach cancer (Kato III), promyelocytic leukemia cell (HL-60) and colon cancer (DLD-1).</td>
<td>Cancer cell apoptosis and genomic DNA fragmentation</td>
<td>Cancer cell apoptosis and genomic DNA fragmentation</td>
<td>The 3,4,5-tri-O-caffeoylquinic acid effectively depressed the growth of three kinds of cancer cells.</td>
<td>(30)</td>
</tr>
</tbody>
</table>

**References:**


2. The extracts of *Ipomoea batatas* purple variety showed anti-inflammatory and anticancer activities. (26)

3. Antioxidant activity is associated with the ability to inhibit tumor cell proliferation. (25)

4. The caspase-independent pathway is the major pathway for cell death in PC-3 cells, whereas LNCaP cell death was both caspase-dependent and caspase-independent. (28)

5. The chromatographic fraction IB F002c had greater anticancer potential. (30)
<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
<th>Activity/Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purple sweet potato (flesh)</strong></td>
<td>Anthocyanins</td>
<td>Inhibition of tumor cell proliferation</td>
</tr>
<tr>
<td><strong>Purple sweet potato (skin) and Anthocyanin-rich extract</strong></td>
<td>Anthocyanins</td>
<td>Antioxidant activity is associated with the ability to inhibit tumor cell proliferation</td>
</tr>
<tr>
<td><strong>Roots</strong></td>
<td>DLA (10, 20, 40, 80, and 160 µg/mL), DL (5, 10, 20, 40, 80, and 160 µg/mL), or DP (10, 20, 40, 80, 160, and 320 µg/mL)</td>
<td>Antiproliferative effect</td>
</tr>
<tr>
<td><strong>Tubers</strong></td>
<td>Anthocyanin-enriched extract</td>
<td>Anthocyanin extract inhibits the growth of cancer cells by inducing cell cycle arrest.</td>
</tr>
<tr>
<td><strong>Leaves</strong></td>
<td>Methanolic extract</td>
<td>Anthocyanin extract inhibits the growth of cancer cells by inducing cell cycle arrest.</td>
</tr>
<tr>
<td><strong>Roots</strong></td>
<td>daucosterol linoleate (DL)</td>
<td>Anthocyanin extract inhibits the growth of cancer cells by inducing cell cycle arrest.</td>
</tr>
</tbody>
</table>

| Roots | Sweet potato pectin (SPP), 200 W and 400 W sonication (SSPP) | 0.1, 0.25, 0.5, 0.75 and 1 mg/ml | Pectin | Antiproliferative assay: HT-29 (human colon cancer) | SSPP of 400 W produces a reduction of cell proliferation by more than 70%. IC50 for 400 W SSPP was 0.5 mg/ml, while for 200 W SSPP it was about 0.75 mg/ml | Caspase-3 involvement in pectin-induced cell death indicates apoptotic cell death. | SPP showed the lowest inhibition, with a maximum of 25% at 0.75 mg/ml, and SSPP 400 W had higher activity than SSPP 200 W |
| Alcoholic extract and fractions of sweet potato tubers | Glucocerebroside, Octadecyl coumarate, 7-hydroxy- coumarin, and 6-methoxy-7-hydroxycoumarin | 100 and 200 µg/ml | Anthocyanins | Antiproliferative assay: MCF-7 (breast cancer), DLD-1 and SW-620 (colon cancer), SK-OV-3 (ovary cancer), A-549 (lung cancer), FaDu (Head and Neck Cancer) | IC50 of IB-F002C values 24.75, 47.91, 52.37, 34.17, 46.07, and 25.89 mg/ml against breast, colon-1, colon-2, ovary, lung, and head/neck cancer cell lines, respectively | Antioxidant activity is associated with the ability to inhibit tumor cell proliferation | The IB-F002c fraction has anticancer potency against breast cancer cell lines-1 and head and neck cancer |
| Acidified ethanolic extract of purple sweet potato anthocyanins (PSPA) | Anthocyanins | 100, 300, 500, 800 and 1000 µg/ml | Phenolic compounds | Antiproliferative assay: 5637 and T24 (Bladder cell lines) | The inhibition rate of the PSPA at 800 µg/ml was > 60% after a 72-h incubation | PSPA produces G2/M arrest which is a DNA damage checkpoint in cell cycle regulation and suppresses cell cycle progression. In addition, there is a decrease in caspase-3, Fas, Fasl, Bcl-2 and inhibition of PI3K / Akt | PSPA exerts antitumor effect through suppression of cell viability, promotion of apoptosis, and induction of cell cycle arrest |
| Extract from baked sweet potato and fractions | Phenolic compounds | 0.5, 1.15 and 2 µg/ml | Glycoprotein | Antiproliferative assay: HL-60 (leukemia) | Maximum inhibition was observed at the concentration of 2 mg/ml, inhibition of 65% with fraction II-a and 57% with fraction III, respectively | Genomic DNA Fragmentation | The antiproliferative effect was dose-dependent. |
| SPG-56 Extract | Glycoprotein | 5 to 320 µg/ml | Phenolic compounds | Antiproliferative assay: Liver Cancer HepG2 Cell | The serum tumor markers CEA, CA125, and CA153 in a 240 mg/kg/d SPG-56 decreased by 54.8%, 91.8%, and 90.3%, respectively. | SPG-56 inhibited the metastasis of breast cancer in MCF-7 and 4T1-bearing mice by altering the expression of MMP2, MMP9, VEGF, Occludin, and Claudin. | SPG-56 may have potential as a novel anti-tumor candidate for breast cancer |
| Ten varieties: YS7, HX22, YS43, WS7, YS25, YY27, YY153, CS1, XY34 and YS15 | Phenolic compounds | 2.4 and 6 mg/ml | Glycoprotein | Antiproliferative assay: Liver Cancer HepG2 Cell | YS43, YS7 and YY27 appeared to show the strongest antiproliferative activity with IC50 values of 4.663 mg/mL, fresh weight (FW), 5.162 mg/mL, FW and 5.287 mg/mL, FW respectively. | Antioxidant activity is associated with the ability to inhibit tumor cell proliferation | Purple-fleshed varieties, such as YS43, YZ7 and YY153, have higher total phenol content and antioxidant capacities, as well as higher antiproliferative activity. |
| SPG-8700 extract | Glycoprotein | 25 and 50 µg/ml | Phenolic compounds | Antiproliferative assay: HCT-116 (colon cancer) - Antiproliferative activity | IC50 of SPG-8700 against HCT-116 cells is 44.7 µg/ml. After SPG-8700 treatment, the three indicators with CA242 decreased by 24.1%, CA199 decreased by 15.7%, CA125 decreased by 34.8% in the therapy group. | SPG-8700 promoted apoptosis in HCT-116 cells by regulating Bcl-2 and Bax expression | SPG-8700 has antitumor activity and had no effect on normal cell growth |
Phenolic compounds

The main phenolic compounds of *Ipomoea batatas* are caffeic acid, p-coumaric acid, ferulic acid and 3-O-cafeoylquinic acid. The polyphenol content in the roots of *Ipomoea batatas* varies from 23.3 to 43.8 mg of caffeic acid/g, and in a range of 146 to 266 mg of gallic acid/100 g. In *Ipomoea batatas* leaves, caffeic acid, 4,5-di-O-cafeoylquinic acid, and 3,4,5-tri-O-cafeoylquinic acid are reported as its main phenolic compounds.

Phenolic compounds are antioxidant molecules; they possess important biological activities such as anti-inflammatory and anticancer activities. The anticancer property includes a wide variety of regulatory mechanisms including cell cycle progression, promotion, modulation of enzyme activities, mitogen-activated protein kinase (MAPK) signaling pathway, apoptosis induction, and metastatic invasion.

Anthocyanins

Anthocyanins are widely distributed in the leaves, flowers, roots, fruits and grains of many colorful fruits and vegetables. Anthocyanins are responsible for the purple coloration of the pulp and peel of *Ipomoea batatas*. The inclusion of anthocyanins in the diet is associated with decreased risk of cardiovascular and metabolic degenerative diseases, improvement of visual and brain function, cancer chemoprevention, decreased risk of cardiovascular and metabolic degenerative diseases, and prevention and therapy, due to its bioactive compounds such as polyphenols, anthocyanins, flavonoids, coumarins and sterols.

Many isolated plant compounds are being rigorously tested for their anti-cancer properties and it is increasingly recognized that the beneficial effects of plants are due to a complex interaction of the composite mixture of bioactive compounds present throughout the plant either by additive or synergistic effect.

Studies need to focus on evaluating the bioavailability of a bioactive compound that is incorporated into the diet as a nutrient. Furthermore, the use of bioactive compounds is limited because insufficient data is available regarding safety and efficacy. Therefore, future studies should encourage the evaluation of pharmacokinetic activities and in silico analyses of bioactive compounds.

CONCLUSIONS

The authors declare no conflicts of interest.

REFERENCES


GRAPHICAL ABSTRACT

Potential anticancer activity of bioactive compounds from *Ipomoea batatas*

Mechanisms of anticancer action:
- Anti-inflammatory
- Antioxidant
- Antiproliferative
- Cell apoptosis
- Cell cycle suppression
- Estrogen receptor
- Genomic DNA fragmentation

ABOUT AUTHORS

Silva–Correa Carmen R. Professor in Department of Pharmacology at Universidad Nacional de Trujillo, holds a degree in Pharmacy and Biochemistry (2011), Master of Chemical Sciences (2017), graduate student at Doctoral program in Biomedical Sciences since 2019. Currently participates in research projects on toxicological and pharmacological evaluation of medicinal plants.

Hilario-Vargas, Julio S. Professor. Departamento de Fisiología, Facultad de Medicina, Universidad Nacional de Trujillo. Master in Physiology and Doctor in Biomedical Science. Research and publishes works on pemphigus, evaluation of medicinal plant extracts, and physiological function in special environments.

Villarreal–La Torre Víctor E. Master of Chemical Sciences, holds a degree in Pharmacy from Universidad Nacional de Trujillo (2011). Professor in the Medicinal Chemistry undergraduate program and the Molecular basis of the Action of Xenobiotics postgraduate program at the Universidad Nacional de Trujillo. He currently executes research projects aimed at the discovery of antimicrobial compounds in medicinal plants. Graduate student at Doctoral program in Pharmacy and Biochemistry since 2019.

Calderón-Peña Abhel A. Doctor in Biological Science and Master of Physiology and Biophysics from Universidad Nacional de Trujillo. Animal Physiology, Human Anatomy, Histology and Biochemistry Professor of undergraduate program at the Universidad Nacional de Trujillo. He is currently conducting research on oxidative stress and the discovery of antioxidant compounds in medicinal plants.
González-Siccha Anabel D. Doctor in Pharmacy and Biochemistry. Master of science in Biochemistry. Magister in Physiology. Pharmacy degree in Spain. Second degree in Clinical and Biological Analysis. Principal Professor of Biochemistry and Molecular Biology undergraduate program of the Department of Biochemistry, Pharmacy and Biochemistry Faculty at the Universidad Nacional de Trujillo. Research Fellow in the Laboratory of Biochemistry and Molecular Biology at the Faculty of Medicine from Albacete, Universidad de Castilla-La Mancha from Spain. Research on Nutritional assessment and anemia in vulnerable populations. Research on medicinal plants on immunomodulatory, antitumor and tumor marker activity. Research on DLK1 and DLK2 proteins and differentiation on mouse tissues through immunohistochemistry.

Aspajo-Villalaz Cinthya L. Master of Food Technology holds a degree in Biological Science from Universidad Nacional de Trujillo. Bromatology and Biochemistry Professor of undergraduate program at the Universidad Nacional de Trujillo. She is currently conducting research on microbiological control of pharmaceutical products, functional foods design and evaluation. Graduate student at Doctoral in the Biological Sciences program.

Cruzado–Razco José L. Master of Physiology and Biophysics, Doctorate studies in Biomedical Sciences. He has participated in research projects on epidemiology of tropical diseases and currently, in research on antimalarial, leishmanicidal and antitypanosomal activity of medicinal plants.