Health Effects of Sweet Potato (*Ipomoea batatas L.*)

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Sweet potato (SP; *Ipomoea batatas* (L.) Lam) is an edible tuber native to America and the sixth most important food crop worldwide. China leads its production in a global market of USD 45 trillion. SP domesticated varieties differ in specific phenotypic/genotypic traits, yet all of them are rich in sugars, slow digestible/resistant starch, vitamins, minerals, bioactive proteins and lipids, carotenoids, polyphenols, ascorbic acid, alkaloids, coumarins, and saponins, in a genotype-dependent manner. Individually or synergistically, SP's phytochemicals help to prevent many illnesses, including certain types of cancers and cardiovascular disorders.

Keywords: antioxidants ; sweet potato ; Ipomoea batatas ; cancer ; carotenoids ; phenolic compounds

1. Introduction

The research of edible roots and tubers (R&T) has attracted the attention of researchers worldwide. Research published to date ranges from their economic and cultural dimensions to their nutritional/functional value as staple foods for certain countries [1][2][3][4]. Among R&T, sweet potato (SP; *I. batatas* (L.) Lam; also known as 'boniato', 'moniato', 'caiapo', 'kumara' or 'kumera') with its >1600 species, has been a major staple food for certain ancient populations for centuries [1][2]. In fact, archaeobotanical and epigraphic evidence allows the researchers to affirm that SP was and continues to be an ingredient widely used to make different drinks and foods, both sweet and salty, in populations of diverse cultures [3][4].

The genus *Ipomoea* belongs to the *Convolvulaceae* family, and 600–800 species have been identified by cytogenetics [5][6]. Most of them exhibit health-promoting bioactivities, such as those related to their phytochemical profile: anti-inflammatory (*I. cairica*), anti-constipation (*I. digitata*), analgesic (*I. stans*), antidiabetic and hypotensive (*I. aquatica*, *I. batatas*), hemostatic and vasoconstrictor (*I. tricolor*), psychotomimetic (*I. muelleri, I. violacea*) and anticancer (*I. horsfalliae, I. turpethum*) activities [7]. Sweet potato (SP; *I. batata*s (L.) Lam), contains a wide range of nutrients and xenobiotic phytochemicals with antioxidant, anti-nyctalopia/xerophthalmia, hepatoprotective/spasmolytic, anticoagulant/anti-HIV antibacterial, and antidiabetic potential. Particularly, specific anticancer bioactives (e.g., phenolic acids, carotenoids, and peptides) present in the aerial (leaves, steams, talks) and non-aerial (storage roots) parts of SP suggest phenotype/varietal-specific benefits [8][9][10][11][12]. It is noteworthy that certain phenotypic traits of SP genotypes are closely related to their functional/nutraceutical value: the peel and flesh (central parenchyma) pigmentation, going from white-creamy to dark purple (**Figure 1**) is related to their phenolic and carotenoid content [13][14][15][16].

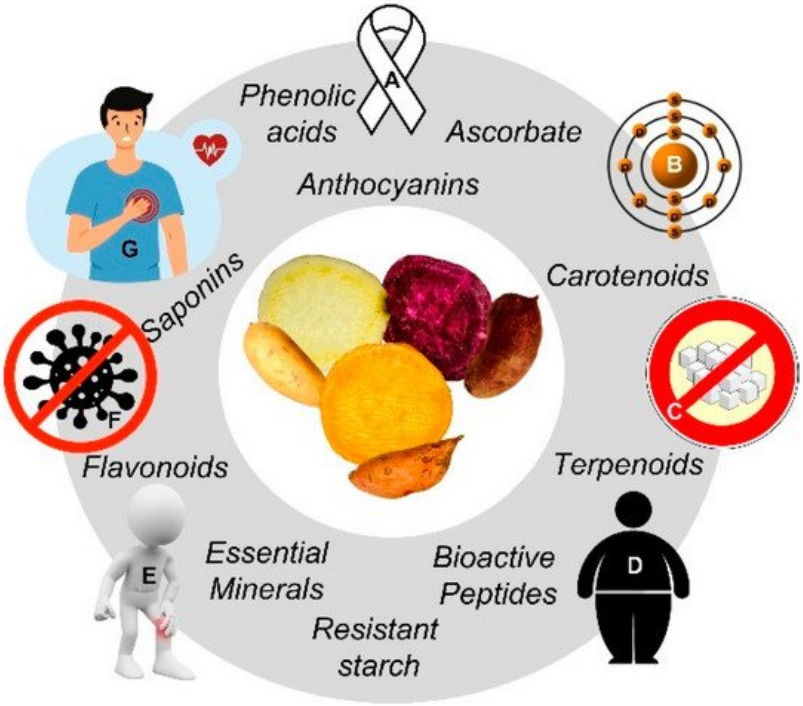

Figure 1. Sweet potato (SP; *Ipomoea batatas* L.) group of phytochemicals with associated health-promoting effects. Preventive actions (clockwise): Immunocompromise (**A**), prooxidant (**B**), diabetes (**C**), adiposity (**D**), inflammatory (**E**), infection (**F**), cardiovascular (**G**) diseases/metabolic rearrangements. Source: The authors (CC (by/nc/sa)-licensed clip art).

However, food processing and preservation [13][14][17][18][19] and the gastrointestinal fate of its phytochemicals [20][21][22] may hinder the health-promoting potential of SP. The aim of this narrative research is to provide an update on SP's botany/molecular phylogeny, agroindustry, and product commercialization/technological diversification, as well as the nutritional/functional value of SP's major genotypes (by flesh color) and certain health effects (cancer chemoprevention and cardiovascular health promotion). Certain physiological considerations to ensure SP's health benefits are discussed shortly.

2. Health Effects and Metabolic Fate of SP's Phytochemicals

Once the diversity of nutrient and non-nutrient compounds has been examined, it is not surprising to find multiple reviews in the literature highlighting the biological activities attributable to SP in the maintenance of optimal nutritional states, and in the prevention of various diseases [8][9][10][11][12][13][14][15][16]. SP's antioxidant, antimicrobial, anti-diabetic, anti-cancer, anti-inflammatory, hepatoprotective, neuroprotective, anti-obesity, and GI-health-promoting properties have been extensively reviewed [23][24][25]. However, the subsequent section focuses on relevant information on the anticancer and anti-cardiovascular disease (CVD), pathologies with the highest morbidity/mortality rates worldwide, in which SP can contribute to conventional clinical treatments as alternative adjuvants.

2.1. SP and Cancer

Plant bioactives exert many benefits in cancer chemoprevention; cyto/genotoxicity, cell cycle arrest, pro-apoptosis, intracellular signaling, immunomodulation, and anti-angiogenesis are probably the most studied mechanisms. Specifically, a robust body of evidence indicates that certain antioxidant phytochemicals, such as phenolic compounds, carotenoids, ascorbate, and antioxidant dietary fiber and RS, can halt the progression of certain types of cancer cells in vitro and ex vivo, although their effectiveness under clinical conditions remains uncertain. Personalized nutrition for cancer patients demands a continuous search for newer sources of phytochemicals to be used in complementary and alternative medicine. Several studies carried out in recent years [26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42][43][44] have reported multiple control points determining the process of initiation, promotion, or the spread of cancer (**Table 1**).

Table 1. Bioactive compounds in SP and their role against cancer.

Variety	Phytochemical	Mechanism	Action
Initiation			
Tainong 57	**Trypsin inhibitor**	**DNA damage reparation**	**↑ P53 leukemic cells**

Variety	Phytochemical	Mechanism	Action
--	Polyphenols	↓ ROS	↓ Oxidative damage induced by H_2O_2 in HepG2 cells.
Mixuan No. 1	Protein hydrolysate	↓ ROS	↑ antioxidant activity, ↓ oxidative damage to DNA
Ayamurasaki	Anthocyanins	↓ROS	↓ Oxidative damage induced by radiation in thymocytes
Tainong 57	Trypsin inhibitor	Cell cycle arrest	Phase G1 arrest
TU-155	Polyphenols	Cell cycle arrest	↓ciclin D1, A y E, ↑ Cip1/p21
Promotion			
NING No. 1	Polysaccharides	Anti-inflammatory	↓ IL-1β, IL-6 y TNF-α
TNG 73	Anthocyanins	Anti-inflammatory	↓ activation of NF-κβ in RAW 264.7 cells induced by LPS
--	Caffeic acid and derivates	Inhibition in cell proliferation	β-catenin and Tcf-4 pathway suppression
Progression			
Bhu Krishna	Anthocyanins	Cell death induction	Apoptosis—↑ caspases
Diverse	Anthocyanins	Cell death induction	↑ caspase 3 in colonic cells
--	Polyphenols	Angiogenesis inhibition	↓ VEGF165 in a dose-dependent manner
--	BSG	Invasion inhibition	PI3K-Akt signaling pathway suppression
Zhongshu-1	SPG-56 Glycoprotein	Invasion inhibition	Regulation in the expression of proteins (MMP2, MMP9, VEGF, ocludin, and claudin) related with metastasis.
TNG 73	Anthocyanins	Invasion inhibition	Cell migration suppression (MCF-7 cells)

Non specified (--), β-Sitosterol-d-glucoside (BSG). Data source: [27][28][29][30][31][35][36][37][38][39][40][41][42][43][44].

In the early stages, the cellular integrity, and in particular the genetic material, can be preserved by various compounds, such as trypsin inhibitors, anthocyanins, protein hydrolysates, or hydroxycinnamic acids present in the various varieties of SP. Damage to genetic material caused by reactive oxygen species ($^{\bullet}OH$ o H_2O_2) o UV/gamma-irradiation can be decreased (if not avoided) after exposure to cells with functional compounds that have a high antioxidant capacity [26]. Additionally, it has been shown that the trypsin inhibitor present in the SP variety Tainong 57 can increase the expression of the protein p53, a nuclear protein known as “the guardian of the genome” due to its role in limiting abnormal cell formation, thus preserving the integrity of the genetic material [27].

If cell integrity is affected, this cell becomes abnormal and must multiply to promote a cancerous process. Cyclins are molecular mediators of the cell cycle; in normal conditions, they require binding with kinases to promote the different phases of cell division. Phenolic extracts of the SP variety Whatle/Loretan can decrease the expression of these proteins and limit complexing with their respective kinases [28]. According to the event and in the case of SP phytochemicals, Huang et al., have demonstrated the potential of trypsin inhibitors present in the Tainong 57 variety to limit cell division after arrest in the early phases (G1 phase) of altered cells [27].

As might be expected, the regulation of signaling pathways is a common and functional mechanism for the modulation of different tumors. The anthocyanins present in SP have been shown to be effective in negatively regulating the signaling pathway of β-catenin, a protein widely recognized for acting as a permanent coactivator of events, such as cell proliferation and differentiation [29][30]. In addition to the role of anthocyanins, phytosterols such as β-Sitosterol-d-glucoside play important roles in the regulation of additional pathways. β-Sitosterol-d-glucoside has been shown to be efficient in negatively regulating the PI3K/AKT/mTOR signaling pathway, a key pathway in processes, such as cell proliferation, apoptosis, metabolism, and angiogenesis [31][32]. The adverse systemic effects associated with the cancer process largely depend on tumor formation, its ability to survive, nutrient acquisition, and location, among other issues. Phenomena such as angiogenesis have been related to the capacity present in transformed cells to produce chemical mediators that promote vascularization and, therefore, the growth of tumor cells and their dissemination throughout the body

(metastasis). Therefore, bioactives combinations with anti-angiogenic capacity seem essential in limiting processes such as the promotion and spread of cancer [33].

Chen et al. [34] demonstrated the ability of SP polyphenols to reduce the expression of the Vascular Endothelial Growth Factor (VEGF165) in a dose-dependent manner. Moreover, it has been shown that the glycoprotein SPG-56 present in the SP variety Zhongshu-1 can modulate the expression of essential proteins in cell attachment and adhesion. Dysregulation in the production of proteins, such as claudins or occludins (essential for the formation of tight junctions between cells), has been reported under in vitro conditions [35]. Beyond cancer promotion or progression stages, cell cytotoxicity on its own deserves attention. In all stages, the induction of cell death by apoptosis is a key tool to stop the number of viable cells in a programmed way. This event has already been reported for SP polyphenols. Particularly, the anthocyanin fractions from SP P40, O'Henry, NC Japanese as well as Bhu Krishna seem to be effective modulators in cell models [36] [37].

The multi-target nature of SP's phytochemicals helps to tackle cancer at many stages; however, future research on this matter should consider the SP varietal richness and plant part [23], gastrointestinal bioavailability [20][21][22][45][46], and pharmacokinetics of a given SP's bioactivity to guarantee the effects observed in vitro/ex vivo conditions.

2.2. SP and Cardiovascular Diseases (CVD)

CVD are the leading cause of worldwide adult mortality. Prevalent cases of total CVD nearly doubled from 271 (CI95% 257–285) to 523 (CI95% 497–550) million deaths and 17.7 to 34.4 million disability-adjusted life years (DALYs) between 1990–2019 [47]. Since CVD and other non-communicable chronic diseases are closely related to lifestyle factors (e.g., unhealthy diet and sedentarism), it is necessary to promote the healthy intake of fruits, nuts, seeds, beans, vegetables, whole grains, and R&T [48], including the aerial/non-aerial parts of SP plant [23]. Numerous investigations indicate that the dietary intake of flavonoids (e.g., quercetin) from plant foods such as purple SP, can reduce the risk for CVD [49] while SP's tannins, flavonoids, alkaloids reducing sugars, anthraquinones, and cardiac glycosides reduces serum creatinine and lactate-dehydrogenase activity, favoring cardiovascular health [23].

Consuming SP leaves reduces the risk for CVD by synergistically reducing lipid peroxidation and DNA damage, and regulating blood glucose, insulin, and lipid levels [50][51]. Such metabolic effects are partially explained by the 1: 2 ratio of linoleic/α-linolenic fatty acids [52], compounds that can protect the cardiovascular system from excessive inflammation and oxidative damage [53]. Moreover, Zhao et al. [51] showed that flavones from an SP leaf powder decreased total cholesterol and triglyceride levels in a dose-dependent manner while its insoluble dietary fiber increased fecal bile acids and cholesterol, reducing serum cholesterol levels [54]. In support of this, a randomized controlled clinical study carried out on 58 humans showed a decrease in circulating cholesterol (7 mg/dL) and triglycerides (2 mg/dL) after the consumption of 132 g of white SP as a meal replacement [55]. Moreover, it has been demonstrated in hamsters that consuming SP leaves increases the presence of favorable biomarkers to reduce the risks for CVD [55] by inducing vascular (aortic) relaxation [56] mediated by nitric oxide (NO) as an inhibitor, in the presence of N ω -nitro-l-arginine (NOLA), an inhibitor nitric oxide synthase (NOS), or by eliminating it from the endothelium [57]. As for SP root, <3 kDa hydrolyzed peptides (VSAIW, AIWGA, FVIKP, VVMPSTF, and FHDPMLR) from sporomin A and B, display a strong anti-ACE (angiotensin-converting enzyme) activity [23][58], while lactic acid bacteria (LAB)-based fermentation of white (Murasaki), orange (Evangeline) and purple (NIC-413)-fleshed SP varieties increases their anti-ACE/antioxidant activity [59]. Additional evidence on the cardioprotective effects of extracts of SP and/or its pure phytochemicals previously identified by chromatographic techniques is summarized in **Table 2**.

Table 2. SP phytochemicals in cardiovascular diseases (CVD).

Phytochemical	Mechanism	Action
Heart		
Anthocyanins	**↓ Malondialdehyde**	**Antioxidant ↓ Lipid peroxidation**
Flavonoids/ anthocyanin	**Vasodilation induction/ ↓ endothelin—1**	**Antihypertensive**
Tannins/saponins/ Flavonoids/terpenoids	**↓ Creatine kinase ↓ Lactate dehydrogenase**	**Prevention in ischemic damage**
Vascular		

Phytochemical	Mechanism	Action
Aqueous extracts	**↑ Telomerase activity preventing cell senescence**	**Prevention of coronary artery disease**
Anthocyanins	**Inhibition of PDGF receptor-β**	**Regulation of platelet aggregation**
Chlorogenic acid	**ACE Inhibition**	**Antihypertensive**
Anthocyanins/ethanolic extract	**↓ VCAM**	**Prevention of atherosclerosis**
SP leaves	**Elongate arterial occlusion time**	**Prevention of thrombotic events**
Purple SP extract	**↓ cyclooxygenase-2, ↓ inducible nitric oxide synthase ↓ tumor necrosis factor-α**	**↓Inflammation**
Brain and Kidney		
Anthocyanins	**↑ BDNF**	**Neuroprotection after ischemic stroke**
Flavonoids/ acetylated anthocyanins	**Blocking VEGFR2/ROS/NLRP3 signaling**	**↓ Kidney damage**

Angiotensin-converting enzyme (ACE), brain-Derived Nuclear Factor (BDNF), NLR family pyrin domain containing 3 (NLRP3), reactive oxygen species (ROS), platelet-derived growth factor (PDGF), sweet potato (SP), vascular cell adhesion molecule (VCAM), vascular endothelial growth factors receptor 2 (VEGFR2). Data source: [60][61][62][63][64][65][66][67][68][69][70][71].

In conclusion, this evidence suggests that several SP bioactives (leaves/root) may individually and synergistically prevent CVD by exerting many cardioprotective mechanisms. Further investigations on the associated molecular events are needed to support the epidemiological and in vivo and in vitro evidence discussed above.

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