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Short Review

Bioactive components of sambo seeds, almonds, and honey and their relationship with prostate cancer

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ABSTRACT

Certain foods rich in bioactive compounds could have dietotherapeutic properties, allowing their use in treating and preventing diseases, including cancer. Popularly, pumpkin seeds, almonds, and honey are used for managing prostate inflammation, which can lead to carcinogenesis. Sambo seeds (*Cucurbita ficifolia*) and almonds (*P. dulcis*) have a nutrient-rich composition that includes unsaturated fatty acids and bioactive components such as vitamins, pigments, and polyphenols, which have been linked to beneficial effects on health and cancer. Currently, more studies exist on cucurbit seeds, such as those from the species *Cucurbita pepo*; however, *C. ficifolia* is abundant in the Andean region, which is why we have focused our study on the effects of *Cucurbita ficifolia*. This review aims to identify the bioactive components and nutrients of the ingredients in sambo seeds, almonds, and honey that are relevant to cancer. It was recognized that linoleic acid and oleic acid present in sambo seeds could prevent and reduce prostate growth; likewise, studies have determined that almonds and sambo seeds possess apoptotic and antiproliferative activity in prostate cancer cells, suggesting that the intake of this food mixture could have more excellent beneficial effects on cancer.

Keywords: Sambo seeds, Almond, Honey, *Cucurbita ficifolia*, *P. dulcis*, Cancer, Prostate

INTRODUCTION

Prostate cancer is the most common cancer in men, after skin cancer. In 2022, around One and a half million cases of prostate cancer were diagnosed worldwide, making it the fourth most diagnosed cancer in the world. In the same year, approximately four hundred thousand people died from the disease[1]. In Ecuador, 13,419 deaths from prostate cancer were recorded between 2004 and 2019, making it the most common cancer among Ecuadorian men [2]. Due to factors such as aging populations and shifts in population size, mortality rates in most Latin American and Caribbean countries are projected to increase by 2030. Ancestral medicine is widely used in various parts of the world as an alternative to current medicine, and plants and foods such as fruits, vegetables, nuts, seeds, oils, and whole grains are rich in bioactive compounds. These chemical substances play roles in health promotion, so they are being studied for cancer prevention [3] Traditional medicine has employed a combination of Sambo seeds, almonds, and honey as a potential preventive agent for prostate cancer. A detailed phytochemical analysis of these components is proposed to evaluate their therapeutic potential and possible mechanism of action in preventing this disease.

Almonds (*Prunus dulcis*)

The almond (*Prunus dulcis*) is a nut instinctive to the Mediterranean climate of the Middle East (Figure 1a). It originated in Central Asia, in countries such as Syria, Turkey, Iran, and Pakistan. Later, it spread to North Africa and Southern Europe[4]. Today, it is produced worldwide in warm and arid Mediterranean climate regions, with the United States being the producer of 80% of the world's almonds, followed by Spain and Australia[5]. The production of this fruit is small in Ecuador, so there is no significant production data. Only small crops are registered in Santa Elena, Sucumbíos, and Orellana6 provinces. There are two types of almonds: sweet almonds and bitter almonds. The sweet almond is edible, while the bitter almond is not and can be poisonous. Morphologically, they differ because the bitter almond is slightly broader and shorter than the sweet almond, which contains 50% oil, while the bitter almond produces hydrogen cyanide[9]. Traditionally, almonds have been considered an excellent nutraceutical for the central nervous system, vision, respiratory tract, gastrointestinal tract, and urinary tract. This fruit has been attributed to pharmacological properties such as antioxidant, anxiolytic, sedative, hypnotic, antimicrobial, cardioprotective, hepatoprotective, and anticancer. Additionally, it has been seen to act as an essential prebiotic[7].

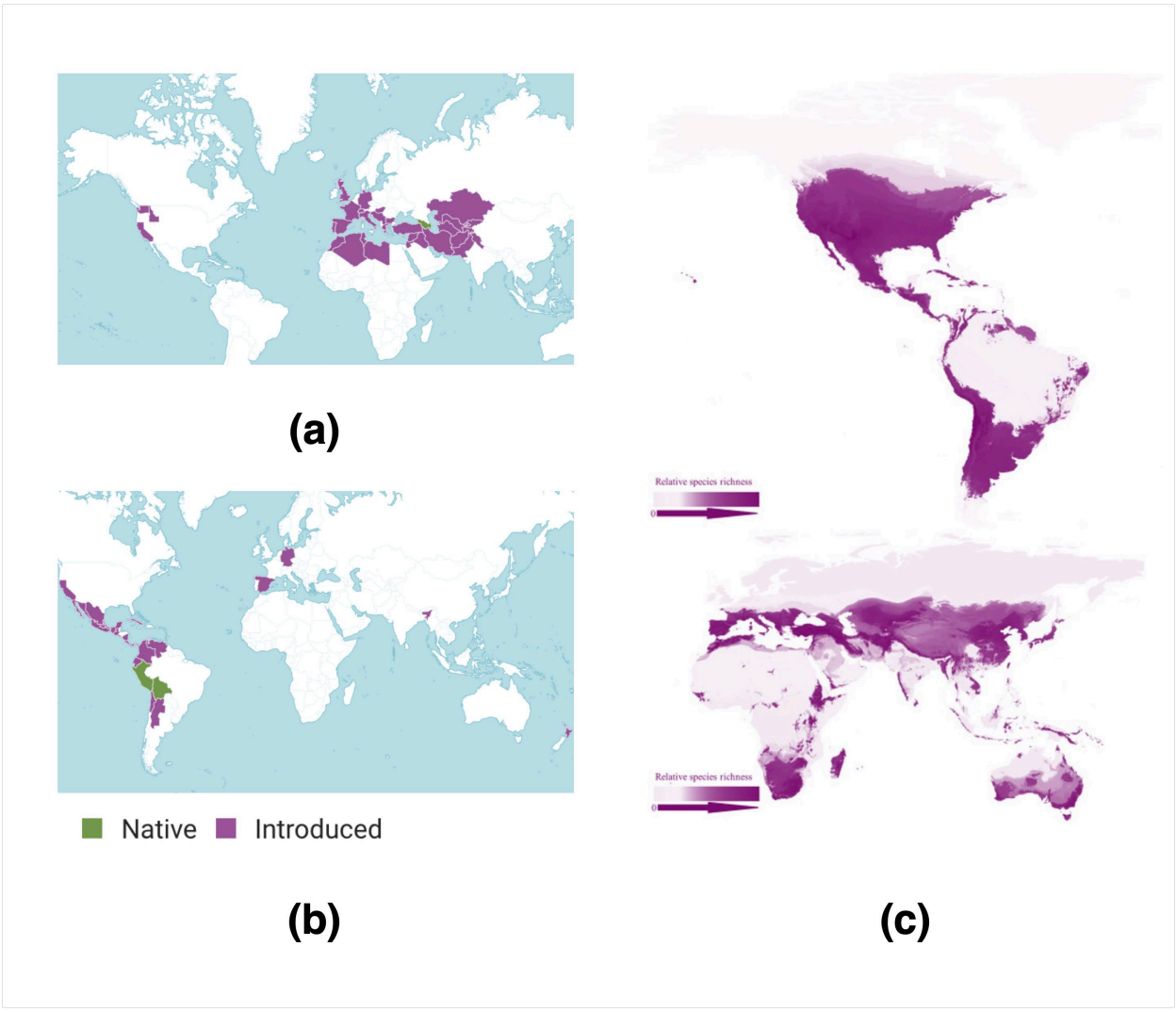

Figure 1. Global distribution of species. Distribution according to POWO. Green Native, Violet Introduced. (a) *P. dulcis* [8] (b) *C. ficifolia* [9] (c) Bee Species Richness Projections of A. mellifera according to Orr et. al 2021 [10]

Almonds (*P. dulcis*) contain phytosterols that delay the cell cycle, induce apoptosis, and inhibit tumor metastasis. They are believed to reduce oxidative stress due to their anti-inflammatory, anticancer, immune-

regulating, and antioxidant functions[11–13]. *P. dulcis* contains compounds such as amygdalin[14,15], which enhances the cytotoxicity of esomeprazole (at a concentration of 10,000 µg/ml) in Hela cells (cervical cancer) and decreases the resistance of these cells to esomeprazole [15]. Amygdalin (**1**) is an aromatic aminoglycoside found in the seeds of fruits from the Rosaceae family. Jumaa et al. reviewed the various antitumor mechanisms of this compound in prostate cancer, noting its effects on proliferation, apoptosis, and the cell cycle during a 24-hour treatment[15]. While amygdalin has been considered controversial due to its potential anticancer properties, it also poses a risk of toxicity due to hydrogen cyanide production from its enzymatic breakdown. There is insufficient clinical evidence to prove its effectiveness against cancer in humans. The conversion of amygdalin to hydrocyanic acid and its subsequent accumulation in the body can lead to harmful toxic effects. Cyanide poisoning can impair the cells' ability to use oxygen, resulting in metabolic acidosis and potentially cardiopulmonary arrest. Symptoms include headache, nausea, and difficulty breathing, and these cannot be addressed with supplemental oxygen. Instead, antidotes like sodium thiosulfate, sodium nitrite, or hydroxocobalamin should be used to neutralize cyanide and facilitate its elimination through the kidneys. Nevertheless, the cyanide content in food is generally low and not considered a significant risk. The CDC states that there is insufficient evidence to support the idea that cyanide causes cancer in humans, and the EPA has concluded that cyanide is not classifiable regarding its carcinogenicity to humans. Fortunately, sweet almonds (*P. dulcis*), the primary type consumed, have amygdalin levels up to 1,000 times lower than bitter almonds. It is estimated that consuming 50 bitter almonds could be fatal for an adult, and 5 to 10 could be toxic to a child. The estimated lethal dose for adults ranges from 0.5 to 3.5 mg/kg of body weight [16–18].

Amygdalin (**1**) and prunasin (**2**) (Figura 2) in almonds show antioxidant, anti-inflammatory, antibacterial, and anticancer effects. Amygdalin can induce apoptosis in tumor cells in prostate cancer[19]. Almond consumption increases the amount of bifidobacteria and lactobacillus related to cancer prevention. Additionally, phenolic compounds and betulinic acid (**3**) with antiproliferative effects in human osteosarcoma and breast cancer cells, respectively, have been observed[20,21].

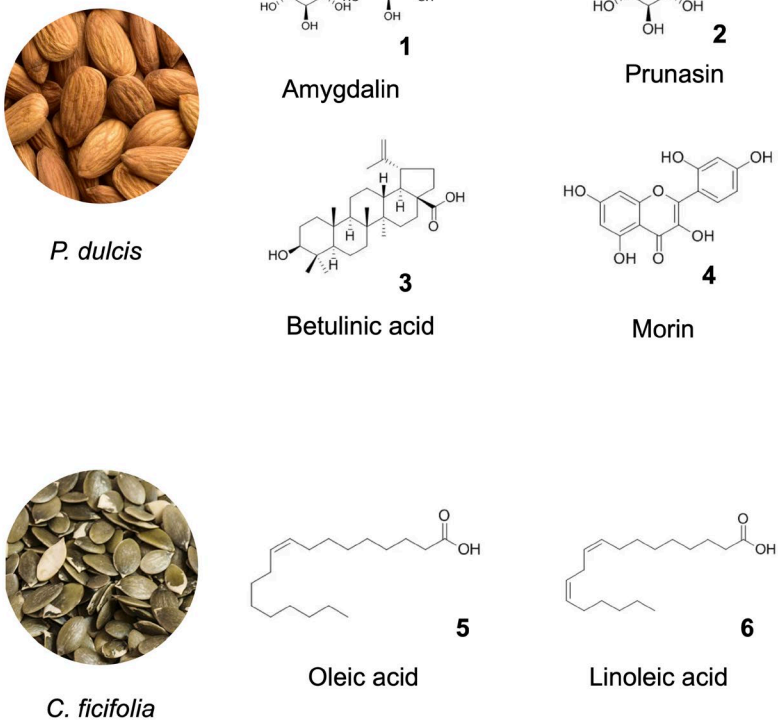

Figure 2. Secondary metabolites from *P. dulcis* and *C. ficifolia* with anti-tumor activity.

Almonds are a source of the bioactive compound morin (**4**), recognized as an anticancer agent due to its ability to suppress the inflammation leading to transformation, proliferation, and initiation of carcinogenesis[22]. Solairaja et al. provided strong evidence of its anticancer role and potential as a therapeutic agent in various cancers, including prostate cancer[23]. Almonds also contain polyphenols that scavenge and neutralize free radicals, intervene in the regeneration of essential vitamins, and modulate Nrf2/EpRE and NF-kB signaling pathways, inducing detoxifying and antioxidant enzymes. These compounds have chemoprotective, cytoprotective, anti-inflammatory, and antitumor effects, acting as inhibitors of carcinogenesis. In prostate cancer, anacardic acid inhibited tumor cell proliferation and induced apoptosis, resveratrol induced cell death, polyphenol caused cell cycle arrest in the G0-G1 phase and induced apoptosis, and genistein dose-dependently repressed DNMT[12,24].

Almonds are a rich source of vitamin E, which helps maintain cell membranes, as well as amygdalin and prunasin, compounds with antioxidant, anti-inflammatory, and anticancer properties. These compounds can trigger apoptosis in prostate cancer cells[12]. Tocopherols regulate key events in lipid metabolism, inflammation, immunity, angiogenesis, cancer, and tumor metastasis. They also benefit intestinal transit, reduce blood pressure, prevent anemia and cancer, and protect against free radicals[25,26]. Due to its linoleic and oleic acid content, almond consumption may reduce the risk of colon cancer through at least one lipid-associated component of almonds[27].

Stilbenes in almonds prevent cardiovascular diseases, have antiatherosclerotic properties, and act against cancer as antiviral and anti-inflammatory agents[28]. Bioactive compounds from *P. dulcis* can be potential selective inhibitors of CYP17A1 lyase in treatments for castration-resistant prostate cancer [22].

Several small, short-term studies have assessed oxidation markers following consuming nuts rich in monounsaturated fats (MUFA), particularly almonds. Although the results were secondary primarily and showed some inconsistency (either a reduction or no change in markers), they never worsened oxidative status compared to other diets. This was also observed in studies with nuts rich in polyunsaturated fats (PUFA), where the antioxidants present in the nuts likely countered any adverse effects. Four recent studies analyzed oxidative stress after consuming meals enriched with nuts versus meals without nuts. Studies with almonds and walnuts showed a beneficial effect on postprandial oxidative stress. Nuts rich in MUFA seem to moderately improve oxidative status, while nuts rich in PUFA have a neutral or slightly positive effect. However, frequent nut consumption has not been shown to reduce antioxidant defenses. In a small study, diets with two doses of almonds compared to a healthy diet without nuts showed that almonds reduced levels of C-reactive protein (CRP) and E-selectin, although they had no impact on IL-6. In the PREDIMED trial sub-study, diets supplemented with 30 g of nuts daily reduced inflammatory markers such as ICAM-1 and soluble IL-6, as well as the expression of pro-inflammatory ligands in monocytes, compared to a low-fat diet. In conclusion, nut consumption has little effect on CRP but reduces other inflammatory biomarkers [29].

Fig-leaf gourd seeds (*Cucurbita ficifolia*)

In Central Europe, dietary supplements based on pumpkin seeds (*Cucurbita pepo*), almonds (*P. dulcis*), and honey are marketed to treat bladder and prostate problems and are used in the Caribbean region. Hydroethanolic extracts of the seeds have shown activities related to urinary incontinence, micturition frequency, and nocturia. However, in the Andean region, within the cucurbit family, one of the most abundant species is *Cucurbita ficifolia*, traditionally known as sambo fruit [30], hence our interest in investigating the possible effects of this species on prostate cancer[31], along with the two components of the mixture and their contribution to prostate-related problems.

C. ficifolia is native to Mesoamerica and the mountainous regions of Latin America (Figure 1b). It is the most widespread cucurbit in temperate and cold areas. According to Álvarez[32], the largest producer of sambo in Ecuador is the province of Bolívar, with a production of 1015 fruits per year, followed by Pichincha (852 fruits), Tungurahua (133 fruits), Imbabura (75 fruits), and finally, Cotopaxi with the lowest production of 27 fruits. Traditionally, sambo has been used to relieve gastrointestinal disorders, hemorrhoids, fever [33], and

urinary tract problems. Its compounds' antioxidant and anti-inflammatory activities [34] could explain its effectiveness in cancer.

C. ficifolia is a natural source abundant in bioactive compounds like carotenoids, tocopherols, phenols, terpenoids, saponins, sterols, fatty acids, and functional carbohydrates. These components offer significant biological benefits and are increasingly being applied in biotechnological fields[35]. *C. ficifolia* oil is rich in unsaturated fatty acids, including linoleic and oleic acids, and contains valuable compounds such as phenolic acids, carotenoids, tocopherols, phytosterols, and squalene [36]. A study examined the anticancer effects of *C. ficifolia* extract on human breast cancer cells (MCF-7). The extract was tested at different concentrations, and the IC_{50} value was determined to be 90 µg/mL. Treated cells showed chromatin condensation and nuclear fragmentation changes, indicating apoptosis. The extract also increased the expression of tumor suppressor genes like p53 and apoptotic markers, leading to programmed cell death. The findings suggest that *C. ficifolia* extract inhibits cell division and induces apoptosis, highlighting its potential as an anticancer agent through gene modulation[37].

C. ficifolia and almonds contain unsaturated fatty acids, mainly oleic and linoleic acids. Research has shown that these fatty acids can inhibit prostate growth and decrease its size. Foods rich in oleic acid (**5**) (Figura 2) have antiproliferative and anticancer effects on colon carcinoma cells[11]. However, a relationship has also been found between the increased incidence of prostate cancer and a diet rich in linoleic acid (**6**) (Figure 2). Huerta-Yépez et al. [38] reported that the ratio of omega-3 to omega-6 fatty acids might be more significant for prostate cancer risk than the overall amount of these fatty acids consumed. Therefore, it is suggested that the recommended dietary ratio of omega-3/omega-6 fatty acids be maintained at 1:1 to 2:1.

There are no clinical studies in humans investigating the effect of *C. ficifolia* on cancer. However, in a population of 1,403 men, all over the age of 50, the effectiveness of pumpkin seed oil (*Cucurbita pepo*) was evaluated. It was observed that phytomedicines with a concentration greater than 50% pumpkin seed extract produced a slight reduction in the International Prostate Symptom Score (IPSS). This reduction showed a low level of heterogeneity but was not clinically significant. Additionally, the phytomedicine showed a positive effect on reducing prostate symptoms compared to a placebo, although this improvement was modest and documented in only one study. Based on this information, it is necessary to conduct human studies on *C. ficifolia* [39].

Soriano-Hernandez et al. reported that high consumption (28 grams at least once a week) of almonds, nuts, or peanuts reduces the risk of breast cancer by 2 to 3 times [40]. However, Balali et al. concluded that there is no significant association between the consumption of nuts and the risk of prostate cancer at any stage, suggesting that more studies are needed[41]. Compounds such as polyphenols present in almonds and sambo seeds, which include flavonoids, stilbenes, and phenolic acids[12,26,28,36,42], have demonstrated antioxidant and anti-inflammatory activity that can be beneficial in cancer prevention, as mentioned by Matsushita et al. [43] . Morin, present in almonds, is a bioflavonoid that suppresses the inflammatory process leading to carcinogenesis. Solairaja et al.[44] provided strong evidence of its anticancer role and potential as a therapeutic agent in various cancers, including prostate cancer[44]. Carotenoids are compounds with cytotoxic and antiproliferative potential, making them possible candidates for chemoprevention and chemotherapy of breast, colorectal, lung, and prostate cancer, as noted by Saini et al.[45] due to their antioxidant properties, tocopherols, especially γ-tocopherol, are compounds present in foods that can help reduce the risk of prostate cancer al. [45,46]. Betulinic acid, extracted from almonds, has been found to have antiproliferative activity. Jiang et al. proposed that this compound has the potential for research and application in current tumor diseases. Furthermore, evaluating the effectiveness of almonds in vitro studies on cell lines such as MCF7 and HepG2 suggests the possibility of studying them on prostate cancer cell lines, expecting similar results [47].

Pumpkin seed oil appears to have a more significant effect than the seeds in reducing prostate enlargement. The carotenoids in pumpkin seeds act as powerful antioxidants, halting the growth of cancerous cells. Omega-3 fatty acids have been studied for their potential benefits to prostate health. Pumpkin seeds may inhibit the production of DHT, which tends to worsen prostate enlargement. Additionally, they are a zinc source, inhibiting the multiplication of prostate cancer cells and preventing cellular damage. Pumpkin seeds are a natural

source of B vitamins and vitamins C, D, E, and K. Minerals found in them include calcium, potassium, and phosphorus [48–54].

In one study, treatment with 320 mg/day of pumpkin seed oil for 12 months improved the quality of life and reduced BPH symptoms in 16 subjects. Therefore, pumpkin seed oil appears to be a promising option for treating BPH symptoms, but further research in larger populations is needed [55]. In another study, the impact of pumpkin seed oil on testosterone-induced prostatic hyperplasia in rats was demonstrated. Oral intake of pumpkin seed oil at a dose of 2 mg/g body weight for 20 days significantly suppressed induced prostate enlargement. This showed that pumpkin seed oil influences enzymes involved in the processing of various endogenous steroids, helping to prevent the conversion of testosterone into DHT.

Additionally, this oil helps relax the bladder sphincter in patients with urination difficulties. Moreover, pumpkin seed extract and β-sitosterol found in seeds have shown the potential to improve urinary symptoms and reduce the growth of prostate cancer cells. It is suggested that the phytoestrogens and unsaturated fatty acids in pumpkin seed oil are responsible for these effects [56].

Bee Honey (*Apis mellifera*)

Honey is a natural product made by honeybees from the nectar of different flowering plants. Honeybees consist of 11 species, genus *Apis*, with *Apis mellifera* as the most extensive species in the world. Honey is primarily produced from the species *A. mellifera*. Figure 1 shows the estimated global distribution of this species. It is composed of a sugar solution in combination with minerals, vitamins, enzymes, free amino acids, flavoring agents, and several volatile organic compounds [57.] The physicochemical characteristics of honey are a function of multiple variables, including the botanical origin of the nectar, the bee species, the geographical conditions (climatic and edaphic), and the post-harvest handling procedures [57.] In this review, we will focus on identifying the biological activities related to prostate cancer in sambo almond seeds and honey, these agents in the prevention and treatment of the disease.

Bee honey contains many flavonoids, known for their anti-inflammatory and antioxidant properties[42]. A positive correlation has been observed between the phenolic compound content in honey, particularly chlorogenic acid, and its antioxidant properties. In vitro studies demonstrate that phenolic acids and flavonoids affect TNF and NO activity. Furthermore, honey exhibits antimetastatic, antiproliferative, anticancer, and chemotherapeutic effects [58].

Honey from bees has anti-inflammatory, antioxidant, antimetastatic, antiproliferative, anticancer, and chemotherapeutic effects. This food stands out for its quantity of phenolic compounds that affect the activity of TNF and NO[42,58]. Z seeds have been used to prevent and reduce prostate growth, and anti-inflammatory and antioxidant properties have been discovered in this food[11,59]. Compounds from almonds and pumpkin seeds can delay cell cycle progression, induce apoptosis, inhibit tumor growth and metastasis, reduce oxidative stress, and decrease the side effects associated with chemotherapy[11]. Sambo seeds have been used to prevent prostate cancer [35,36,59], and it has been observed that the oil from these seeds decreases the International Prostate Symptom Scores (IPSS) by 41.1%[19]. Almonds can induce apoptosis and inhibit the proliferation of tumor cells in prostate cancer[19,24]. Almonds act as a prebiotic, increasing the amount of bifidobacteria and lactobacillus, which is beneficial in cancer prevention[12].

The role of honey in cancer has demonstrated antimetastatic, antiproliferative, anticancer, and chemotherapeutic effects of its phenolic compounds. However, evidence also suggests a direct link between sugar and cancer, as high sucrose or fructose diets activate inflammation [60]. According to Castillo-Martínez et al.[61], the average concentration of fructose and glucose is 36.4 and 28.9 g/100 g for *A. mellifera* honey.

Some human studies have indicated that natural honey may interact with specific isoenzymes of the cytochrome P450 system, which are crucial for metabolizing many antineoplastic drugs. It has been found that regular consumption of honey might increase the activity of the CYP3A4 enzyme without affecting others like CYP2D6 or CYP2C19. This suggests that honey could alter the efficacy of drugs metabolized by CYP3A4. However, another clinical study found that daily honey consumption did not affect the activity of CYP3A4 or

P-glycoprotein, which acts as an efflux pump for various drugs. Acacia honey (ACH), produced by *A. mellifera* feeding on acacia flowers, has shown antiproliferative properties. A study by Aliyu et al. assessed these effects on prostate cancer cells (PC-3), and the MTT assay results indicated IC_{50} values of 1.9% for PC-3 cancer cells and 3.7% for normal NIH/3T3 cells. Conversely, a study by Tsiapara and colleagues analyzed the viability of PC-3 cells and found significant differences in the effects of various honey extracts, highlighting that only thyme honey significantly reduced cell viability. Based on current evidence, natural honey and its bioactive components may have anticancer effects through various mechanisms. However, these mechanisms are not yet fully understood. Some studies suggest that honey's anti-inflammatory and antioxidant properties might help prevent cancer initiation, promotion, and progression. Future research could clarifyoney's anti-cancer role, allowing for more specific and safe use in treating cancer patients [62].

Excessive sugar consumption is a recognized risk factor for increased body fat, obesity, and cardiometabolic disorders, which in turn elevate the risk of developing various types of cancer. Obesity contributes to the disruption of several hormonal pathways, leading to increased levels of insulin, estradiol, and inflammatory cytokines while decreasing levels of adiponectin, testosterone, and sex hormone-binding globulin [63–66]. It was found that diabetes is inversely associated with the incidence of prostate cancer [67].

It has also been suggested that sugars (monosaccharides and disaccharides) are associated with other cancer risk factors, including prostate cancer, through IGF-1-mediated inflammation[64,66], such as oxidative stress and inflammation or insulin resistance. In their latest report, the World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR) concluded that the available evidence was insufficient to link sugar with cancer. Few studies have explored the associations between sugars and prostate cancer. In the present human study, no significant association was found between sugar intake and prostate cancer [64].

High sugar consumption is linked to the onset of low-grade chronic inflammation, which may increase the risk of autoimmune diseases. Glucose can affect the immune system through B cell proliferation and T cell regulation. It has also been observed that glucose supports the development of B lymphocytes and protects them from apoptosis via the mTOR pathway, while fructose does not appear to have the same effect [68]. Therefore, sugar consumption should be limited in cancer compared to healthy tissue; tumor cells consume and transport more glucose and amino acids, while mitochondrial respiration is reduced. This leads to an increase in glycolysis and lactic acid production. Depending on the type of cell and the oncogenes involved, there is also more significant activity in the pentose phosphate pathway, increased de novo nucleotide synthesis, and higher synthesis of proteins, ribosomes, and fatty acids [69].

Prostate cancer prevention of combination of *P. dulcis, C. ficifolia* and *Apis mellifera*

The Mediterranean diet, characterized by olive oil and high consumption of fiber, fish, fruits, vegetables, legumes, and grains, with moderate to low consumption of dairy products and moderate wine intake, is a diet rich in antioxidants that can prevent prostate cancer [70]. The Sustainable Development Goal (SDG) 3, 'Good Health and Well-being,' aims to ensure healthy lives and promote well-being. Prostate cancer is directly linked to this goal, as it represents one of the leading causes of death in older men. Working on the prevention of prostate cancer is key to reducing mortality, improving quality of life, and reducing inequalities in access to early diagnosis and treatments, particularly in countries with fragile healthcare systems [71]. A risk factor for prostate cancer is excessive energy intake, often related to high consumption of saturated fatty acids (SFAs) and sugars and low intake of complex carbohydrates, polyunsaturated fatty acids (PUFAs), fruits, and vegetables.

Additionally, certain food products (such as processed and smoked meats) may be sources of carcinogenic compounds (polycyclic aromatic hydrocarbons, N-nitroso compounds, and heterocyclic aromatic amines), which can initiate and promote prostate carcinogenesis. A diet rich in antioxidants and other nutrients, such as oleic acid, has anticancer properties [72]. In addition to these findings, this review underscores the promising potential of natural compounds found in Zambo seeds (*Cucurbita ficifolia*), almonds (*Prunus dulcis*), and honey as complementary treatments in the context of cancer, particularly prostate cancer. The bioactive components, such as linoleic and oleic acids, vitamins, pigments, and polyphenols, demonstrate significant

antiproliferative and apoptotic activities against prostate cancer cells, suggesting a synergistic effect when consumed together. These foods can be part of the Mediterranean diet adapted to local customs.

Table 1 presents the nutritional composition of almonds and sambo seeds. The nutrient amounts detailed below are per 100 g of food. Nutritional values from the Food Composition Tables of Peru, Colombia, Ecuador, and INCAP were compared. Fats are the predominant nutrient in sambo seeds and almonds; they also contain many minerals, almost doubling the amount in almonds except for calcium. Combining honey with almonds and sambo seeds is beneficial because the consumption of honey in adequate quantities, due to its flavonoid content, combined with foods rich in saturated fatty acids, allows for synergy between anti-inflammatory components.

Nutrient	Almond			Sambo Seeds	
	INCAP [a]	**Peru [b]**	**Colombia [c]**	**INCAP [a]**	**Ecuador [d]**
Ash (g)	3.02	3.2	1.4	4.37	-
Moisture (g)	4.47	5.1	12	7.1	-
Protein (g)	21.94	23.4	18.6	32.07	24.5
Fat (g)	50.62	54.1	54.1	42.13	46.00
Carbohydrate (g)	19.94	14.3	13.9	13.43	12.5
Calcium (mg)	216	195	228	43	-
Iron (mg)	3.72	3.72	3.4	14.94	15
Zinc (mg)	3.12	3.12	3.1	7.44	-
Magnesium (mg)	275	-	271	534	-

[1] Note. a (INCAP & OPS, 2012) [73]. b (MINSA, 2017) [74]. c (Instituto Colombiano de Bienestar Familiar, 2018) [75]. d (Herrera et al., 2021) [76].

Table 1. Nutritional Composition of Almond (*P. dulcis*) and Sambo Seeds (*C. ficifolia*)

Honey, being a food rich in sugar, should be consumed in moderation. The WHO recommends reducing the intake of free sugars, whether added or from natural sources such as fruit juices, honey, and syrups, to 5% of total daily caloric intake [77]. However, due to its bioactive compounds related to cancer, for a 2000 kcal daily diet, it is suggested that honey consumption be limited to 25 grams of sugar or about two tablespoons. No more than two tablespoons per day. Including nuts and seeds in the diet is beneficial because essential fatty acids are also provided apart from the bioactive compounds in these three foods.

Unsaturated fatty acids, abundant in fish and vegetable oils, reduce the risk of prostate cancer. Diet influences the gut microbiome, and dysbiosis can lead to prostate cancer. The gut-prostate axis is essential for prostate cancer prevention. Promoting prebiotics and/or probiotics can foster beneficial gut bacteria that may reduce the risk of developing prostate cancer [78,79,80]. Almonds and Sambo seeds, due to their rich nutritional composition and bioactive components, are crucial in preventing cancer. These foods are rich in unsaturated fatty acids and fiber, contributing to intestinal health. The high fiber content in these seeds supports a healthy gut microbiome, promoting beneficial bacteria that can play a role in reducing inflammation and potentially lowering cancer risk. Consumption of almonds and almond skins can enhance the profile of the intestinal microbiota and alter intestinal bacteria's activities, promoting health-beneficial factors and suppressing harmful ones [80]. This integrative approach aligns with the growing trend towards personalized nutrition and medicine, where diet and lifestyle play pivotal roles in disease management and prevention.

Figure 3 shows the primary mechanisms by which the combination of the three components inhibits cancer development, according to the hallmarks of a tumor cell. The three components primarily act by inhibiting inflammatory processes and inducing apoptosis in tumor cells, decreasing their ability to survive and proliferate.

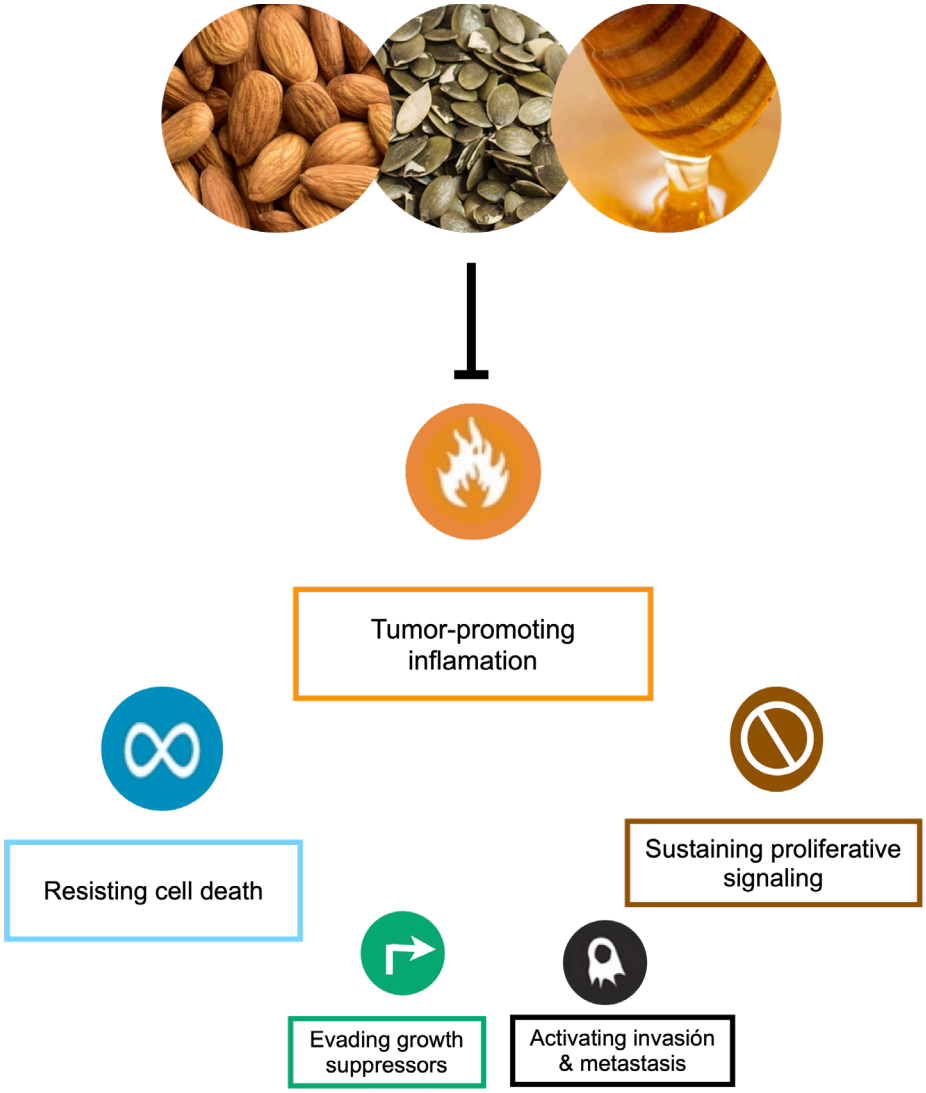

Figure 3. The mixture of almonds, sambo, and honey on tumor cells modulates the main hallmarks of tumor cells.

The findings of this review emphasize the promising potential of natural compounds found in sambo seeds (*C. ficifolia*), almonds (*P. dulcis*), and honey as complementary agents in cancer management, particularly pros-tate cancer. The bioactive components, such as linoleic and oleic acids, vitamins, pigments, and polyphenols, exhibit notable antiproliferative and apoptotic effects on prostate cancer cells, suggesting a synergistic impact when consumed in combination. Among the analyzed articles, bioactive compounds against cancer were con-sistently reported in both sambo seeds and almonds, with almonds receiving more extensive mentions. These findings indicate that both sambo seeds and almonds hold potential as agents for the prevention and treatment of cancer.

However, while the bioactive compounds in honey, particularly flavonoids, show potential benefits, the effectiveness of honey in cancer and inflammation management remains controversial. This is due to the direct association between high-sucrose or fructose diets and adverse health outcomes, given honey's high content of these sugars.

Despite the positive findings, it is critical to acknowledge the limited research on *C. ficifolia*, particularly when compared to other cucurbit species such as *Cucurbita pepo*. This gap highlights the need for more extensive scientific exploration. Future research should prioritize robust clinical trials to confirm the efficacy and safety

of these natural compounds in cancer therapy. Investigating the molecular mechanisms behind their anticancer effects could offer valuable insights into their therapeutic potential.

Advancing research in this area is essential to integrate natural compounds with conventional cancer therapies, potentially enhancing treatment effectiveness, reducing adverse effects, and improving patient outcomes. Such an integrative approach resonates with the growing emphasis on personalized medicine and nutrition, where dietary and lifestyle interventions play key roles in disease management and prevention. While this review establishes the groundwork for understanding the potential benefits of sambo seeds, almonds, and honey in cancer therapy, it also paves the way for future research opportunities. Expanding knowledge in this field is scientifically enriching and vital for advancing public health and innovative cancer treatment strategies.

CONCLUSIONES

The reviewed articles highlight the presence of bioactive compounds with anticancer properties in both sambo seeds and almonds, with almonds receiving more frequent mentions. These beneficial effects suggest that both foods could serve as preventive and therapeutic agents against cancer. However, while flavonoids in honey show potential benefits, their overall effectiveness in cancer and inflammation remains debatable due to the direct link between high-sucrose or fructose diets and the high sugar content in honey. This underscores the need for further research to clarify these effects and establish guidelines for their use in cancer therapy.

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