Scientia Pharmaceutica

Review

A Review of the Biological Properties of Purple Corn (*Zea mays* L.)

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Abstract: In the food and beverage industries, replacing synthetic colorants with plant-based colorants has become popular in recent times. Purple corn (*Zea mays* L.) is an important source of natural colorants due to its range in color from orange to purple. The whole plant of purple corn has a high amount of anthocyanin content. Anthocyanin is the water-soluble pigment found in various fruits and vegetables. The color pigments are chiefly found in the pericarp or kernels, in addition to corn cobs. Purple corn is rich in various health-promoting compounds, mainly anthocyanins such as cyanidin-3-*O*-glucoside, perlagonidin-3-*O*-glucoside, peonidin 3-*O*-glucoside, and their malonylated forms. This review emphasized recent updates regarding the in vitro and in vivo biological properties of extracts and compounds from purple corn. Purple corn color extracts possess a variety of biological properties, including antioxidant, anti-inflammatory, anticancer, anti-diabetic, anti-obesity, etc. The results of in vitro and in vivo studies of the biological properties of purple corn could lead to the development of different health-promoting products in the near future.

Keywords: purple corn; anthocyanins; biological activity; corn kernels; cyanidin-3-*O*-glucoside; phenolics

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Citation: Kim, H.Y.; Lee, K.Y.; Kim, M.; Hong, M.; Deepa, P.; Kim, S. A Review of the Biological Properties of Purple Corn (*Zea mays* L.). *Sci. Pharm.* **2023**, *91*, 6. https://doi.org/10.3390/scipharm91010006

Academic Editor: Matthias Hamburger

Received: 3 December 2022
Revised: 9 January 2023
Accepted: 13 January 2023
Published: 19 January 2023

1. Introduction

Purple corn (*Zea mays* L.) is an annual grass that belongs to the family of Poaceae. It is a group of flint maize varieties (*Z. mays* var. *indurata*; also called Indian corn or calico corn) descended from a common ancestral variety termed "k'culli" in Quechua. Purple corn originated in Peru and is now widely distributed in the markets of Asia, the United States, and Europe. The cob and pericarp of the purple corn grain contain a concentrated purple color (Figure 1). The colored corn is extensively used in the preparation of traditional drinks and desserts [1,2]. Purple corn is extensively utilized in the food and pharmaceutical industries due to the presence of various bioactive compounds [3]. In recent times, several studies have focused on purple corn varieties due to their rich source of anthocyanin pigments in the aleurone or pericarp with well-known health-promoting properties. In addition, the natural pigment is used in the food industry for coloring beverages, jellies, and candies [4,5].

Anthocyanins are water-soluble pigments from the phenolic family. They are glycosylated polyhydroxy or polymethoxy derivatives of 2-phenylbenzopyrilium. Anthocyanins are composed of a basic C6–C3–C6 skeleton. Numerous anthocyanin components have been isolated from different plant species [6,7]. Further, these components have a variety of colors depending on pH, temperature, and light intensity [8]. In purple corn, anthocyanins impart different color profiles, from dark purple to red [9]. Previous studies demonstrated the chemical composition obtained from kernel, cob, husk, and silk extracts of purple corn [10–12]. Figure 2 illustrates the biosynthesis pathways of anthocyanins in corn.

Figure 1. Kernels of purple corn.

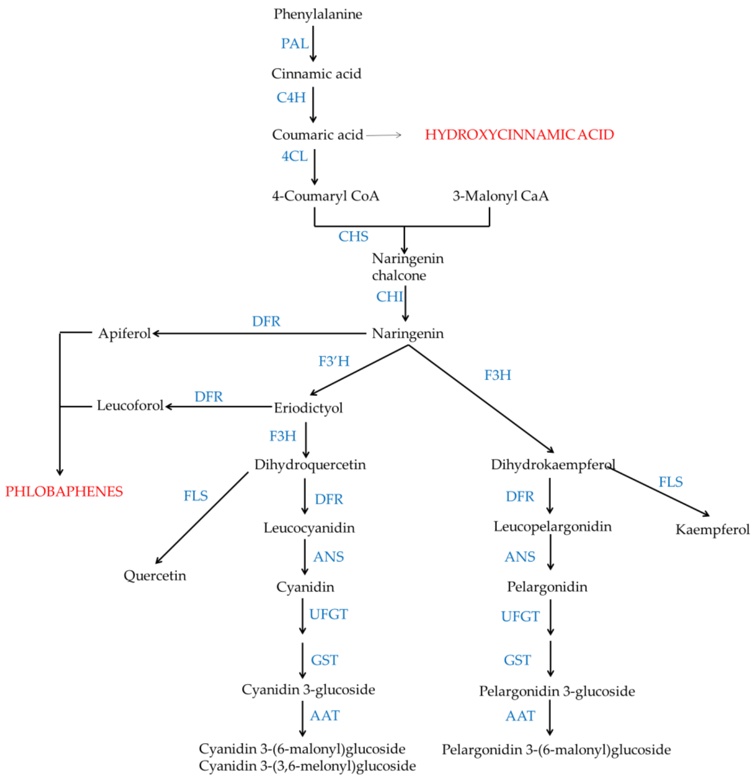

Figure 2. The biosynthesis pathways of anthocyanins in corn. AAT, anthocyanin acyltransferase; ANS, anthocyanidin synthase; 4CL, 4-coumaroyl; C4H, cinnamate 4-hydroxylase; CHS, chalcone synthase; CHI, chalcone isomerase; DFR, dihydroflavonol 4-reductase; F3H, flavanone 3-hydroxylase; F3′H, flavonoid 3′-hydroxylase; FLS, flavonol synthase; GST, glutathione S-transferase; PAL, phenylalanine ammonia lyase; UFGT, flavonoid 3-*O*-glucosyltransferase.

The extracts of purple corn contain six major anthocyanin compounds such as cyanidin-3-*O*-β-D-glucoside, pelargonidin-3-*O*-β-D-glucoside, peonidin-3-*O*-β-D-glucoside, cyanidin-3-*O*-β-D-(6-malonyl-glucoside), pelargonidin-3-*O*-β-D-(6-malonyl-glucoside), and peonidin-3-*O*-β-D-(6-malonyl-glucoside). Among them, cyanidin 3-*O*-β-D-glucoside is the major anthocyanin found in purple corn [10,13,14]. In addition, some other derivatives such as catechin-(4,8)-pelargonidin-3,5-di-*O*-glucoside, afzelechin-(4,8)-pelargonidin-3,5-di-*O*-glucoside, cyanidin-3-*O*-succinylglucoside, and cyanidin-3,5-di-*O*-glucoside have been identified in purple corn [1,11,15].

The anthocyanin-rich extracts obtained from purple corn exhibit potent antioxidant activities [16–18]. Previous studies reported that purple corn extracts also have various pharmacological properties such as being anti-inflammatory [19], anti-carcinogenic [20,21], and anti-angiogenic [22], in addition to ameliorating obesity [23] and diabetes-related complications [24,25].

The present review aimed to describe the biological properties of purple corn in both in vitro and in vivo studies. For this purpose, a literature search was performed to retrieve information regarding the biological activities of purple corn from different websites, including PubMed, Science Direct, MDPI, Google Scholar, and others. The collection of literature was restricted to publications in the English language. The search for the literature collection was carried out until November 2022.

2. In Vitro Biological Activities of Purple Corn

Purple corn color is a widely utilized food colorant that is reported to have a number of therapeutic uses. The in vitro biological activities of extracts and compounds obtained from purple corn are presented in Figure 3 and Table 1.

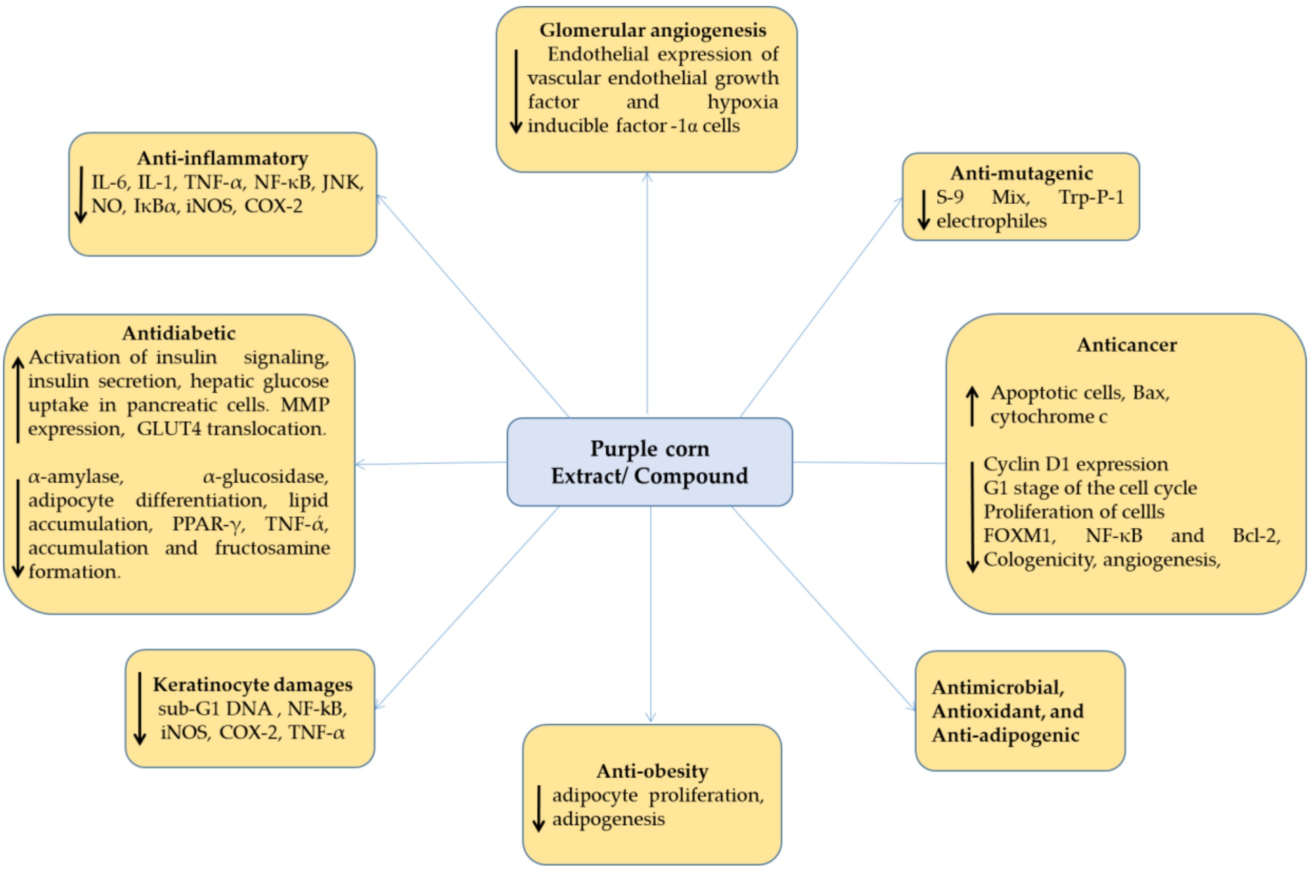

Figure 3. In vitro biological properties and mechanisms of purple corn.

Table 1. In vitro biological properties of extracts and compounds from purple corn.

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
Antioxidant activity	Free phenolic fractions	Andean region, Arequipa	DPPH and ABTS assays	Radical scavenging activity	[26]
	Methanol water extract	Cajamarca, Peru	DPPH, ABTS, FRAP, and deoxyribose assays	Radical scavenging and antioxidant activities	[27]
	Water extract	Beirut, Lebanon	DPPH, FRAP and cupric-reducing antioxidant capacity assays	Radical scavenging and antioxidant activities	[4]
	Methanol extract from corn silk and corn cob	Khon Kaen University, Thailand	DPPH and TEAC radical scavenging assays	Radical scavenging and antioxidant activities	[28]
	Waxy purple corn cob ethanol extract	Khon Kaen University, Thailand	ABTS radical scavenging assay	Radical scavenging activity	[29]
	Free phenolic compounds	Lima, Peru	ABTS and ORAC methods	Radical scavenging and antioxidant activities	[30]
	Ethanol extract	Khon Kaen University, Thailand	TEAC, FRAP, ORAC assays	Antioxidant activity	[31]
	Methanol extract	Ministry of Agriculture and Forestry Maize Research Institute, Republic of Turkey	DPPH assay	Radical scavenging activity	[32]
	Purple corn	New Delhi, India	DPPH and ABTS assays	Radical scavenging activity	[33]
	Pigment (Ver 42 genotype)	Texcoco, Mexico	ABTS, peroxy radical absorbance capacity	Radical scavenging and antioxidant activities	[34]
	Ethanol extract	Beijing, China	DPPH assay	Radical scavenging activity	[35]
	Water and ethyl acetate fractions	Lima, Peru	DPPH assay	Radical scavenging activity	[36]
	Aqueous and ethanol extracts	Mexico	Nitric oxide and oxyradical-scavenging activity	Radical scavenging activity	[37]
	Ethanol extract	Sun Valley, CA, USA	DPPH assay	Radical scavenging activity	[38]
	Extract corn cob	Spain	DPPH, ABTS and FRAP assays	Radical scavenging and antioxidant activities	[39]
	0.3% purple corn pigment	Guiyang, China	DPPH, superoxide anion and hydrogen peroxide activities	Radical scavenging and antioxidant activities	[40]
	Purple corn pigment	Milan, Italy	DPPH and TEAC assays	Radical scavenging and antioxidant activities	[5]
	Fresh purple waxy corn	National Institute of Crop Science, Republic of Korea	DPPH, FRAP, ABTS, and CHE assays	Radical scavenging and antioxidant activities	[17]
	Anthocyanin purified extracts waxy purple corn cob	Khao Tha Phra, Thailand	DPPH and FRAP assays	Radical scavenging and antioxidant activities	[41]
	Methanol extract from the seed and cob	Anhui Province, China	DPPH, FRAP and TEAC assays	Radical scavenging and antioxidant activities	[42]

Table 1. *Cont.*

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
	Extract husk and cobs of the Seakso 1	Chuncheon, Republic of Korea	DPPH and ABTS assays	Radical scavenging activity	[43]
	Anthocyanin-rich purple corn stover silage extract	Bang Kruai, Thailand	DPPH assay	Radical scavenging activity	[44]
	Andean purple corn cob	Sun Valley, CA, USA	DPPH assay	Radical scavenging activity	[38]
	Anthocyanins	Osaka, Japan	DPPH assay	Radical scavenging activity	[45]
	Ethanol extract	Braila County, Romania	DPPH assay	Radical scavenging activity	[46]
	Anthocyanin-rich husk ethanol extract	Chuncheon, Republic of Korea	BHT and EDTA	Antioxidative performance in mayonnaise during storage	[47]
	Purple waxy raw and thermal ethanol extract	Khon Kaen, Thailand	FRAP assay	Antioxidant activity	[16]
	Purple waxy corn	Khon Kaen province, Thailand	TEAC, FRAP, and ORAC	Radical scavenging and antioxidant activities	[48]
	0.3% purple corn pigment	Guiyang, China	Milk during storage	In light-protected milk, prevented lipid oxidation, enhanced antioxidant activity, maintained volatile compounds, and increased the sensory scores.	[40]
Anticancer	Purple corn color	Chiba, Japan	Androgen-dependent prostate cancer cell line, (LNCaP cells)	Decreased Cyclin D1 expression and inhibited the G1 stage of the cell cycle.	[49]
	Ethanol extract	Beijing, China	Human colorectal cancer cell, HT-29	Inhibited the proliferation of cells.	[50]
	Water extract	Swanson, CT, USA	Human colorectal cancer cells, HCT-116 and HT-29	Increased apoptotic cells and impacted on apoptotic markers such as BAX, Bcl-2, cytochrome c, and TRAILR2/D5. Inhibited the proliferation of cells by enhancing apoptosis and suppressing angiogenesis.	[21]
	Methanol extracts	Chorrillos-Lima, Peru	Human colorectal cancer cell, HT-29	Inhibited the proliferation of cells.	[51]
	Anthocyanin complex nanoparticle	Khon Kaen, Thailand	Cholangio carcinoma KKU213 cells	Induced apoptosis and the production of mitochondrial superoxide. Decreased clonogenicity and downregulated FOXM1, NF-κB and Bcl-2. Inhibited KKU214GemR cell proliferation.	[52]

Table 1. *Cont.*

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
Anti-diabetic activity	Free phenolic fractions	Southern Andes, Peru	α-Amylase and α-glucosidase enzymes	Inhibited α-amylase activity. No effect on α-glucosidase activity.	[26]
	Aqueous and ethanol extracts	Mexico	Yeast α-glucosidase activity	Inhibited α-glucosidase activity.	[37]
	Free phenolic compounds	Lima, Peru	α-Glucosidase and α-amylase assay	Inhibited α-glucosidase and α-amylase activities.	[30]
	Ethanol extract	Beijing, China	α-Glucosidase activity	Inhibited α-glucosidase activity.	[35]
	Water extract from purple corn pericarp, pure cyanidin-3-*O*-glucoside, pelargonidin-3-*O*-glucoside, peonidin-3-*O*-glucoside	Irvine, CA, USA	The 3T3-L1 cells	Prevented adipocyte differentiation, lipid accumulation, and reduced PPAR-γ transcriptional activity. Ameliorated TNF-α-induced inflammation and insulin resistance in adipocytes through the activation of insulin signaling. and enhanced GLUT4 translocation.	[53]
	By product extract	Milan, Italy	BSA-methylglyoxal, glucose, fructose, and ribose systems. α-amylase and α-glucosidase	Inhibited the accumulation of advanced glycation end products. Inhibited fructosamine formation and exhibited anti-glycative properties.	[54]
	Anthocyanins	Angelina's Gourmet, Swanson, CT, USA	HepG2 cells	Enhanced insulin secretion and hepatic glucose uptake in pancreatic cells and hepatocytes by activating free fatty acid receptor-1 and glucokinase.	[55]
	Ethanol extract	Zana Export Co. (Lima, Peru)	HIT-T15 cells	Protected pancreatic β-cell death	[56]
	Anthocyanins	Chuncheon, Republic of Korea	High-glucose induced human renal mesangial cell	Boosted membrane type-1 MMP expression and dampened MMP-2 expression through disturbing transforming growth factor β–SMAD signaling, facilitating extracellular matrix degradation. Dampened NF-κB translocation.	[57]

Table 1. *Cont.*

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
	Ethanol extract of the kernel from purple corn. 7 nonanthocyanin phenolic compounds and 5 anthocyanins	Seoul, Republic of Korea	Rat lens aldose reductase (RLAR) inhibitory assays. Kinetic analyses of recombinant human aldose reductase (rhAR)	Hirsutrin showed the most potent RLAR inhibitory activity. Competitive inhibition against rhAR. Hirsutrin inhibited galactitol formation in rat lens and erythrocytes sample incubated with a high concentration of galactose. Prevented osmotic stress in hyperglycemia.	[58]
	Ethanol extracts	Seoul, Republic of Korea	Human renal mesangial cells	Activated interleukin-8 by eliciting Tyk2-STAT signaling pathway.	[59]
Anti-inflammatory effects	Anthocyanins from purple waxy corn cob	Khon Kaen University, Thailand	LPS-stimulated RAW 264.7 cells	Reduced expression of IL-6, IL-1, and TNF- mediators. Inhibited NO production.	[19]
	Cyanidin-3-*O*-glucoside; peonidin-3-*O*-glucoside; pelargonidin-3-*O*-glucoside; anthocyanin-rich extracts	Genay, France	RAW264.7 cells and 3T3-L1 pre-adipocytes	Inhibited the activation of NF-κB and JNK pathways by regulating the phosphorylation of IκBα and JNK. Restored inflammation-mediated oxidative stress and insulin resistance in adipocytes.	[60]
	Proanthocyanidins	Swanson, CT, USA	iNOS and COX-2 activities	Inhibited iNOS and COX-2 activities.	[61]
Inhibitory activity	Extract husk and cobs of the Seakso 1	Chuncheon, Republic of Korea	α-amylase and α-glucosidase assay	Inhibitory activity of α-amylase and α-glucosidase	[43]
	Seakso 1 corn husk and cob extracts	Korea	Pancreatic lipase activity and adipocyte differentiation in 3T3-L1 cells.	Inhibited measured adipocyte differentiation and lipid accumulation. Decreased the mRNA expression and protein level of obesity-related factors—PPARγ and CCAAT (C/EBPα).	[62]
	Free phenolic compounds	Lima, Peru	Lipase enzyme activity	High lipase inhibitory activity	[30]
Oxidative stress	Methanol water extract	Cajamarca, Peru	CAT, TPX, SOD, and TBARS levels in albino male mice organs	Increased the levels of endogenous enzymes such as SOD, CAT, and TPX and decreased MDA formation	[27]
Antimicrobial activity	Free and bound phenolic fractions	Lima, Peru	*Lactobacillus helveticus* and *Bifidobacterium longum* and *Helicobacter pylori*	Beneficial probiotic lactic acid bacteria such as *L. helveticus* and *B. longum* were not inhibited by the free and bound phenolic fractions.	[63]
	Ethanol extracts	Beijing, China	*Salmonella enteritidis*, *Staphylococcus aureus*, and *Candida albicans*	Strong antimicrobial activity	[50]

Table 1. *Cont.*

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
Anti-mutagenic activity	Water and ethyl acetate fraction	Lima, Peru	Ames test	Blocked the S-9 mix and scavenged Trp-P-1 electrophiles.	[36]
Glomerular angiogenesis	Ethanol extract	Seoul, Republic of Korea	High-glucose-induced human endothelial cells	Decreased endothelial expression of vascular endothelial growth factor and hypoxia inducible factor—1a cells. Attenuated the induction of the endothelial marker of platelet endothelial cell adhesion molecule—1 and integrin b3. Endothelial tube formation promoted by anthocyanin-rich purple corn extract was disrupted in the presence of purple corn extract.	[22]
Anti-adipogenic	Water extract	Siskiyou Seeds, Williams, AZ, USA	Mouse cell lines (3T3-L1 pre-adipocytes and RAW264.7 cells)	Downregulated pro-inflammatory mediator production, modulated diabetes-related key enzymes, and improved insulin sensitivity.	[64]
Collagen production	Anthocyanins from silk of purple waxy corn	Khon Kaen University, Thailand	Human skin fibroblasts	Stimulated collagen production due to the amount of melatonin in the silk extracts.	[65]
Rumen fermentation	Anthocyanin-rich purple corn stover silage	Bang Kruai, Thailand	Ruminal fluid was obtained from goats before morning feeding	Better silage fermentative quality. Higher levels of crude protein and high yield of dry matter.	[44]
Anti-obesity	Slk water extract	Khon Kaen, Thailand	Murine 3T3-L1 cell line	Inhibited adipocyte proliferation and adipogenesis. Induced lipolysis and apoptosis at high concentration.	[66]
Maintain unsaturated fatty acid level	0.3% purple corn pigment	Nanjing, China	During milk storage	Maintained unsaturated fatty acid concentrations in milk during the storage period.	[67]
Keratinocyte damages	Purple corn silk propylene glycol extract	Khonkaen province, Thailand	UVB-induced cell death in HaCaT cells	Decreased the sub-G1 DNA content. Attenuated NF-kB activity by suppressing NF-kB nuclear translocation and protein expression. Decreased c-Jun phosphorylation and decreased proinflammatory cytokines, iNOS and COX-2 levels in UVB-treated cells.	[68]

Table 1. *Cont.*

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
	Ethanol extract	Gangwon-do, Republic of Korea	HaCaT cells	Suppressed TNF-α induced NF-κB activation.	[69]

2.1. Antioxidant Activity

It is well known that antioxidants, mainly phenolic components, are considered for their potential to reduce the risk of various ailments. Further, these antioxidant compounds play a major role in the development of functional food products. A study found that purple corn extract obtained from a Peruvian Andean highland location registered a high 2,2-diphenyl-1-picrylhydrazyl (DPPH) antioxidant capacity [26]. Another study reported the antioxidant potential of 22 Peruvian corn samples using ABTS and ORAC assays [30]. Anthocyanins of purple corn extract obtained using methanol: water (80:20) acidified with 1% HCl (1 N) exhibited strong antioxidant activity in terms of DPPH, ABTS, FRAP, and deoxyribose assays [27]. Anthocyanin-rich water and ethyl acetate fractions of Andean purple corn showed antioxidant activities [36]. Aqueous extracts obtained from corn kernels scavenged nitric oxide (NO) and superoxide (O_2^-) at the concentrations of 0.25 mg/mL and 1.5 mg/mL, respectively [37]. Andean purple corn had a higher DPPH scavenging capacity [38].

Extracts of husks and cobs of Seakso 1 showed DPPH and ABTS radical scavenging activities [43]. Purple corn cob exhibited notable antioxidant activity in terms of DPPH, ABTS, and FRAP methods, and moderate xanthine oxidase inhibitory activity [39]. Xing-Zhou et al. [44] observed that anthocyanin-rich purple corn stover extract registered a higher DPPH scavenging activity during the storage period compared to that of sticky corn stover. The extracts from the seed and cob of Chinese purple corn showed considerable antioxidant activity using DPPH, FRAP, and TEAC methods [42]. Anthocyanin-rich extract from Thai waxy purple corn cobs exhibited DPPH scavenging and FRAP activities [41]. In light-protected milk, Tian et al. [40] found that anthocyanin-rich purple corn extract inhibited lipid oxidation, increased antioxidant capacity, maintained the level of volatile compounds, and increased sensory scores.

A previous study found that anthocyanin-rich colored grains such as red, purple, and black rice, purple corn, black barley, and black soybean showed antioxidant activity [35]. Trehan et al. [33] demonstrated that purple corn accessions registered higher total phenolic content and antioxidant activity (DPPH and ABTS) than yellow and white accessions. Among different corn varieties, the Veracruz 42 genotype contained the highest level of total phenolic and anthocyanin content and antioxidant potential, in addition to QR-inducing activity using the hepatoma cell line, Hepa 1 c1c7 [34]. Kano et al. [45] reported that the antioxidative activity of anthocyanins from the extract of purple sweet potato tuber exhibited stronger DPPH scavenging activity when compared with anthocyanins from red cabbage, grape skin, elderberry, and purple corn.

Simla et al. [28] reported that anthocyanin content, phenolic content, and antioxidant activity were found to be higher during the seed stage when compared with the edible stage. The developmental stage of the corn kernel highly influenced the anthocyanin content and antioxidant level of purple corn [17]. Saikaew et al. [31] found that variety and maturity highly influenced chemical composition and antioxidant activity (FRAP, TEAC, and ORAC assays) of purple waxy corns. The extract from the husk of purple corn registered the strongest antioxidative performance in mayonnaise during storage in terms of peroxide, *p*-anisidine, total oxidation, acid, and iodine values [47]. Harakotr et al. [16] found that steam cooking preserved the loss of more antioxidant compounds as compared to boiling. Another study reported that pressure treatment at 700 MPa registered strong antioxidant activity due to the higher amount of extractable total phenolic and anthocyanin contents [48].

2.2. Anticancer Activity

Cancer is the most important public health problem in developing and certain developed countries. Purple corn color extract exhibited antiproliferative activity against the androgen-dependent prostate cancer cell line, LNCaP, by downregulating Cyclin D1 expression and suppressing the G1 stage of the cell cycle. In addition, anthocyanin compounds identified from purple corn colors such as cyanidin-3-glucoside and pelargonidin-3-glucoside inhibited the proliferation of LNCaP cells [49]. A study indicated that anthocyanin-rich purple corn extract effectively inhibited the proliferation of human colon cancer cells (HCT-116 and HT-29 cells) by promoting apoptosis and suppressing angiogenesis [21].

Jing et al. [51] found that nonacylated monoglycosylated anthocyanins from purple corn showed a greater inhibitory effect on the proliferation of HT-29 cells. Further, anthocyanin extracts from Chinese purple corn exhibited an inhibitory effect on HT-29 cells with IC_{50} of 0.525 μg/mL [50]. Anthocyanin complex nanoparticles developed from the extracts of cobs of purple waxy corn and petals of the blue butterfly pea inhibited the proliferation of the cholangiocarcinoma cell line (KKU213), a deleterious bile duct tumor, by suppressing the forkhead box protein M1 (FOXM1), nuclear factor-κB (NF-κB), B-cell lymphoma-2 (Bcl-2), and the endoplasmic reticulum stress response, in addition to the induction of mitochondrial superoxide production. Further, the complex nanoparticle sensitized gemcitabine-resistant KKU214GemR cells [52].

2.3. Anti-Diabetic Activity

Diabetes is a chronic metabolic disease, and now about 3% of the world's population is affected by this disease. Purple corn from the Andean location showed α-glucosidase-inhibitory activity [26]. Another study showed that the ethanol extracts of corn inhibited yeast α-glucosidase activity [37]. Twenty-two Peruvian corn samples with five corn races were evaluated for hyperglycemia and obesity under in vitro conditions. The study revealed that a positive correlation was observed between the a-glucosidase and lipase inhibitory activities with anthocyanin content [30]. The inhibitory activity of extracts from the husks and cobs of Seakso 1 (10 mg/mL) against α-amylase and α-glucosidase was 95.86% and 76.92%, respectively [43]. However, Yao et al. [35] found that black rice had the highest α-glucosidase inhibitory activity over other colored grains, including purple corn. Aldose reductase inhibitors are one of the treatments used against diabetes complications without increasing the risk of hypoglycemia. Hirsutrin compounds isolated from the ethanol extract of purple corn kernels showed potent inhibitory activity against rat lens aldose reductase at IC_{50} of 4.78 μM by inhibiting galactitol formation in the rat lens. Based on these findings, the authors demonstrated that hirsutrin from purple corn kernels may effectively prevent osmotic stress in hyperglycemia [58].

In BSA-sugars and BSA-methylglyoxal assays, a Moradyn phytocomplex of corn and its purified anthocyanin fraction effectively inhibited the formation of fructosamine and exhibited antiglycative properties [54]. In 3T3-L1 adipocytes, anthocyanin-rich extracts and pure anthocyanins from purple corn pericarp ameliorated inflammation induced by TNF-α and insulin resistance by activating insulin signaling and enhancing GLUT4 translocation [53]. Luna-Vital and Mejia [55] investigated the effect of an anthocyanin-rich extract of purple corn pericarp on insulin secretion and hepatic glucose uptake in pancreatic cells and hepatocytes. The authors demonstrated that the anthocyanin-rich extract enhanced the activity of free fatty acid receptor-1 (FFAR1) and glucokinase (GK), and potentially ameliorated type-2 diabetes comorbidities. In a pancreatic beta cell line (HIT-T15) model, purple corn anthocyanins efficiently protected against cell death in HIT-T15 cell cultures [56].

Diabetic nephropathy is the major diabetic complication and the leading cause of end-stage renal disease. In human endothelial cells and THP-1 monocytes, purple corn extract antagonized the infiltration and accumulation of macrophages in diabetic kidneys by regulating the mesangial IL-8-Tyk-STAT signaling pathway [70]. Anthocyanin-rich purple corn and its butanol fraction attenuated the proliferation of high-glucose-promoted mesangial cell and matrix accumulation by regulating TGF-β–SMAD and NF-κB pathways [57,59].

2.4. Anti-Inflammatory Activity

Inflammation is a typical response to the injury of tissues. However, if uncontrolled, it leads to various complications. In adipocyte-macrophage cocultures, purple and red corn extracts showed anti-inflammatory potential by inhibiting pro-inflammatory cytokine production and lipolysis and enhancing glucose transporter 4 membrane translocation [60]. Anthocyanins from purple corn showed anti-inflammatory effects by inhibiting inducible nitric oxide synthase and cyclooxygenase-2 activities [61]. A recent study indicated that sericin-alginate hydrogel formulations with purple waxy corn cob extract significantly inhibited the production of nitric oxide and reduced the expression of inflammatory mediators such as IL-6, IL-1β, and TNF-α [19].

2.5. Antimicrobial Activity

Regulating the growth of probiotic gut bacteria and inhibiting the growth of pathogenic bacteria are major beneficial effects of phenolic bioactive-rich foods. The free and bound phenolic fractions from Peruvian purple corn were compatible with beneficial probiotic bacteria such as *Lactobacillus helveticus* and *Bifidobacterium longum*. However, the growth of the pathogenic bacterium, Helicobacter pylori, was not inhibited by both free and bound phenolic forms of purple corn [63]. Another study indicated that anthocyanin-rich extracts from Chinese purple corn exhibited potent antimicrobial activity against *Salmonella enteritidis*, *Staphylococcus aureus*, and *Candida albicans* [50].

2.6. Protection against Keratinocyte Damage

Ultraviolet B (UVB) radiation is an important causative factor in skin damage, such as cell aging, death, and inflammation, because UVB easily infiltrates the epidermal layer of human keratinocyte cells. A previous study found that the extract of purple corn silk inhibited keratinocyte damage in UVB-treated cells. In this context, Poorahong et al. [68] investigated the protective effects of purple corn silk extract against inflammation in HaCaT cells induced by UVB. The purple corn silk extract attenuated NF-B activity by suppressing NF-κB nuclear translocation and protein expression. Further, purple corn silk extract markedly decreased the phosphorylation of c-Jun and suppressed proinflammatory cytokines, in addition to iNOS and COX-2 levels, in UVB-treated cells. A novel purple corn extract, FB801, suppressed the expression of nuclear factor-κB proteins (NF-κB) in TNF-α-stimulated human keratinocyte (HaCaT) cells [69].

2.7. Miscellaneous Activities

Lee et al. [62] investigated the effect of purple corn husk and cob extracts on the pancreatic lipase inhibitory effect and anti-adipogenic effect in 3T3-L1 cells. The extract effectively decreased mRNA expression and protein levels of obesity-related factors PPARγ and CCAAT enhancer-binding protein α (C/EBPα). In the Ames test, an anthocyanin-rich ethyl acetate fraction (IC_{50} of 321.7 μg of chlorogenic acid equiv/plate) from purple corn showed higher antimutagenic behavior against the food mutagen Trp-P-1 than a water fraction (and 95.2 μg of chlorogenic acid equiv/plate) [36]. Zhang et al. [64] evaluated the anti-adipogenic activity of anthocyanin-rich water extracts from 20 purple maize genotypes in RAW 264.7 macrophages and 3T3-L1 adipocytes. The result revealed the anti-adipogenic properties of purple corn water extract by inhibiting the transition of preadipocyte–adipocyte. The cob and silk of purple waxy corn also contain anthocyanins. Silk extracts of purple corn highly stimulate collagen production when compared with cob extracts; this may be due to the higher amount of melatonin in the silk extracts [65]. Corn silk or the stigma of corn has been traditionally used to stimulate weight loss and treat cystitis, urinary infections, and obesity. In the murine 3T3-L1 cell line, the ethanol extract of purple corn silk showed anti-obesity properties by inhibiting adipocyte proliferation and adipogenesis as well as inducing lipolysis and apoptosis [66]. Unsaturated fatty acids in milk increase the formation of radicals and lead to the oxidation of lipids during storage, resulting in the reduction of the commercial value of milk. The addition of purple corn pigment maintained the concentration of unsaturated fatty acids in milk during storage time [67].

3. In Vivo Biological Activities of Purple Corn

The in vivo biological activities of extracts and compounds obtained from purple corn are presented in Figure 4 and Table 2.

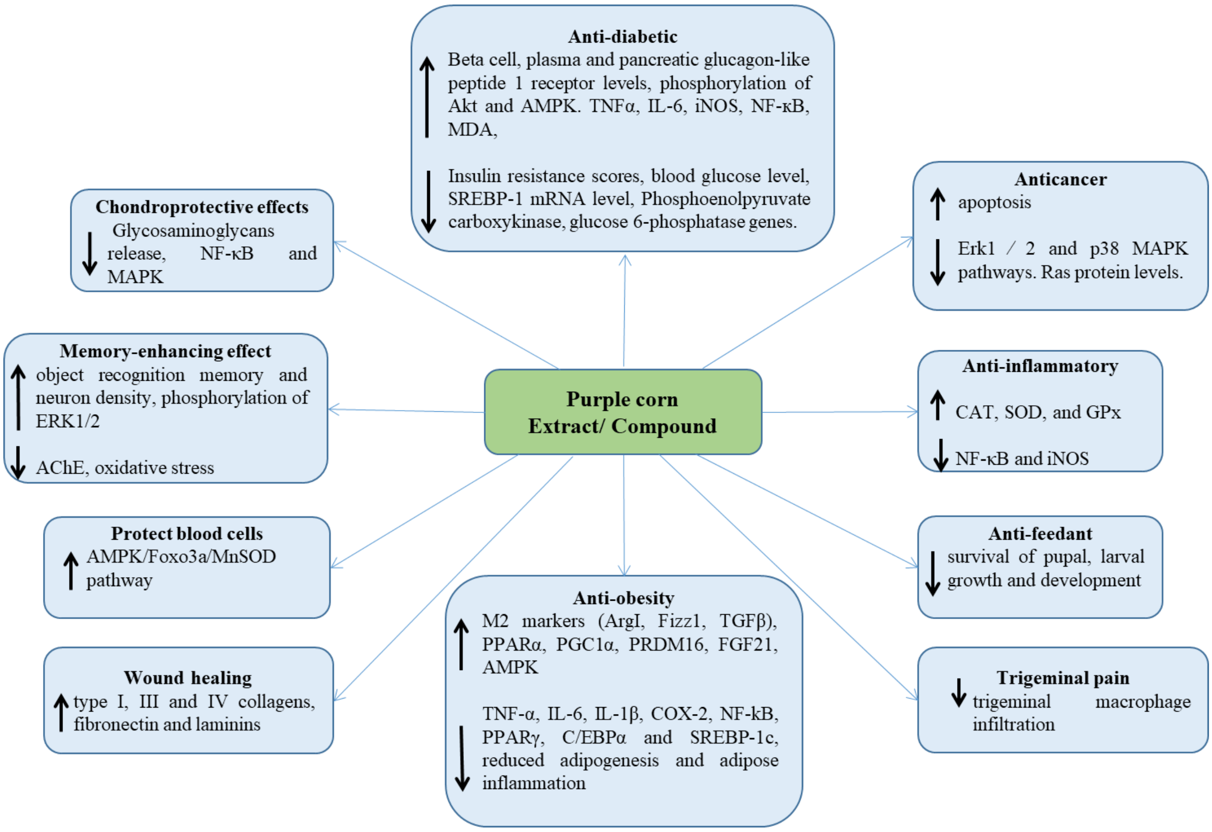

Figure 4. In vivo biological activities and mechanisms of purple corn.

Table 2. In vivo biological properties of extracts and compounds from purple corn.

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
Anticancer	Purple corn color	Chiba, Japan	Male TRAP rats	Suppressed the activation of Erk1/2 and p38 MAPK pathways.	[49]
	Anthocyanin corn seeds, and color	Osaka, Japan	7,12 dimethylbenz[a]anthracene-induced mammary carcinogenesis in Hras128 rats	Modulated cell proliferation and apoptosis in mammary neoplastic lesions by reducing Ras protein levels.	[71]
	Corn color, enzymatically modified Isoquercitrin, and Isoquercitrin	Osaka, Japan	Male F344 rats/i.p. injection of diethylnitrosamine (200 mg/kg b.w.)	Antioxidant activity. Induced RNA expression of P450 (cytochrome) oxidoreductase, phosphatidylinositol 3-kinase, and phospholipase A2.	[72]
	Purple corn color	Tokyo, Japan	Male F344/DuCrj rats	Suppressed the development of lesions.	[73]

Table 2. *Cont.*

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
Anti-diabetic activity	Ethanol extract	Zana Export Co. (Lima, Peru)	Male C57BL/KsJ db/db mice	Protected pancreatic beta cell death.	[56]
	Anthocyanin extract	Yogyakarta, Indonesia	Fed high-fat and fructose diet/male Wistar rats	Reduced insulin resistance scores and blood glucose levels. Increased plasma and pancreatic glucagon-like peptide 1 receptor levels and improved pancreatic morphology.	[74]
	Purple corn extract	Pohang, Republic of Korea	High-fat diet induced obesity in C57BL/6 mice	Decreased glucose intolerance by increasing the phosphorylation of Akt and reducing macrophage infiltration into the epididymal adipose tissue.	[23]
	Cyanidin 3-*O*-beta-D-glucoside-rich purple corn	Osaka, Japan	Male C57BL/6J mice	Suppressed the mRNA levels of the enzymes of fatty acid and triacylglycerol synthesis. Reduced of the SREBP-1 mRNA level in white adipose tissue.	[75]
	Purple corn anthocyanin	Tianjin, China	Male C57BL/6 mice	Increased fecal butyric acid levels, elevated 22 hepatic SOD and GPX activities, decreased lipid peroxidation, and downregulated the gene expression levels of TNFα, IL-6, iNOS, and NF-κB.	[76]
	Purple waxy corn (50% hydroalcoholic solvent)	Khon Kaen, Thailand	Male Wistar rats/glucose 55 mM	Decreased lens opacity together with the decreased malondialdehyde level. Decreased oxidative stress and aldose reductase.	[77]
	Purple waxy corn 50% hydroalcoholic extract	Khon Kaen, Thailand	Streptozotocin-diabetic rats	Protected diabetic cataract and diabetic retinopathy. Decreased lens opacity, MDA, and aldose reductase in the lens.	[78]
	Ethanolic extract	Seoul, Republic of Korea	Adult male db/db mice	Alleviated glomerular angiogenesis of diabetic kidneys by attenuating the induction of vascular endothelial growth factor F and HIF-1a. Antagonized glomerular angiogenesis through disturbing the Angpt-Tie-2 ligand-receptor system linked to the renal vascular endothelial growth factor receptor 2 signaling pathway.	[22]
	Purple corn extract (30% ethanol-water)	Gangwon Province, Republic of Korea	C57BL/KsJ db/db mice	Prevented pancreatic β-cell damage and higher insulin content. Increased the phosphorylation of AMPK and decreased phosphoenolpyruvate carboxykinase, glucose 6-phosphatase genes.	[25]
Obesity	Methanol extract of corn cob	Milan, Italy	Male C57BL/6J mice/high-fat diet	Upregulated M2 markers (ArgI, Fizz1, TGFβ), downregulated inflammatory mediators (TNF-α, IL-6, IL-1β, COX-2). Suppressed NF-kB signaling. Attenuated Adipose tissue inflammation.	[79]
	Anthocyanins	Jilin, China	High-fat diet-induced obese mice	Downregulated the expression of PPARγ, C/EBPα, and SREBP-1c. Upregulated the expression of PPARα, PGC1α, PRDM16, and FGF21. Promoted hepatic AMPK activity.	[80]
	Water extract from pericarp	Angelina's Gourmet (Swanson, CT, USA)	C57BL/6 mice	Modulated of TLR and AMPK signaling pathways, reduced adipogenesis and adipose inflammation, and promoted energy expenditure.	[81]

Table 2. *Cont.*

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
Chondroprotective effects	Anthocyanin (cyanidin-3-*O*-glucoside, pelargonidin-3-*O*-glucoside and peonidin-3-*O*-glucoside) content in purple corn extract	Chiang Mai, Thailand	Advanced glycation end products induced human articular chondrocytes	Reduction in glycosaminoglycans released from advanced glycation end products induced cartilage explants, corresponding with diminishing of uronic acid loss of the cartilage matrix. Inactivation of the NF-κB and MAPK signaling pathways.	[82]
Anti-inflammatory effects	Anthocyanins extracted from cobs of purple waxy corn	Khon Kaen province, Thailand	*Opisthorchis viverrini*-infected hamsters	Decreased the expression of oxidant-related genes (NF-κB and iNOS) and increased the expression of antioxidant-related genes (CAT, SOD, and GPx).	[83]
Memory-enhancing effect	Water extract of purple waxy corn cob	Khon Kaen, Thailand	Female Wistar rats	Increased object recognition memory and neuron density but decreased oxidative stress status in prefrontal cortex. Increased phosphorylation of ERK1/2 in prefrontal cortex.	[84]
	Purple corn cob water extract	Khon Kaen, Thailand	Wistar rats	Suppression of AChE and the increase in ERK signaling in the hippocampus.	[85]
Chronic liver injury	Purified purple corn cob anthocyanins (cyanidin 3-*O*-glucoside)	Hei Longjiang Province, China	CCl_4-induced chronic liver injury in mice	Reduced liver index, serum total bilirubin, alanine transaminase, and aspartate transaminase and malondialdehyde levels. Increased SOD activity. Downregulated the expression of caspase-3, Bax, and cytochrome P450 2E1 proteins in the liver and upregulated the expression of Bcl-2.	[86]
Oxidative stress	Purple plant pigment	Shenyang, China	Fluoride-induced oxidative damage in rat brains	Alleviated oxidative damage in the rat brain. Reduced the elevated malondialdehyde levels, increased SOD activity, and attenuated histopathological alterations and mitigated neuronal apoptosis. Reversed changes in Bax and Bcl-2.	[87]
	Purple plant pigment rich in anthocyanins	Shenyang, China	Fluoride-induced oxidative damage of liver and kidney in Wistar rats	Attenuated these fluoride-induced pathological changes. Reduced the elevation of MDA levels in blood and liver and increased the SOD and GSH-Px activities in kidneys. Alleviated the decrease in Bcl-2 protein expression and the increase in Bax protein expression.	[88]
Aphrodisiac activity	Aqueous extract	Ixtenco Tlaxcala, Mexico	Sexually vigorous male Wistar rats	Facilitated the arousal and execution of male rat sexual behavior without significant influences on the ambulatory behavior.	[89]
Metabolic syndrome	Methanol extract	Spectrum Ingredients Pte Ltd., Singapore	Wistar rats	Reduced visceral adiposity index, total body fat mass, and systolic blood pressure; improved glucose tolerance, liver, and cardiovascular structure and function. Decreased plasma triacylglycerols and total cholesterol. Reduced inflammatory cell infiltration in heart and liver.	[90]
Anti-hypertensive effects	Coors	Osaka, Japan	Spontaneously hypertensive rats	Inhibited the increase in blood pressure.	[91]
	Purple corn extract capsule	Lima, Peru	Blood pressure Peruvian adults	Blood pressure readings decreased from baseline levels to end of study.	[92]
Improvement of mutton flavor	Purple corn pigment	Nanjing Herd Source Bio-technology Co., Ltd., Nanjing, China	Goats/feeding anthocyanin-rich purple corn pigment	Improved mutton flavor by decreasing plasma lipid metabolism parameters and by modulating the abundance of several flavor-related genes.	[93]
Growth performance	Purple corn pigment	Nanjing, China	Goats	Improved meat quality, muscle antioxidant status, and polyunsaturated fatty acid profile.	[18]

Table 2. *Cont.*

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
Infliximab infusion	Purple corn supplement with a high anthocyanin content.	Castellana Grotte, Bari, Italy	Crohn's disease and ulcerative colitis patients	Improved IFX-mediated disease remission in terms of circulating inflammatory markers.	[94]
Toxicity study	Purple corn color	San-Ei Gen F.F.I., Tokyo, Japan	F344/DuCrj rats	Total cholesterol, phospholipid, and triglycerides were significantly lowered. No adverse effect.	[95]
Hepatic desaturase activity	Purple corn extract	GlobeNatural, Chorrillos, Peru	Female Sprague Dawley rats	Showed an anti-adipogenic effect. Desaturase activity was inhibited by anthocyanins.	[96]
Wound healing	Anthocyanin complex from purple corn	Sisaket Province, Thailand	Human gingival fibroblasts, male or female (18–60 years) with oral inflammatory lesion(s) within the areas of labial and/or buccal mucosa	Scratched cells showed accelerated wound healing activity. Upregulation of type I, III, and IV collagens, fibronectin, and laminins. Accelerated wound closure, reduced pain due to the oral wounds, and improved participants' quality of life.	[97]
Glomerulosclerosis	Ethanol extracts	Seoul, Republic of Korea	Adult male db/db mice	Lowered plasma glucose level and ameliorated severe albuminuria. Lessened collagen fiber accumulation in kidney glomeruli and connective tissue growth factor expression via retarding tissue growth factor-β signaling.	[59]
	Ethanol extract	Seoul, Republic of Korea	Human umbilical vein endothelial cells. Adult male db/db mice	Decreased the human mesangial cells exposed to 33 mM glucose-conditioned, media-induced expression of endothelial vascular cell adhesion molecule-1, E-selectin, and monocyte integrins-1 and-2 through blocking the mesangial Tyk2 pathway. Attenuated CXCR2 induction and the activation of Tyk2 and STAT1/3.	[70]
Protect blood cells	Ethanol extract	Zana Export Co., Lima, Peru	Cigarette smoke-induced DNA damage in rodent blood cells	Removal of ROS via activation of the AMPK/Foxo3a/MnSOD pathway.	[98]
Anti-atopic dermatitis	Purple corn ethanol extract	Gangwon-do, Republic of Korea	Dorsal skin and right ear of BALB/c mice	Regulated Th1 and Th2 responses in the skin lesions in mice.	[69]
Trigeminal pain	Corn cob ethanol extract	Appiano Gentile, Italy	Male adult Sprague Dawley rats	Reduced trigeminal macrophage infiltration and the shift of microglia cell polarization.	[99]
Anti-feedant activity	Pericarp extract	Texas, USA	Tobacco hornworm (*Manduca sexta* L.)	Lowered the survival of pupa.	[100]
	Polyphenol-rich liquid extract from purple corn pericarp	Andes region of Peru	Fall armyworm (*Spodoptera frugiperda*)	Inhibited larval growth and development.	[101]
	Purple corn pericarp water extract	Texas, USA	Tobacco hornworm (*Manduca sexta* L.)	Reduced insect feedant activity.	[102]
Cardioprotective activity	Cyanidin 3-glucoside	Milanese, Italy	Doxorubicin-induced cardiotoxicity in C57BL/6J mice.	Survived longer and reduced histopathological alterations.	[103]
Ruminal fluid fermentation	Purple corn pigment anthocyanin	Nanjing, China	Goat/feeding purple corn pigment	Increased antioxidant potential, improved rumen volatile fatty acids, and induced a shift in the structure and relative abundance of ruminal microbiota in growing goats.	[104]
	Purple field corn residue stover	Khon Kaen, Thailand	Thai native beef cattle/feeding purple corn stover	Modulated rumen fermentation and feed digestion in Thai native beef cattle.	[105]

Table 2. *Cont.*

Biological Activity	Extract/Compound	Collection Place of the Sample	Model	Mechanism	References
Lactating dairy cows	Anthocyanin-rich purple corn	Pioneer Hi-Bred Japan, Tokyo, Japan	Feeding anthocyanin-rich corn to lactating dairy cows	Lowered aspartate aminotransferase activity and enhanced SOD activity in lactating dairy cows.	[106]
	Feeding purple corn silage	Yabuki, Fukushima, Japan	Lactating cows	Increased milk yield and blood superoxide dismutase concentrations. Increased antioxidant capacity and milk production in dairy cows.	[107]
Lactating dairy goats	Purple corn stover silage	Nanjing, China	SOD and total antioxidant capacity	Higher level of SOD in plasma and milk. Enhanced the amount of antioxidants in lactating dairy goats.	[108]
Nutrient utilization—dairy goats	Anthocyanin-rich purple corn stover silage, purple corn pigment	Nanjing, China	Goats/feeding anthocyanin rich purple corn stover silage	DPPH scavenging activity and SOD in plasma were greater. Increased the abundance of nuclear factor (erythroid-derived 2)-like 2. Decreased the level of TNF in the mammary gland. Increased the levels of SOD2, GPX1, and GPX2 mRNA expression in the mammary gland.	[109]

3.1. Anticancer Activity

The administration of purple corn color in transgenic rats with adenocarcinoma of the prostate for eight weeks decreased the incidence of adenocarcinoma. Purple corn color treatment lowered the Ki67 positive rate, decreased the expression of cyclin D1, and down-regulated Erk1/2 and p38 MAPK activation [49]. Purple corn color significantly inhibited 7,12-dimethylbenz[a]anthracene (DMBA)-induced mammary carcinogenesis in human c-Ha-ras proto-oncogene transgenic (Hras128) rats and their non-transgenic counterparts. Purple corn color and cyanidin 3-*O*-β-D-glucoside inhibited cell viability and induced apoptosis by activating caspase-3 and reducing Ras protein levels in tumor cells [71]. Purple corn color reduced 1,2-dimethylhydrazine-induced colorectal carcinogenesis in rats [73]. In addition, purple corn color showed a protective effect against diethylnitrosamine-induced hepatocarcinogenesis in rats by upregulating RNA expressions such as P450 (cytochrome) oxidoreductase, phosphatidylinositol 3-kinase, and phospholipase A2 [72].

3.2. Anti-Diabetic Activity

Purple corn anthocyanins (PCA) registered excellent antihyperglycemic activity by decreasing blood glucose levels and exhibiting HbA1c-decreasing activity when compared with db/db mice [24]. Administration of anthocyanin-rich purple corn reduced blood glucose levels, increased HOMA-β and HOMA-IS scores, plasma GLP1 and pancreatic GLP1R levels, and improved pancreatic morphology in rats fed a diet high in fat and fructose [74]. In C57BL/KsJ db/db mice, purple corn extract exhibited anti-diabetic effects by protecting pancreatic β-cells, increasing insulin secretion, and activating AMPK in the liver [25]. Cyanidin 3-glucoside-rich purple corn color prevented hyperglycemia, hyperinsulinemia, and hyperleptinemia in high-fat diet-induced mice. Purple corn color-diet normalized TNF-mRNA levels and these findings revealed that dietary purple corn color may ameliorate high-fat-diet–induced insulin resistance in mice [75].

Anthocyanin-rich purple corn extract reduced plasma glucose levels in db/db mice and improved severe albuminuria. In addition, purple corn extract decreased the accumulation of collagen fiber in kidney glomeruli and CTGF expression by retarding the TGF-β signaling pathway [59]. In db/db mice, purple corn extract inhibited diabetes-associated glomerular monocyte activation and macrophage infiltration via attenuation of CXCR2 induction and the activation of Tyk2 and STAT1/3 [70]. In experimental diabetic cataracts, purple waxy corn registered an anticataract effect by decreasing lens opacity and MDA levels in addition to increasing GPx activity [77]. The mixture of purple waxy corn and ginger showed a protective effect against diabetic eye complications in streptozotocin-induced diabetic rats. The mixture efficiently decreased lens opacity, MDA, and AR in the lens of diabetic rats [78]. Purple corn extract prevented the glomerular angiogenesis of diabetic kidneys by reducing VEGF and HIF-1a induction [22].

3.3. Anti-Obesity Activity

Obesity is one of the important chronic inflammatory disorders and is an important risk factor for the onset of several chronic syndromes. Adipose tissue plays a critical role in the development of obesity. Tomay et al. [79] demonstrated that purple corn cob extract showed anti-obesity activity in a diet-induced obesity model in mice. Purple corn anthocyanin effectively exhibited anti-obesity activity in C57BL/6 mice fed a high-fat diet by increasing fecal butyric acid levels, elevating hepatic SOD and GPx activity, decreasing lipid peroxidation, and suppressing the expression of TNFα, IL-6, iNOS, and NF-κB levels [76]. Purple corn extract alleviated high-fat diet-induced obesity and glucose intolerance by increasing the phosphorylation of Akt and reducing macrophage infiltration into epididymal adipose tissue [23]. A recent study reported that anthocyanins from purple corn showed antiobesity effects via the activation of the hepatic AMP-activated protein kinase (AMPK) pathway, thereby decreasing fatty acid synthase and increasing fatty acid oxidation [80]. In a murine model of obesity, the administration of phenolic-rich water extract from purple maize pericarp for 12 weeks prevented obesity by modulating TLR and AMPK signaling pathways [81]. Purple corn color downregulated the mRNA levels of enzymes associated with fatty acid and triacylglycerol synthesis and decreased the mRNA level of the sterol regulatory element binding protein-1 in white adipose tissue [75].

3.4. Anti-Inflammatory Activity

Intuyod et al. [83] developed an anthocyanin complex by mixing anthocyanins extracted from purple waxy corn cobs, blue butterfly pea petals, and turmeric extract. The anthocyanin complex showed a protective effect against inflammation and periductal fibrosis in hamsters infected with *Opisthorchis viverrini* through the downregulation of oxidant-related gene (NF-κB and iNOS) expressions and upregulation of antioxidant-related gene (CAT, SOD, and GPx) expressions. The anti-inflammatory effect of purple corn anthocyanins and the metabolite, protocatechuic acid (PCA), on advanced glycation end product-induced human articular chondrocytes occurs by inactivating the NF-κb and MAPK signaling pathways [82].

3.5. Memory-Enhancing Effect

For menopause-related issues, neuroprotectant and memory-enhancing supplements are required due to the adverse effects of hormonal therapy. Kirisattayakul et al. [84] studied the synergistic effect of purple waxy corn cob and pandan leaves on memory impairment in experimental menopause. The combined extract showed neuroprotective and memory-enhancing effects by improving the oxidative stress status and cholinergic function, in addition to signal transduction through ERK in the prefrontal cortex. In another study, a functional drink containing the extracts of purple corn cob and pandan leaves exhibited a memory-enhancing effect partly via the suppression of AChE and the upregulation of ERK signaling in the hippocampus of rats induced by bilateral ovariectomy [85].

3.6. Oxidative Stress

It was reported that exposure to high levels of fluoride causes neurotoxicity, including memory impairment. Purple corn color alleviated the adverse effects induced by fluoride on the liver and kidneys of rats via reduction in the elevation of MDA levels in the blood and liver, and upregulation of SOD and GSH-Px activities in the kidneys and the GSH level in the liver. Further, purple corn color reversed changes in the expression of Bcl-2 and Bax proteins [88]. Similarly, purple corn extract alleviated fluoride-induced oxidative damage in rat brains [87].

3.7. Anti-Hypertensive Effects

Continuous administration of purple corn extract decreased the blood pressure and heart rate of spontaneously hypertensive rats [91]. In Peruvian adults with mild to moderate hypertension, the administration of a concentrated dose of anthocyanin from purple corn extract (300 mg once a day for 3 weeks) showed a reduction in systolic and diastolic readings [92].

3.8. Anti-Feeding Effects

Purple corn pericarp extract shows cascading negative effects on pupal, adult, and second generation *Manduca sexta*, a common insect herbivore [100]. In another study, purple corn pericarp extract affected *M. sexta* egg hatching and larval mass gain, thereby increasing developmental time [102]. Further, Singh and Kariyat [101] reported that polyphenol-rich purple corn pericarp extract inhibited the growth and development of larvae and affected the pupal stages of *Spodoptera frugiperda* (the fall armyworm).

3.9. Ruminal Fluid Fermentation

In growing goats, the inclusion of anthocyanin-rich purple corn improved antioxidant potential and rumen volatile fatty acids, and induced a shift in the structure and relative abundance of ruminal microbiota [104]. In Thai native beef cattle, purple field corn stover treated with *Pleurotus ostreatus* and *Volvarialla volvacea* enhanced the quality of purple field corn stover and regulated rumen fermentation and feed digestion [105].

3.10. Lactating Dairy Cows

In lactating dairy cows, feeding anthocyanin-rich corn silage effectively reduced aspartate aminotransferase (AST) activity and increased SOD activity in plasma [106]. In another study, feeding purple corn silage increased the yield of milk and blood SOD concentrations. However, anthocyanin concentration in purple corn silage may degrade during storage [107].

3.11. Improving Dairy Goats

In dairy goats, Tian et al. [109] observed that the consumption of anthocyanin-rich purple corn stover silage improved antioxidant capacity in plasma and regulated inflammation-related and antioxidant genes in mammary glands. Purple corn stover silage enhanced the amount of antioxidants, and there was a stronger positive correlation between antioxidant enzymes and anthocyanin composition in milk [108].

3.12. Miscellaneous Activities

Purple corn extract prevented the development of orofacial allodynia [99]. Petroni et al. [103] reported that dietary intake of cyanidin 3-glucoside from purple corn protected mice against doxorubicin-induced cardiotoxicity. In 2,4-dinitrochlorobenzene (DNCB)-treated BALB/c mice, a novel purple corn extract, FB801, inhibited the development of atopic dermatitis-like skin symptoms through the regulation of Th1 and Th2 responses in skin lesions [69]. Purple corn extract effectively alleviated cigarette smoke-induced oxidative DNA damage by activating the AMPK/Foxo3a/MnSOD pathway [98]. In oral wounds, anthocyanin complex (composed of extracts of purple waxy corn and blue butterfly pea petals) niosome gel accelerated wound closure, reduced pain due to the oral wounds, and improved participants' quality of life [97]. In addition, anthocyanin-rich extract exerted a protective effect on desaturase activity [96].

In a subchronic oral toxicity study, no adverse effect was observed at the concentration of 5.0% purple corn color in the diets of both male (3542 mg/kg/day) and female (3849 mg/kg/day) rats [95]. Purified anthocyanins from purple corn cob improved CCl4-induced chronic liver injury via downregulation of caspase-3, Bax, and cytochrome P450 2E1 protein expressions in the liver and upregulation of Bcl-2 expression [86]. In rats with diet-induced metabolic syndrome, Bhaswant et al. [90] studied the measurement of cardiovascular, liver, and metabolic parameters following chronic administration of anthocyanins from purple corn.

For maintenance of inflammatory bowel diseases, administration of a purple corn supplement improved the infliximab response in patients with Crohn's disease but not in patients with ulcerative colitis [94]. A study reported that anthocyanin-rich purple corn extract enhanced mutton flavor by decreasing plasma lipid parameters and regulating the flavor-related genes of goats [18]. In goat muscles, anthocyanin-rich purple corn improved growth performance and the quality of meat, and enhanced muscle antioxidant status and unsaturated fatty acid profiles [18]. Aqueous purple corn extract showed aphrodisiac properties in male rats [89].

4. Conclusions and Future Perspectives

In the last decade, the utilization of purple corn has increased steadily due to the presence of health-promoting anthocyanin compounds. Previous studies demonstrated that anthocyanin-rich purple corn extract showed numerous biological properties under both in vitro and in vivo conditions. In particular, purple corn extracts exhibited significant antioxidant, anticancer, anti-diabetic, anti-obesity, and anti-inflammatory potentials. The findings summarized in this review offer a basis for the development of novel strategies for functional food-related applications of purple corn anthocyanins. Although these in vitro and in vivo animal studies figure out the health benefits of purple corn extracts, mechanistic, bioavailability and clinical studies are warranted to confirm these effects. Furthermore, studies concerning efficient anthocyanin extraction methods are required to enhance the nutritional and health benefits of purple corn.

Author Contributions: Conceptualization, S.K. and H.Y.K.; methodology, P.D., M.H., and M.K.; validation, K.Y.L.; resources, P.D., M.H., K.Y.L. and M.K.; writing—original draft preparation, P.D.; writing—review and editing, P.D. and S.K.; supervision, S.K. All authors have read and agreed to the published version of the manuscript.

Funding: Rural Development Administration (Project No. PJ015140), Republic of Korea.

Institutional Review Board Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: This work was supported by "Quality characteristics of health function and development of breeding material lines of purple corn (PJ015140)" from Rural Development Administration, Republic of Korea.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

ABTS, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); AChE, acetylcholinesterase; AMPK, AMP-activated protein kinase; BAX, BCL2-associated X protein; Bcl-2, B-cell lymphoma 2; BHT, butylated hydroxytoluene; BSA, bovine serum albumin; C/EBPα, CCAAT/enhancer binding protein α; CCAAT, enhancer-binding proteins (C/EBPs); CCl4, carbon tetra chloride; COX-2, cyclooxygenase-2; CTGF, connective tissue growth factor; CXCR2, CXC chemokine receptor 2; DPPH, 2,2-diphenylpicrylhydrazyl; ERK1/2, extracellular signal-regulated kinase 1/2; FGF21, fibroblast growth factor 21; FOXM1, forkhead box protein M1; Foxo3a, forkhead box class O 3a; FRAP, ferric reducing antioxidant power assay; GLP1, glucagon-like peptide-1; GLUT4, glucose transporter type 4; IL-1β, interleukin-1 beta; IL-6: interleukin 6; iNOS, inducible nitric oxide synthase; IκBα, nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha; JNK, Jun N-terminal kinase; MAPK, mitogen-activated protein kinase; MMP-2, matrix metalloproteinase-2; MnSOD, manganese superoxide dismutase plasmid; NF-κB, nuclear factor kappa-B; NO, nitric oxide; ORAC: oxygen-radical absorbance capacity; p38 MAPK, p38 MAP kinase; PPARγ, peroxisome proliferator-activated receptor gamma; ROS, reactive oxygen species; SOD, superoxide dismutase; SREBP-1, sterol regulatory element-binding protein-1; TBARS, thiobarbituric acid reactive substances; TGFβ, transforming growth factor beta; Th1, type 1 T helper; TLR, toll-like receptor; TNF-α, tumor necrosis factor alpha; Tyk2, tyrosine kinase 2; VEGF: vascular endothelial growth factor.

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