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Review

A Review of the Phytoconstituents, Phytochemistry, and Bioactivities of *Sorbus commixta* Hedl.

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Abstract

Sorbus commixta Hedl. is a deciduous plant in the Rosaceae family known for its traditional medicinal uses. Despite increasing evidence of its distinct phytoconstituents and biological activities, its potential as a functional food remains underexplored. This review synthesizes the available evidence on phytoconstituents, phytochemistry, and bioactivities of this plant. Relevant literature was identified through searches of Google Scholar, PubMed, and Embase using terms related to *Sorbus commixta*, health promotion, nutritional composition, botanical characteristics, and pharmacological potential. Approximately 110 phytoconstituents have been identified in different parts of the plant, including the bark, stem bark, leaves, fruits, seeds, and roots. The principal classes include phenylpropanoids, lipids and oxylipins, terpenoids, flavonoids, phenolic glycosides, and cyanogenic glycosides. The review also highlights compounds first identified in this species. In vitro and in vivo studies have reported antioxidant, anti-inflammatory, anticancer, skin-protective, neuroprotective, antiviral, cardiovascular, bone-protective, and antidiabetic activities, as well as protection against alcohol-induced toxicity. Because clinical evidence remains limited, well-designed human studies are needed to evaluate these potential benefits in humans.

Keywords: Japanese rowan; traditional plant; antioxidant; anti-inflammatory; neuroprotection

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1. Introduction

Sorbus commixta Hedl., a deciduous tree species of the genus *Sorbus*, is commonly known as Japanese rowan, Japanese mountain ash, or Korean magamok [1,2]. Several botanical synonyms have been reported, including *S. commixta* var. *pilosa* Nakai, *S. amurensis* var. *rufa* Nakai, *S. commixta* var. *rufoferruginea* Shirai ex CKSchneid., *S. amurensis* var. *lanata* Nakai, and *S. amurensis* var. *latifoliolata* Nakai, according to the National Bioresource Natural Products Cluster Herbal Medicine Resource Hub Bank, Republic of Korea [3]. This member of the phylum Streptophyta and family Rosaceae is widely distributed in East Asia, including Japan, Korea, and China [4]. It is particularly associated with Ulleungdo Island in Korea. Recently, Park et al. [5] examined its ecological niche alongside other plant species in subalpine vegetation associated with *Abies* sp. in Korea and China [5]. The species is also cultivated in North America and Europe [6].

The species is valued for both ornamental and medicinal uses. It bears creamy-white flowers and dark green leaves. Traditionally, the plant has been propagated from seeds; however, under natural conditions, most seeds do not germinate without being ingested by birds. Passage through birds facilitates germination by removing fruit pulp containing germination inhibitors [7]. Micropropagation has therefore been used to propagate plants with unique characteristics [8]. The orange-to-red fruits develop in berry-like clusters and contribute to the plant's ornamental and medicinal uses. Known as rowanberries, the fruits ripen in autumn. They are traditionally eaten as a side dish or processed into jam, either alone or with other Korean fruits. The fruits are also used to make alcoholic beverages, particularly country wine [9].

Sorbus commixta has a history of ethnopharmacological use, and its potential functional properties have attracted growing research interest, with in vitro and in vivo studies examining the health-related effects of its extracts and bioactive constituents. The plant is reported to contain numerous distinctive phytochemicals alongside more widely occurring constituents [10,11]. Previous comprehensive reviews have discussed species across the genus *Sorbus* [1,4]. Despite increasing reports of its distinctive bioactive constituents, the plant remains underexplored as a potential functional food. A dedicated review of the traditional uses, phytoconstituents, and therapeutic potential of *S. commixta* Hedl. has yet to be reported. Accordingly, this review compiles evidence on the phytoconstituents, phytochemistry, and potential health-promoting properties of *S. commixta* Hedl.

2. Literature Search Approach

The literature search used the following search terms: "*Sorbus commixta* and health promotion," "*Sorbus commixta* and nutritional composition," "*Sorbus commixta* and botanical description," "*Sorbus commixta* and pharmacological potential," and "*Sorbus commixta* extract and health promotion" in Google Scholar, PubMed, and Embase. English-language articles were included. Korean-language articles were also considered if they had English abstracts or provided sufficient information about the plant's traditional uses.

3. Traditional Knowledge

In traditional medicine, *S. commixta* has been used to treat neuralgia, tuberculosis, liver disorders, cough, pain, bruising, the common cold, arthralgia, and tingling, and to improve blood circulation, among other conditions. Its bark, in particular, has been used to treat bronchial disorders, cough, asthma, gastritis, and dropsy [12]. Traditional preparations of the stem, bark, fruits, and leaves included brewed drinks, soups, and decoctions [2]. Table 1 summarizes documented traditional uses of *S. commixta*.

Table 1. Traditional uses of *Sorbus commixta*.

Used Parts	Ailments	Preparation	Application	Ref.
Stem	Arm pain	Drink #	Oral	[13]
	Leg pain	Drink #	Oral	
	Shoulder pain	Drink #	Oral	

Table 1. *Cont.*

Used Parts	Ailments	Preparation	Application	Ref.
Fruit	Arthralgia	Brewing	Oral	[2]
	Neuralgia	Brewing	Oral	
	Common cold	Brewing	Oral	
	Cough	Brewing	Oral	
Fruit, leaf, and stem	Liver diseases	Brewing	Oral	
		Decoction	Oral	
Leaf	Blood circulation	Decoction	Oral	
Stem	Liver diseases	Soup	Oral	
	Pain	Decoction	Oral	
	Pulmonary tuberculosis	Decoction	Oral	
	Tingling	Decoction	Oral	
Fruit	Asthma	Brewing	Oral	[14]
	Bronchitis	Brewing	Oral	
	Women diseases	Brewing	Oral	
Stem	Bone diseases	Decoction	Oral	
Fruit	Bronchitis	Brewing	Oral	[15]
Stem	Bone diseases	Decoction	Oral	
	Leg pain	Infusion	Oral	
Stem	Asthma	Decoction	Oral	[16]
	Pulmonary tuberculosis		Oral	
Fruits	Common cold	Brewing rice wine of fruit	Oral	
	Cough		Oral	
Fruit, leaf, and stem	Liver diseases	Decoction, tea	Oral	[17]

A sweet drink made from fermented rice. A decoction is a liquid prepared by boiling plant material in water.

4. Phytochemical Profile

Previous studies have isolated numerous phytoconstituents from *S. commixta*. Phenylpropanoids, lipids, oxylipins, and triterpenoids have been among the most frequently reported classes. Other documented constituents include phenolic glycosides, cyanogenic glycosides, and flavonoids. Table 2 summarizes phytoconstituents identified in different parts of *S. commixta*, including the seeds, stem, bark, stem bark, whole plant, leaves, fruits, and roots. Several analytical techniques have been used to characterize and identify these constituents, including gas-liquid chromatography, mass spectrometry, liquid chromatography coupled to mass spectrometry, ultraviolet and infrared spectroscopy, nuclear magnetic resonance spectroscopy, ultra-high-performance liquid chromatography tandem mass spectrometry, high-resolution mass spectrometry, and high-performance liquid chromatography. As shown in Table 2, approximately 110 compounds have been reported across several classes: phenolic acids and their derivatives, phenylpropanoids and their derivatives, lignans and their glycosides, coumarins, lipids and oxylipins, terpenoids, flavonoids, phenolic glycosides, cyanogenic glycosides, sterols and their derivatives, and other compound classes.

Among these compounds, caffeoylquinic acid (CA) isomers, including chlorogenic and neochlorogenic acids, can differ in biological activity. For instance, the concentrations of chlorogenic and neochlorogenic acids were 3.92 ± 0.02% and 0.76 ± 0.01%, respectively, in *S. commixta* inflorescences, versus 0.79 ± 0.01% and 0.05 ± 0.01%, respectively, in leaf extracts.

Differences in CA isomers, proanthocyanidins, and flavonoids were associated with differences in antioxidant activity [18]. In a comparison of inflorescences from different *Sorbus* species and cultivars, chlorogenic acid was most abundant, whereas neochlorogenic acid was least abundant [11]. Another study investigated the effects of different ethanol concentrations (25%, 50%, 75%, and 100%) on the concentrations of several polyphenolic compounds, including chlorogenic acid, rutin, ferulic acid, protocatechuic acid, and hydroxybenzoic acid. Among these compounds, chlorogenic acid had the highest reported concentration (μg/g), and its concentration increased with increasing ethanol concentration. Specifically, the chlorogenic acid concentrations were 127.14 ± 1.56, 150.70 ± 3.40, 176.72 ± 4.58, and 344.70 ± 7.18 at ethanol concentrations of 25%, 50%, 75%, and 100%, respectively [19].

Kim et al. [20] first reported caffeic acid in the *S. commixta* fruit water extract (SFW, 1.56 mg/g) and ethanol extract (SFE, 0.55 mg/g) along with other phenolic compounds, including chlorogenic acid, rutin, gallic acid, and *p*-coumaric acid. In the stem bark of *S. commixta*, 6′-O-benzoylprunasin (sorcomiside A) and 3,4,5-trimethoxyphenyl-(6′-O-benzoyl)-O-β-D-glucopyranoside (sorcomiside B) were identified for the first time, alongside 10 other phytoconstituents [21]. Another study first isolated the coumarin scopoletin from dried *S. commixta* bark, together with three other constituents, including ursolic acid, β-sitosterol, and lupeol [22]. Similarly, a phytochemical study first isolated the fatty acid sorcomic acid from the stem bark, along with nine other compounds [23]. Another newly identified compound, 1,2,4-trimethoxydibenzofuran-3,9-diol (a dibenzofuran derivative), was first isolated from *S. commixta* bark alongside six known compounds: β-sitosterol, betulin, betulinic acid, lupeol, ursolic acid, and β-pyrufuran [24].

Two further studies first reported neosakuranin, a chalcone glycoside, and the cyanogenic glycosides prunasin and sambunigrin in the fruits of *S. commixta* [9,25]. More recently, Rutkowska et al. [6] identified 78 phytochemical constituents in leaf extracts of *S. commixta*, of which 30 were reported for the first time, including a quercetin triglycoside, two flavalignans, three flavanones, eight proanthocyanidin hexosides, and sixteen caffeic acid derivatives (Table 2) [6].

The reported extraction yields (% dry weight) for dried inflorescences and their fractions were as follows: chloroform extract (6.1), 70% methanol extract (26.3), diethyl ether fraction (0.6), ethyl acetate fraction (2.6), *n*-butanol fraction (6.1), and water residue (17.0). For the methanol extract, diethyl ether fraction, ethyl acetate fraction, *n*-butanol fraction, and water residue, total phenolic content (expressed as gallic acid equivalents [GAE]) and total proanthocyanidin content (%) were reported as 16.81 ± 0.19, 1.26 ± 0.07, 15.53 ± 0.19, 51.20 ± 1.24, and 2.72 ± 0.08 and 23.77 ± 0.30, 36.67 ± 0.49, 53.55 ± 1.13, 48.52 ± 0.53, and 11.00 ± 0.12, respectively [10]. Jin et al. [19] reported lower total phenolic (GAE, μg/mg of extract) and total flavonoid (quercetin equivalent [QE], μg/mg of extract) contents in the aqueous fruit extract (50.27 ± 4.2 and 2.49 ± 0.25) than in the absolute ethanol extract (67.98 ± 4.28 and 8.65 ± 0.5, respectively). Moreover, the highest total phenolic content was found in the butanol fraction (87.15 ± 4.66 μg GAE/mg of extract), whereas the lowest was found in the hexane fraction (19.89 ± 2.65 μg GAE/mg of extract). The butanol fraction was followed by the ethyl acetate fraction (72.59 ± 5.34 μg GAE/mg of extract) and the aqueous fraction (44.07 ± 2.77 μg GAE/mg of extract). Total flavonoid content (μg QE/mg of extract) decreased in the following order: 22.25 ± 0.77 (butanol fraction) > 13.54 ± 0.43 (ethyl acetate fraction) > 6.25 ± 1.25 (hexane fraction) > 5.96 ± 1.11 (aqueous fraction) [19].

Overall, these findings indicate that phytoconstituent profiles may vary with cultivar, geographic location, plant part, extraction solvent, and solvent concentration. Although the phytochemical composition and potential health-related properties of *S. commixta* have been widely investigated, studies of extract absorption, metabolism, and bioavailability remain scarce.

Table 2. Phytoconstituents isolated or identified from *Sorbus commixta*.

S No.	Compounds	Technique	Plant Part	Location	Ref.
Phenolic acids or derivatives					
Caffeoylquinic acids					
1.	Chlorogenic acid (5-*O*-Caffeoylquinic acid)	HPLC	F	CNU, Korea	[19]
		HPLC	F	Jecheon, Korea	
		HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
		HPLC-PDA, UVS	I	Poland	[10]
		RP-HPLC	I, L	Poland	[18]
		UHPLC-MS/MS	L	WULS, Poland	[6]
2.	Cryptochlorogenic acid (4-*O*-Caffeoylquinic acid)	UHPLC-MS/MS	L	WULS, Poland	[6]
		HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
		HPLC-PDA, UVS	I	Poland	[10]
3.	Neochlorogenic acid (3-*O*-Caffeoylquinic acid)	UHPLC-MS/MS	L	WULS, Poland	[6]
		HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
		HPLC-PDA, UVS	I	Poland	[10]
		RP-HPLC	I, L	Poland	[18]
4.	p-Hydroxybenzoic acid	UHPLC-MS/MS	L	WULS, Poland	[6]
5.	*p*-Coumaric acid	HPLC	F	Jecheon, Korea	[20]
		UHPLC-MS/MS	L	WULS, Poland	[6]
		HPLC-PDA, UVS	I	Poland	[10]
6.	Gallic acid	HPLC	F	Jecheon, Korea	[20]
		HPLC	F	CNU, Korea	[19]
7.	Caffeic acid	HPLC	F	Jecheon, Korea	[20]
		UHPLC-MS/MS	L	WULS, Poland	[6]
		HPLC-PDA, UVS	I	Poland	[10]
8.	Protocatechuic acid	HPLC	F	CNU, Korea	[19]
		HPLC-PDA, UVS	I	Poland	[10]
9.	Protocatechuic acid hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
10.	Hydroxybenzoic acid	HPLC	F	CNU, Korea	[19]
11.	Caffeoylmalic acid	UHPLC-MS/MS	L	WULS, Poland	[6]
12.	Caffeoylshikimic Acid	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
13.	Vanillic acid	UHPLC-MS/MS	L	WULS, Poland	[6]
14.	Ferulic acid	HPLC	F	CNU, Korea	[19]
15.	Sinapinic acid	HPLC	F	CNU, Korea	[19]
16.	Ferulic acid isomer	UHPLC-MS/MS	L	WULS, Poland	[6]
17.	Caffeic acid derivative	UHPLC-MS/MS	L	WULS, Poland	[6]
18.	Dicaffeoylquinic acid derivative 1	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
		RP-HPLC	I	Poland	[18]
19.	Dicaffeoylquinic acid derivative 2	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
		RP-HPLC	I	Poland	[18]

Table 2. *Cont.*

S No.	Compounds	Technique	Plant Part	Location	Ref.
Phenylpropanoids or derivatives					
20.	2,3-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-1-propanone	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
21.	5-*O*-Caffeoylquinic acid hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
22.	Caffeic acid hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
23.	Caffeic acid acetyl-hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
24.	5-*O*-p-Coumaroylquinic acid	UHPLC-MS/MS	L	WULS, Poland	[6]
25.	5-*O*-Caffeoylshikimic acid	UHPLC-MS/MS	L	WULS, Poland	[6]
26.	Caffeic acid hexoside derivative	UHPLC-MS/MS	L	WULS, Poland	[6]
27.	5-*O*-Feruloylquinic acid	UHPLC-MS/MS	L	WULS, Poland	[6]
28.	Cinchonain I isomer	UHPLC-MS/MS	L	WULS, Poland	[6]
29.	3,5-*O*-Dicaffeoylquinic acid	UHPLC-MS/MS	L	WULS, Poland	[6]
30.	Caffeic acid acetyl-hexoside derivative	UHPLC-MS/MS	L	WULS, Poland	[6]
31.	1,5-*O*-Dicaffeoylquinic acid	UHPLC-MS/MS	L	WULS, Poland	[6]
32.	4,5-*O*-Dicaffeoylquinic acid	UHPLC-MS/MS	L	WULS, Poland	[6]
33.	Cinchonain I isomer derivative	UHPLC-MS/MS	L	WULS, Poland	[6]
Lignan and glycosides					
34.	(−)-Lyoniresinol 3α-*O*-*β*-D-xylopyranoside	Silica gel CC, NMR	SB	Mt. Sulak, Korea	[26]
35.	(+)-Lyoniresinol	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
36.	Lyoniside	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
37.	Prupaside	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
38.	Tiliamurosides A	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
39.	Ssioriside	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
40.	Nudiposide	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
41.	Lyoniresinol	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
42.	(7*S*,8*R*)-dihydrodehydrodiconiferyl alcohol 9-*O*-α-L-rhamnoside	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
Coumarins					
43.	Scopoletin	Silica gel CC	B	Hamyang, Korea	[22]
Lipids and Oxylipins					
44.	Methyl (3*S*,5*S*)-3,5-dihydroxyhexanoate	NMR, MS	B	Yangyang, Korea	[23]
45.	Methyl 9-hydroxynonanoate	NMR, MS	B	Yangyang, Korea	[23]
46.	3(*R*)-hydroxyoctanoic acid	NMR, MS	B	Yangyang, Korea	[23]
47.	9-Hydroxynonanoic acid	NMR, MS	B	Yangyang, Korea	[23]
48.	(*S*)-(*E*)-4-hydroxy-2-nonenoic acid	NMR, MS	B	Yangyang, Korea	[23]

Table 2. *Cont.*

S No.	Compounds	Technique	Plant Part	Location	Ref.
49.	(9*S*,12*R*,13*R*)-(*E*)-9,12,13-trihydroxy-10 octadecaenoic acid	NMR, MS	B	Yangyang, Korea	[23]
50.	Sorcomic acid	NMR, MS	B	Yangyang, Korea	[23]
51.	(9*S*,12*S*,13*R*)-(*E*)-9,12,13-trihydroxy-10-octadecaenoic acid	NMR, MS	B	Yangyang, Korea	[23]
52.	Azelaric acid	NMR, MS	B	Yangyang, Korea	[23]
53.	Monomethyl azelate	NMR, MS	B	Yangyang, Korea	[23]
Terpenoids					
54.	Ursolic acid	Silica gel CC, NMR	SB	Mt. Sulak, Korea	[26]
		NMR	B	Kangwon Province, Korea	[24]
		Silica gel CC	B	Hamyang, Korea	[22]
55.	Lupeol	Silica gel CC, NMR	SB	Mt. Sulak, Korea	[26,27]
		NMR	SB	Yangnyeong, Korea	[28]
		NMR	B	Kangwon Province, Korea	[24]
		Silica gel CC	B	Hamyang, Korea	[22]
56.	3β-acetoxy ursolic acid	Silica gel CC, NMR	SB	Mt. Sulak, Korea	[26]
57.	Lupenone	Silica gel CC, NMR	SB	Mt. Sulak, Korea	[26,27]
58.	Cecropiacic acid	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
59.	Betulin	NMR	B	Kangwon Province, Korea	[24]
60.	Betulinic acid	NMR	B	Kangwon Province, Korea	[24]
Flavonoids					
61.	Catechin-7-*O*-*β*-D-xylopyranoside (flavanol glycosides)	Silica gel CC, NMR	SB	Mt. Sulak, Korea	[26,29]
62.	(Epi)catechin-B-(epi)catechin	UHPLC-MS/MS	L	WULS, Poland	[6]
63.	(+)-Catechin	UHPLC-MS/MS	L	WULS, Poland	[6]
64.	(Epi)catechin-B-(epi)catechin hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
65.	(−)-Epicatechin	UHPLC-MS/MS	L	WULS, Poland	[6]
66.	Quercetin *O*-rhamnosyl-hexosyl-hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
67.	(Epi)catechin-B-(epi)catechin-B-(epi)catechin	UHPLC-MS/MS	L	WULS, Poland	[6]
68.	Quercetin *O*-dihexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
69.	Quercetin 3-*O*-β-sophoroside	UHPLC-MS/MS	L	WULS, Poland	[6]
70.	Kaempferol *O*-dihexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
71.	Kaempferol coumaroyl glucoside	HPLC, UPLS with MS detection	I	Southeastern region of Lithuania	[11]
72.	Quercetin *O*-hexosyl-pentoside	UHPLC-MS/MS	L	WULS, Poland	[6]
73.	Eriodictyol *O*-hexoside 1	UHPLC-MS/MS	L	WULS, Poland	[6]
74.	Eriodictyol *O*-hexoside 2	UHPLC-MS/MS	L	WULS, Poland	[6]
75.	Quercetin 3-*O*-β-D-(6″-O-α-L-rhamnosyl)-glucoside	UHPLC-MS/MS	L	WULS, Poland	[6]

Table 2. *Cont.*

S No.	Compounds	Technique	Plant Part	Location	Ref.
76.	Quercetin 3-*O*-β-D-galactoside	UHPLC-MS/MS	L	WULS, Poland	[6]
77.	Quercetin 3-*O*-β-D-glucoside	UHPLC-MS/MS	L	WULS, Poland	[6]
78.	Kaempferol *O*-hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
79.	Kaempferol *O*-rhamnosyl-hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
80.	Kaempferol acetyl hexoside	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
81.	(Epi) catechin derivative	UHPLC-MS/MS	L	WULS, Poland	[6]
82.	(Epi)catechin-B-(epi)catechin-B-(epi) catechin hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
83.	Naringenin *O*-hexoside	UHPLC-MS/MS	L	WULS, Poland	[6]
84.	Astragalin	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
85.	Eriodictyol	UHPLC-MS/MS	L	WULS, Poland	[6]
86.	Quercetin	UHPLC-MS/MS	L	WULS, Poland	[6]
		HPLC-PDA, UVS	I	Poland	[10]
87.	Isorhamnetin rutinoside	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
88.	Quercetin dihexoside 3	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
89.	Hyperoside	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
		HPLC-PDA, UVS	I	Poland	[10]
90.	Isoquercitrin	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
		HPLC-PD, UVS	I	Poland	[10]
91.	Quercetin 3-*O*-Malonylglucoside	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
92.	Procyanidin B2	UHPLC-MS/MS	L	WULS, Poland	[6]
93.	Catechin-7-*O*-*β*-D-apiofuranoside (flavanol glycosides)	Silica gel CC, NMR	SB	Mt. Sulak, Korea	[26]
94.	Neosakuranin (chalcone glycoside)	MS, IR, UV, NMR	F	Iksan, Korea	[25]
95.	Sakuranetin	NMR, Lc-MS	P	Daejeon, Korea	[30]
96.	Sexangularetin Derivative	HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
97.	Sexangularetin 3-*O*-glucopyranoside	HPLC-PDA, UVS	I	Poland	[10]
98.	Rutin	HPLC	F	CNU, Korea	[19]
		HPLC	F	Jecheon, Korea	[20]
		HPLC, UPLC-MS	I	Southeastern region of Lithuania	[11]
		HPLC-PDA, UVS	I	Poland	[10]
Phenolic glycosides					
99.	Benzyl *β*-D-glucopyranoside	NMR, CC	F	Jecheon, Korea	[9]
100.	Methyl syringate *α*-L-rhamnoside	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
101.	3,4,5-trimethoxyphenyl-(6′-*O*-benzoyl)-*O*-*β*-D-glucopyranoside (sorcomiside B)	NMR, HR-MS	SB	Gangwon-do, Korea	[21]

Table 2. *Cont.*

S No.	Compounds	Technique	Plant Part	Location	Ref.
102.	6′-*O*-benzoylprunasin (sorcomiside A)	NMR, HR-MS	SB	Gangwon-do, Korea	[21]
Cyanogenic glycosides					
103.	Prunasin	GLC, UV, IR, NMR	R, B, S, L	Japan	[31]
		NMR, CC	F	Jecheon, Korea	[9]
104.	Amygdalin	GLC, UV, IR, NMR	R, B, S, L	Japan	[31]
105.	Sambunigrin	NMR, CC	F	Jecheon, Korea	[9]
Sterol and derivatives					
106.	*β*-sitosterol	Silica gel CC, NMR	SB	Mt. Sulak, Korea	[26]
		Silica Gel CC	B	Hamyang, Korea	[22]
107.	β-sitosteryl-3-*O*-*β*-glucopyranoside	LC-MS	B	NG	[12]
Others					
108.	1,2,4-trimethoxydibenzofuran-3,9-diol	NMR	B	Kangwon Province, Korea	[24]
109.	β-pyrufuran	NMR	B	Kangwon Province, Korea	[24]
110.	Lyoniresinol 3a-*O*-β-D-Xylopyranoside	HPLC	St	Commercial source	[32]

GLC: gas-liquid chromatography; UVS: ultraviolet spectrophotometry; IR: infrared; NMR: nuclear magnetic resonance; MS: mass spectrometry; LC-MS: liquid chromatography coupled to mass spectrometry; NG: not given; HR-MS: high-resolution mass spectrometry; HPLC: high-performance liquid chromatography; RP-HPLC: reversed-phase HPLC; CNU: Chungbuk National University; CC: column chromatography; LR-MS: low-resolution electron-impact mass spectrometry; WULS: Warsaw University of Life Sciences; UHPLC: ultra-high-performance liquid chromatography; UPLC: ultra-performance liquid chromatography; HPLC-PDA: HPLC coupled to a photodiode array detector; F: fruit; I: inflorescence; L: leaves; SB: stem bark; B: bark; P: whole plant; R: roots; S: seeds; St: stem.

5. Biological Activities

5.1. Antioxidant Activity

Oxidative stress arises when the generation of reactive oxygen species (ROS), reactive nitrogen species, and other radicals exceeds the capacity of antioxidant defenses. The resulting accumulation of reactive species contributes to the pathogenesis of many diseases [33]. Increasing evidence suggests that phytoconstituents may help mitigate diseases associated with oxidative stress [34–36].

Olszewska et al. [18] assessed the antioxidant activity of inflorescence and leaf extracts of *S. commixta* using two complementary assays: a single-electron-transfer (SET)-based 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging assay and a hydrogen-atom-transfer (HAT)-based test of AAPH-induced linoleic acid (LA) peroxidation. In the DPPH assay, inflorescence extract had a lower EC_{50} (µg/mL), whereas leaf extract showed a lower percentage inhibition of LA peroxidation (Table 3). Overall, activity was lower than that of the reference standards quercetin and Trolox, with EC_{50} values of 1.44 ± 0.05 and 3.27 ± 0.10 for DPPH and percentage inhibition values of 88.38 ± 1.15 and 92.74 ± 1.10 for LA, respectively [18]. The antioxidant activity of *S. commixta* inflorescence methanol extract and its diethyl ether, ethyl acetate, and *n*-butanol fractions and water residue was reported as 3.52 ± 0.13 to 7.16 ± 0.22 for DPPH EC_{50} values (µg/mL) and 1.26 ± 0.05 to 3.40 ± 0.08 for TEAC (mmol Trolox®/g of aqueous extract). The reference standards included chlorogenic acid, rutin, butylated hydroxyanisole, butylated hydroxytoluene,

tertiary butylhydroquinone, and Trolox and had DPPH EC_{50} values ranging from 2.73 ± 0.12 to 6.54 ± 0.28 and TEAC values ranging from 2.56 ± 0.08 to 6.01 ± 0.24. For the remaining standards, namely, caffeic acid, (+)-catechin, gallic acid, and quercetin, activity was two to three times higher in the DPPH assay (0.95 ± 0.05 to 2.17 ± 0.11) and TEAC (9.51 ± 0.53 to 22.36 ± 0.63). Ferric reducing antioxidant power (FRAP) assay (mmol Fe^{2+}/g) values ranged from 2.70 ± 0.13 to 12.23 ± 0.07 across extracts (Table 3), whereas comparable or higher values were reported for the reference standards, 10.83 ± 0.32 to 44.17 ± 0.98 [10].

Table 3. Antioxidant and anti-inflammatory activities of *Sorbus commixta*.

Plant Part/Compounds	Biological Activities/Model	Results	Ref.
Leaves and inflorescence (70% methanol)	DPPH assay	DPPH (EC_{50} value µg/mL): Inflorescence: 23.22 ± 0.33; Leaves: 28.56 ± 0.64 TEAA (mmol/g) Inflorescence: 0.56; Leaves: 0.46	[18]
	LA peroxidation	(% inhibition) Inflorescence: 78.21 ± 1.61; Leaves: 58.65 ± 1.28	
Inflorescence (70% methanol) and fractions diethyl ether, ethyl acetate, *n*-butanol, and water residue	DPPH assay	DPPH (EC_{50} value µg/mL): Methanol: 7.16 ± 0.22; Diethyl ether: 5.72 ± 0.20; Ethyl acetate: 3.52 ± 0.13; *n*-butanol: 3.53 ± 0.16; Water residue: 9.66 ± 0.25 TEAC (mmol Trolox®/g) Methanol:1.70 ± 0.10; Diethyl ether: 2.14 ± 0.05; Ethyl acetate: 2.62 ± 0.13; *n*-butanol: 3.40 ± 0.08; water residue: 1.26 ± 0.05	[10]
	FRAP assay	FRAP (mmol Fe^{2+}/g): Methanol: 5.04 ± 0.24; Diethyl ether: 7.58 ± 0.10; Ethyl acetate: 12.23 ± 0.07; *n*-butanol: 11.01 ± 0.59; Water residue: 2.70 ± 0.13	
Leaves extract (methanol and water) and fractions: DEF; EAF, BF, water residue	Antioxidant/human plasma (ex vivo), extracts (1, 5, 50 µg/mL), water residue (5 µg/mL), 37 °C, 15 min, followed by ONOO− (100–150 µM). Inhibition of plasma proteins nitration	↑ inhibition up to 42%	[6]
	Lipid peroxidation inhibition (hydroperoxides, LOOHs)	↑ inhibition up to 62%	
	Effects on the plasma lipids oxidation and the formation of thiobarbituric acid reactive substances (TBARS)	Inhibition up to 26–37%	
	Non-enzymatic antioxidant capacity (NEAC, FRAP test)	↑ non-enzymatic antioxidant activity	
Stem bark (methanol) catechin-7-*O*-β-D-xylopyranoside (1), catechin-7-*O*-β-D-apiofuranoside (2)	DPPH, NBT, TBA methods	Compound 1: IC_{50} value (µM) DPPH: 3.6, Superoxide: 8.5; LPIA: 9.0	[29]
		Compound 2: IC_{50} value (µM) DPPH: 4.0 Superoxide: 9.2; LPIA: 9.2	
Cortex (methanol)	Inflammation/in vivo: Male SD rats, Frc, dose: 100, 200 mg/kg/day, 7 weeks	↓ TG, ↔ ecNOS, ↔ nitrite, ↔ cGMP, ↔ NF-κB p65, ↔ MCP-1, ↓ VCAM-1, ↓ ICAM-1, ↓ E-selectin, ↑ endothelin-1 (ET-1)	[37]
Plant extract (70% ethanol)	Inflammation/in vitro: RAW264.7, LPS (1 µg/mL), extract (0, 25, 50, 100, 200, 300, 400 µg/mL, 24 h HEK293 cells (Luciferase assay)	↓ NO, ↓ PGE_2, ↓ iNOS, ↓ COX-2, ↓ AP-1, ↓ p-JNK	[38]

Table 3. *Cont.*

Plant Part/Compounds	Biological Activities/Model	Results	Ref.
Plant extract (water)	Inflammation/in vitro, RAW264.7, LPS (1 µg/mL), extract (25, 50, 100, 200, 300, 400 µg/mL), 24 h HEK293 cells, in vivo: ICR mice, pretreatment with extract (100 mg/kg) or indomethacin (1 mg/kg), 7 days arachidonic acid (2%, *w*/*v*): 25 µL/ear	↓ NO, ↓ PGE_2 (dose-dependent), ↓ iNOS, ↓ COX-2, ↓ MyD88, ↓ NF- κB p65, ↓ p-IκBα, ↓ p-IKKα/β, ↓ p-PDK1, ↓ p-p85/PI3K, ↓ p-Src, ↓ p-Syk ↓ Ear thickness	[39]
Cortex/ *β*-sitosteryl-3-*O*-*β*-glucopyranoside	Inflammation/in vitro: RAW 264.7, LPS, (1 µg/mL), compound (12.5, 25, 50 µM),	↓ NO, ↓ PGE_2, ↓ iNOS, ↓ COX-2, ↓ TNF-α, ↓ IL-6, ↓ IL-1β, ↓ NF-kB	[12]
	in vivo: Paw edema mice, carrageenan (25, 100 mg/kg (p.o.))	↓ Paw swelling	
Leaves extract (methanol and water) and fractions: DEF, EAF, BF, water residue	Anti-inflammatory/PBMCs, pretreatment of extracts (1, 5, 50 µg/mL), water residue and DEF (5 µg/mL), 1 h + concanavalin A (10 µg/mL), 24 h. Positive control (5 µg/mL) treated	↓ IL-2, ↓TNF-α, ↓1L-1β (methanol 5 and 50 µg/mL), BF and EAF (50 µg/mL)	[6]

↓ = suppressed; ↔ = normalize; ↑ = enhanced; NBT: nitro blue tetrazolium; TBA: thiobarbituric acid; LPIA: lipid peroxidation inhibitory activity; DPPH: 2,2-diphenyl-1-picrylhydrazyl; TEAA: Trolox equivalent antioxidant activity (mmol Trolox equivalents/g of dry plant material). TEAC: Trolox equivalent antioxidant capacity (mmol Trolox equivalents/g of dry plant material). FRAP: ferric reducing antioxidant power (mmol Fe^{2+} equivalents/g of dry plant material). SD: Sprague-Dawley; Frc: high-fructose diet; TG: triglyceride; ecNOS: endothelial nitric oxide synthase; cGMP: cyclic guanosine monophosphate; NF-κB p65: nuclear factor kappa-light-chain-enhancer of activated B cells p65 subunit; MCP-1: monocyte chemoattractant protein-1; VCAM-1: vascular cell molecule-1; ICAM-1: intercellular adhesion molecule-1; E-selectin: endothelial leukocyte adhesion molecule 1; ET-1: endothelin-1; LPS: lipopolysaccharide; p-IκBα: phosphorylated inhibitor of kappa B alpha; RAW264.7: mouse macrophage cell line; HEK293: human embryonic kidney 293; NO: nitric oxide; PG: prostaglandin; TNF-α: tumor necrosis factor-alpha; iNOS: inducible NO synthase; COX-2: cyclooxygenase-2; JNK: c-Jun N-terminal kinase; AP-1: activator protein 1; MyD88: myeloid differentiation primary response 88; Src: non-receptor protein tyrosine kinase; Syk: spleen tyrosine kinase; IκBα: inhibitor of kappa B alpha; PDK1: 3-phosphoinositide-dependent protein kinase 1; p85/PI3K: phosphoinositide 3-kinase with p85 subunit; IL-6: interleukin 6; IL-1β: interleukin-1 beta; DEF: diethyl ether fraction; EAF: ethyl acetate fraction; BF: *n*-butanol fraction; EC_{50}: half-maximal effective concentration; IC_{50}: half-maximal inhibitory concentration; $ONOO^-$: peroxynitrite; LOOHs: lipid hydroperoxides; TBARS: thiobarbituric acid-reactive substances; NEAC: nonenzymatic antioxidant capacity; PBMCs: peripheral blood mononuclear cells; ICR: Institute of Cancer Research; PGE2: prostaglandin E2.

One study evaluated the radical-scavenging activity of two compounds isolated from *S. commixta* stem bark using superoxide and DPPH assays and a lipid-peroxidation inhibition assay. Compounds 1 and 2, catechin-7-*O*-β-D-xylopyranoside and catechin-7-*O*-β-D-apiofuranoside, showed strong radical-scavenging activity, with IC_{50} values of 3.6 µM and 4.0 µM against DPPH radicals, 8.5 and 9.2 µM against superoxide radicals, and 9.0 and 9.2 µM for inhibition of lipid peroxidation, respectively. Both compounds showed greater antioxidant activity than the reference antioxidants, namely, butylated hydroxyanisole and α-tocopherol [29]. Overall, the reported antioxidant activity supports further investigation of *S. commixta* as a potential functional food ingredient.

A recent study evaluated the antioxidant effects of *S. commixta* leaf methanol extract and its fractions. Depending on the extract and concentration, inhibitory effects were reported for plasma protein nitration and lipid peroxidation, measured by lipid hydroperoxide (LOOH) formation and thiobarbituric acid-reactive substances (TBARS) (Table 3). The observed effects were comparable to or greater than those of Trolox at equivalent extract weights. The extract and fractions also increased total nonenzymatic antioxidant capacity in plasma. The methanol extract and *n*-butanol fraction (BF) provided the strongest protection of human plasma components in an ex vivo model against peroxynitrite ($ONOO^-$)-induced nitrative and oxidative stress.

Correlation analyses showed mostly nonsignificant positive associations between redox-related measures, including TBARS and plasma nonenzymatic antioxidant capacity (NEAC), and individual phenolic acids, flavanones, flavonols, flavanols, and flavalignans. Significant associations were observed only between NEAC and total phenolic acids, total phenolics, or total flavonoids, and between TBARS and naringenin *O*-hexoside. Plasma lipid oxidation and LOOH formation showed strong but nonsignificant negative correlations with simple phenolic acids and flavonoid aglycones. The protective effects of the extract may reflect its capacity to scavenge $ONOO^-$ and secondary radicals generated by ONOO– [6]. Together, these findings support the antioxidant potential of *S. commixta*, although further in vitro and in vivo research is needed to characterize its biological effects.

5.2. Anti-Inflammatory Activity

Inflammation is a primary defense response to pathogens, physical injury, and tissue damage [40]. Acute inflammation helps protect the body, whereas persistent inflammation can disrupt physiological processes and contribute to disease [41]. Metabolic syndrome is associated with endothelial dysfunction and increased circulating inflammatory markers [42].

Kang et al. [37] examined the effects of methanolic *S. commixta* cortex extract on endothelial inflammation in rats with high-fructose-induced metabolic syndrome. Relative to the control group, extract treatment enhanced the endothelial nitric oxide synthase/nitric oxide (NO)/cyclic guanosine monophosphate (cGMP) pathway and restored the levels of the vasoactive peptide endothelin-1, inflammatory mediators such as nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) p65 subunit and monocyte chemoattractant protein-1 (MCP-1), and adhesion molecules such as vascular cell molecule-1 (VCAM-1), endothelial leukocyte adhesion molecule-1 (E-selectin), and intercellular adhesion molecule-1 (ICAM-1) [37]. These changes were associated with reduced vascular inflammation, suggesting *S. commixta* cortex's potential as an anti-inflammatory agent. Another study examined the anti-inflammatory effects of a 70% ethanolic *S. commixta* extract in lipopolysaccharide (LPS)-stimulated RAW264.7 mouse macrophages. The extract reduced prostaglandin (PG) E_2, NO, cyclooxygenase-2 (COX-2), and inducible nitric oxide synthase levels relative to LPS-treated RAW264.7 cells. It inhibited activator protein-1 (AP-1) translocation by reducing c-Jun N-terminal kinase (JNK) phosphorylation. However, extract treatment did not inhibit the translocation of NF-κB p65 up to 300 μg/mL (Table 3) [38]. These findings suggest potential anti-inflammatory activity, but animal studies and toxicity assessments are needed before therapeutic applications can be considered.

In a related study, researchers evaluated the anti-inflammatory properties of *S. commixta* in both in vitro and in vivo models. The extract reduced the inflammatory mediator PGE_2 in LPS-stimulated RAW264.7 cells and mice with arachidonic acid-induced edema. In contrast to the preceding report, the extract inhibited myeloid differentiation primary response 88-dependent NF-κB activation in response to the interaction between LPS and toll-like receptor 4, and reduced inflammatory responses. High-performance liquid chromatography showed differences in the constituent profiles of the water and ethanol fractions, including retention times and relative component amounts. These findings suggest that extraction conditions may affect phytochemical composition and associated biological activity [39].

Another study reported the anti-inflammatory activity of bark-derived β-sitosteryl-3-*O*-β-glucopyranoside in LPS-treated RAW264.7 cells. Treatment with the compound reduced the production of proinflammatory cytokines and mediators by inhibiting the mitogen-activated protein kinase (MAPK) signaling pathway and suppressing NF-κB activation without detectable cytotoxicity. In addition, in rats with carrageenan-induced edema of the right hind paw, the compound reduced paw inflammation 1 h after administration. At 3 h, paw edema was reduced by 63.2% at 25 mg/kg, compared with a 50.4% reduction in

the ibuprofen-treated group [12]. Further animal studies and clinical trials are needed to assess the compound's potential as an anti-inflammatory agent.

More recently, *S. commixta* leaf extracts and fractions were evaluated for several activities, including anti-inflammatory effects. Pretreatment with the extracts reduced proinflammatory cytokine release from concanavalin A-stimulated human peripheral blood mononuclear cells in vitro [6]. Together, these studies suggest anti-inflammatory activity, although additional work is needed to identify the responsible *S. commixta* constituents.

5.3. Anticancer Activity

Cancer affects approximately one-third of the global population. It involves uncontrolled cellular proliferation and may invade and damage surrounding tissues [43]. Cancer-cell invasion involves multiple pathways, and understanding these mechanisms is important for developing anticancer agents. Growing evidence suggests that plant extracts and bioactive constituents may provide candidates for anticancer drug development [44]. Accordingly, *S. commixta* extracts and constituents have been investigated for anticancer activity.

Metastasis contributes substantially to cancer-related mortality, motivating research into agents that inhibit tumor spread. In this context, Park et al. [45] investigated the effects of aqueous extracts of *S. commixta* Hedl. on invasion and migration in highly metastatic Hep3B hepatocellular carcinoma cells and the underlying mechanisms. The extract reduced the expression and activity of matrix metalloproteinase-9 (MMP-9), a protein associated with tumor invasion, and chemokine receptors, while altering cytoskeletal organization. The findings implicated phosphorylated extracellular signal-regulated kinase (ERK) and p38 mitogen-activated protein kinase signaling in the observed cellular effects. The findings support further investigation of *S. commixta* extracts as potential inhibitors of tumor invasion and migration. Future research should examine extract toxicity and safety in animal models (Table 4) [45].

Inducing apoptosis in cancer cells is one strategy for limiting tumor growth. Apoptotic effects of *S. commixta* fruit and bark extracts have been reported in cancer cell models [9,46]. Lee et al. [9] examined cytotoxic effects of *S. commixta* fruit extract in four human lung cancer cell lines. The ethanolic fruit extract produced cytotoxic and apoptotic effects, including cell shrinkage and membrane blebbing, in the Calu-6, H1299, H1264, and A549 lung cancer cell lines, regardless of p53 status (mutant, wild-type, or null). Cell viability decreased in a concentration-dependent manner, with IC_{50} values (mg/mL) of 0.81 ± 0.07 (Calu-6), 1.34 ± 0.15 (A549), 1.35 ± 0.02 (H1299), and 2.01 ± 0.33 (H1264) (Table 4). Three bioactive constituents were also reported—sambunigrin, prunasin, and β-$_D$-glucopyranoside—in the fruit extract [9]. These cell-based findings warrant further investigation of the anticancer potential of *S. commixta* fruit extract. However, efficacy and safety require assessment in animal models.

Another study reported proapoptotic activity of stem and bark extracts of *S. commixta* in human colon carcinoma cells (HCT116). The extract showed cytotoxic effects in three cancer cell lines (HCT116, HepG2, and Hep3B); the most responsive cell line was selected for further investigation. Treatment increased the proportion of HCT116 cells in the sub-G1 phase and increased levels of signaling proteins (p53, p27, and p21) and altered the processing of apoptosis-related proteins (poly(ADP-ribose) polymerase, caspase-3, and caspase-9). The findings suggested that extract-induced apoptosis involved mitochondrial ROS generation (Table 4) [46]. The study suggests that *S. commixta* extracts merit further investigation into proapoptotic anticancer activity; however, their efficacy and safety must be assessed in animal models.

Table 4. Anticancer activity of *Sorbus commixta*.

Plant Part/Compounds	Biological Activities/Model	Results	Ref.
Air-dried stem and cortex (water)	Anti-metastatic potential/Hep3B cells, extract (0, 50, 100 μg/mL), 24 h	↓ MMP-9, ↓ invasion, ↓ migration, ↓ CXCR-4, ↓ CXCR-6, ↓ p-ERK, ↓ p-p38, ↑ p-JNK (slightly)	[45]
Fruit extract (50% ethanol)	Anti-cancer/Calu-6, H1299, H1264, and A549 cells, extract (0.5, 1.0, 1.5, 2.0 mg/mL)	↑ cytotoxicity, ↑ apoptosis	[9]
Stem and bark extract (water)	Anti-cancer/HCT116 cells, extract (0, 50, 100, 200 mg/mL), 48 h	↑ sub-G1 phase cells (dose-dependent), ↑ apoptosis, ↓pro-PARP, ↑ cleaved PARP, ↓pro-caspase-3, ↑ cleaved caspase-3, ↓ pro-caspase-9, ↓ MMP, ↑ p21, ↓ MDM2 ↑ p27, ↑ p53, ↑ Bax, ↓ Bcl-2	[46]
Bark extract (ethyl acetate) Ursolic acid (4), betulinic acid (3), betulin (2)	Anti-cancer/HEp-2, MCF-7, A549, PC-3 and SKOV-3, 7 Compounds (1, 50, 100 μM)	Compounds 2,3, and 4 at 100 μM: excellent cytotoxicity against HEp-2 and A549 at 4 h post-UV irradiation	[24]
Fruit/ethanol (butanol)	Anti-cancer/SK-MEL-2 cells, Butanol fraction (25, 50, 100 μg/mL), 48 h	Butanol extract: ↑cytotoxicity (dose-dependent), TPC: 87.15 μg GAE/mg of extract, TFC: 22.25 μg QE/mg of extract, chlorogenic acid: 912.72 μg/g ↓ p-ERK, ↓ p-MEK, ↑ caspase-3	[19]

↓ = suppressed; ↑ = enhanced; Calu-6, H1299, H1264, A549: human non-small cell lung cancer cells; Hep3B: immortalized human liver cancer cells; MMP-9: matrix metalloproteinase-9; CXCR-4/6: C-X-C chemokine receptors 4 and 6; ERK: extracellular signal-regulated kinase; p38: p38 mitogen-activated protein kinase; HCT116: human colon cancer cell line; PARP: poly(ADP-ribose) polymerase; caspase-3/9: aspartate-specific cysteine proteases 3/9; MMP: mitochondrial membrane potential; p21: cyclin-dependent kinase inhibitor 1; p27: cyclin-dependent kinase inhibitor 1B; p53: tumor protein p53; Bcl2: B-cell lymphoma 2; Bax: Bcl-2-associated X protein; HEp-2: human epithelial type 2; MCF-7: Michigan Cancer Foundation-7; MDM2: mouse double minute 2 homology; SKOV-3: human ovarian cancer cells; PC-3: prostate cancer cells; SK-MEL-2: human melanoma cells; TPC: total phenolic content; GAE: gallic acid equivalent; TFC: total flavonoid content; QE: quercetin equivalent; MEK: mitogen-activated protein kinase.

A further study isolated seven compounds—(1) lupeol, (2) betulin, (3) betulinic acid, (4) ursolic acid, (5) β-sitosterol, (6) β-pyrufuran, and (7) 1,2,4-trimethoxydibenzofuran-3,9-diol from the bark of *S. commixta* Hedl.—and assessed their cytotoxic activity in five cancer cell lines: human epithelial type 2 (HEp-2), Michigan Cancer Foundation-7 (MCF-7), A549, prostate cancer cells (PC-3), and human ovarian cancer cells (SKOV-3) (Table 4). Of these, compounds 2, 3, and 4 showed significant cytotoxicity in HEp-2 (compound 2 = 43.5 ± 2.32, compound 3 = 37.2 ± 3.08, compound 4 = 84.8 ± 0.23) and A549 (compound 2 = 38.0 ± 3.26, compound 3 = 41.0 ± 4.75, compound 4 = 80.8 ± 0.31) cells, relative to untreated control cells. The positive control, docetaxel, showed cytotoxic effects on HEp-2 and A549 cells (83.6 ± 1.69 and 64.8 ± 3.52, respectively). Compound 4 also showed significant cytotoxicity against MCF-7 (80.8 ± 0.22), PC-3 (76.6 ± 3.89), and SKOV-3 (77.1 ± 0.36) [24]. Further animal studies are needed to evaluate the anticancer properties of these compounds. Cytotoxicity testing in noncancerous human cell lines is also warranted.

Melanoma is a potentially fatal skin cancer arising from uncontrolled proliferation of melanocytes. Jin et al. [19] reported antimelanoma activity of an ethanolic fruit extract of *S. commixta* against human melanoma (SK-MEL-2) cells. The *n*-butanol fraction showed greater antimelanoma activity than the other solvent fractions. Activity decreased in the following order: butanol fraction (83.47%), ethyl acetate fraction (33.57%), hexane fraction (9.43%), and aqueous fraction (5.56%). The butanol fraction was associated with reduced MAPK and ERK signaling and increased caspase-3 activity, suggesting involvement of these pathways in cancer cell death. HPLC analysis identified rutin, chlorogenic acid, gallic acid, ferulic acid,

hydroxybenzoic acid, protocatechuic acid, and sinapinic acid (Table 4) [19]. The butanol fraction had the highest chlorogenic acid concentration (912.72 ± 68.04 μg/g), which may contribute to its relatively strong antimelanoma activity, as chlorogenic acid is recognized for its antioxidant, anti-inflammatory, and anticancer properties. These in vitro findings support further exploration of *S. commixta* fruit constituents as potential antimelanoma agents.

Across these studies, *S. commixta* extracts and constituents showed promising effects on cancer cell invasion, apoptosis, and viability. Because the evidence is primarily from in vitro studies, animal research is needed to establish the safety and potential efficacy of these extracts and compounds.

5.4. Skin-Protective Activity

Ultraviolet (UV) irradiation increases ROS production in the skin and activates tissue-degrading enzymes. These processes contribute to skin damage associated with photosensitivity, photoaging, phototoxicity, and malignancy [47]. Herbal extracts have therefore been investigated for potential skin-protective effects.

Bae et al. [48] reported that treating *S. commixta* cortex extract with β-glucanase, a carbohydrate-hydrolyzing enzyme, enhanced ROS-scavenging activity in UVB-irradiated human dermal fibroblast (HDF) cells. The enzyme-treated extract also reduced UVB (6.3 J/cm^2)-induced MMP-1 expression in a dose-dependent manner. At 20 μg/mL, its inhibitory effect was greater than that of trans-retinoic acid, a known inhibitor of UVB-induced MMPs. The enhanced activity was attributed to increased total phenolic content (TPC; μg GAE/mg extract) and flavonoid content (μg quercetin equivalents/mg extract). Enzymatic treatment also increased the extract's radical-scavenging activity. The findings suggest that enzymatic treatment may improve the skin-protective effects of *S. commixta* extract by enhancing its antioxidant activity [48] (Table 5).

Table 5. Skin-protective, neuroprotective, and antiviral properties of *Sorbus commixta*.

Plant Part/Compounds	Biological Activities/Model	Results	Ref.
Cortex extract (ethanol)	Skin protection/HDFs cells, ROS test: UVB (20 mJ/cm^2), β-GSCoE dose (1, 10, 100 μg/mL) MMP-1 expression: UVB (6.3 J/cm^2), β-GSCoE dose (2.5, 5, 10, 20 μg/mL)	↓ ROS ↓ MMP-1(%) (2.5 = 7.4, 5 = 16.5, 10 = 32.4, 20 = 55.9)	[48]
Twig extract (70% ethanol)	Skin protection/NHDF cells, Cell viability: extract pretreatment (6.3, 12.5, 25, 50, 100, 200 μg/mL), 24 h + UVB (80 mJ/cm^2), 24 h ROS: extract pretreatment (12.5, 25, 50 μg/mL) + UVB (80 mJ/cm^2) + DCFH-DA dye, 30 min	↑ cell viability ↓ ROS (dose-dependent) ↓ MMP-1, ↓ MMP-2, ↓ MMP-3, ↓ c-Fos, ↓ p-p38, ↓ p-ERK, ↓p-JNK	[49]
Twig extract (70% ethanol)	Skin protection/B16 cells: extract (3.125, 6.25, 12.5 μg/mL), 48 h Melanin production: extract (2.5, 5, 10, 20 μg/mL), 72 h	↑ cell proliferation, ↑ melanin content	[50]
	NHDF cells: extract pretreatment (12.5, 25, 50, 100 μg/mL) + TNF-α (10 ng/mL)	↓ IL-6, ↓ IL-8, ↓ TNF-α	
	HaCaT cell: extract pretreatment (2.5, 5, 10, 20 μg/mL) + TNF-α (10 ng/mL)	↓ IL-6	
Stem extract (30% ethanol)	Neuroprotective/In vivo: Drosophila, Aβ42, TDP-43, extract (5, 50 μg/mL)	↑ survival rate, ↑ decreased eye size, ↑ pupariation rates, ↑ motor activity, ↓ ROS, ↓ rough eye	[32]
	In vitro: SH-SY5Y cells, extract (5, 25, 50 μg/mL), Aβ (25 μM)	↓ Aβ42-induced cell death	
	DPPH, dose: 0.1 to 100 μg/mL	IC_{50} values (μg/mL): 23.4	

Table 5. *Cont.*

Plant Part/Compounds	Biological Activities/Model	Results	Ref.
Stem bark extract (80% aqueous methanol), sorcomic acid *(1), 9-hydroxynonanoic acid (5), azelaic acid (7)	Neuroprotective/C6 glioma cells	↑ NGF	[23]
Compound 10 *	Anti-neuroinflammation/BV2 cells	↓ NO (IC_{50} = 71.25 μM), ↓ NF-κB	
Fruit extract (water and ethanol 70%)	Neuroprotective/BV2 cells, extract pretreatment (12.5, 25, 50, 100, 200 μg/mL), 1 h and LPS (200 ng/mL), 24 h	↓ NO, ↓ TNF-α, ↓ IL-6, ↓iNOS, ↓ COX-2, (dose-dependent) ↓ p-JNK, ↓ p-ERK, ↓ p-p38, ↓ p-IκBα, ↓ nuclear translocation of NF-κB	[20]
Caffeic acid	Neuroprotective/BV2 cells, caffeic acid pretreatment (12.5, 25, 50, 100 μg/mL), 1 h, LPS (200 ng/mL), 18 h	↓ NO, ↓ iNOS, ↓ COX-2	
Dried whole plant (methanol), sakuranetin	Antiviral/HeLa cells, HRV3, sakuranetin (0.1, 1, 10, 100 μg/mL), 48 h Ribavirin (an antiviral drug)	Antiviral activity(100 μg/mL) = Compound: 67% Drug: 60% ↓ CPE	[30]
Branch and stem/water (SCW) and ethanol (SCE) extracts	Antiviral/A/MA81 (H5N2) virus + water extract (312.5, 625, 1250, 2500 μg/mL), ethanol extract (31.3, 62.5, 125, 250, 500, 1000 μg/mL), 30 min, MDCK cells, 48 h	Inhibited viral entry (dose-dependent) Showed hemagglutination inhibition activity (ethanol extract > water extract), suppressed viral replication, exhibited hemolysis inhibition activity	[51]
	DPPH Water extract (78.1–2500 μg/mL) Ethanol extract (31.3–1000 μg/mL)	Antioxidant: EC_{50} (μg/mL) SCE = 392.2, SCW = 241.0	

↓ = suppressed; ↑ = enhanced; HDFs: human dermal fibroblasts; HaCaT: human keratinocyte cell line; Aβ42: amyloid beta 42; TDP-43: TAR DNA-binding protein 43; β-GSCoE: β-glucanase-treated *S. commixta* Hedl. cortex extract; NHDF: normal human dermal fibroblast; ROS: reactive oxygen species; SH-SY5Y: human neuroblastoma cell line; DPPH: 2,2-diphenyl-1-picrylhydrazyl; B16: mouse melanoma cell line; IC_{50}: half-maximal inhibitory concentration; NGF: nerve growth factor; BV-2: mouse microglia cell line; NO: nitric oxide; HRV3: human rhinovirus 3; CPE: cytopathic effect; MDCK: Madin–Darby canine kidney cells; A/MA81 (H5N2): strain of H5N2 avian influenza A virus; IL-6: interleukin 6; iNOS: inducible NO synthase; TNF-α: tumor necrosis factor-alpha; LPS: lipopolysaccharide; MMP: matrix metalloproteinase; p-ERK: phosphorylated extracellular signal-regulated kinase; p38: p38 mitogen-activated protein kinase; p-IκBα: phosphorylated inhibitor of kappa B alpha; c-Fos: a proto-oncogene; COX-2: cyclo-oxygenase-2; p-JNK: phosphorylated c-Jun N-terminal kinase; NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells; DCFH-DA: 2′,7′-Dichlorodihydrofluorescein diacetate; UVB: ultraviolet B; EC_{50}: half-maximal effective concentration; SCW: *Sorbus commixta* water extract; SCE: *Sorbus commixta* ethanol extract. * Compound 1: sorcomic acid, 5: 9-hydroxynonanoic acid, 7: azelaic acid, 10: (9S,12R,13R)-(E)-9,12,13-trihydroxy-10-octadecaenoic acid.

Another study examined the photoprotective effects of ethanolic *S. commixta* twig extract and their underlying mechanisms. The extract had a total phenolic content (TPC) of 54.9 ± 0.9 gallic acid mg/g, a total flavonoid content (TFC) of 292.2 ± 0.1 quercetin mg/g, and an extraction yield of 4.1%. The extract reduced intracellular ROS levels in HDF cells after UVB exposure. The extract treatments up to 100 μg/mL did not show any cytotoxicity; however, high-concentration supplementation (200 μg/mL) drastically reduced (54.3%) the HDF cell's viability compared to the untreated control. Notably, pretreatment with 200 μg/mL extract followed by UVB exposure (80 mJ/cm^2) exhibited significantly higher (83.1%) cell viability than the group treated with the extract (at 200 μg/mL) alone. The findings indicated reduced expression of the proto-oncogene c-Fos and downstream MMP-1/2/3 levels in fibroblasts (Table 5). These protective effects might be associated with extract-induced inhibition of MAPK signaling. The study therefore suggests potential antiphotoaging activity of *S. commixta* twig extract [49]. Further, in vivo studies are needed to evaluate these effects.

A separate study examined *S. commixta* twig extract for potential applications in vitiligo, an autoimmune condition characterized by skin depigmentation. The extract increased B16 melanocyte proliferation and melanin production compared to untreated cells. Keratinocytes and fibroblasts contribute to the regulation of melanocyte function. In cells stimulated with recombinant human TNF-α, extract treatment reduced proinflammatory cytokine levels and ERK phosphorylation in normal human dermal fibroblasts (NHDF) and HaCaT keratinocytes. The extract also showed radical-scavenging activity in a DPPH assay, supporting further investigation of its potential relevance to vitiligo [50]. Further animal studies are needed to investigate whether *S. commixta* extracts protect against photoaging or vitiligo-related changes. The bioactive constituents responsible for these effects also require identification.

5.5. Neuroprotective Activity

Neurodegenerative disorders, including Alzheimer's disease (AD) and Parkinson's disease, involve multiple pathophysiological changes. These may include progressive neuronal loss, amyloid beta (Aβ) plaque accumulation, increased ROS production, cellular dysfunction, and cognitive impairment [52]. Numerous medicinal plants and their constituents have been investigated for neuroprotective effects [53]. *S. commixta* has also been examined in this context.

One study screened 23 medicinal plants for protective activity against Aβ42-associated neurotoxicity in a *Drosophila* model of AD. Five extracts, including that of *S. commixta*, showed protective activity. *S. commixta* stem extract reduced Aβ42-associated cell death in *Drosophila* larval brains and human neuroblastoma (SH-SY5Y) cells treated with Aβ42. The extract also reduced ROS levels in eye imaginal discs from the *Drosophila* AD model. Lyoniresinol 3a-*O*-β-D-xylopyranoside was reported as the principal constituent of the extract. The extract also exhibited DPPH radical-scavenging activity, with an IC_{50} of 23.4 μg/mL. The findings suggested protection against Aβ42-associated toxicity and abnormalities involving transactive response DNA-binding protein 43 (TDP-43) [32] (Table 5). These preclinical findings suggest that *S. commixta* constituents warrant further study for neuroprotective applications.

Another group isolated 10 compounds from *S. commixta* bark. The compounds were evaluated for their ability to stimulate nerve growth factor (NGF) secretion in C6 glioma cells. Among these, compound 1 (sorcomic acid, 233.40 ± 12.82%), compound 5 (9-hydroxynonanoic acid, 194.40 ± 8.05%), and compound 7 (azelaric acid, 185.74 ± 10.25%) increased NGF release from C6 glioma cells to levels above those obtained with the positive control, 6-shogaol (168.58 ± 7.16%). In addition, compound 10 ((9S,12R,13R)-(E)-9,12,13-trihydroxy-10-octadecaenoic acid) reduced NO production and NF-κB protein levels in LPS-stimulated BV-2 microglial cells (Table 5). The other compounds (1–9) showed weak or no activity in this assay. These results suggest potential antineuroinflammatory and neuroprotective effects of *S. commixta*-derived compounds [23]. Kim et al. [21] reported that 12 compounds isolated from *S. commixta* bark did not inhibit NO production or affect other examined neuroprotective markers. These contrasting findings indicate that neuroprotective activity may vary among phytoconstituents [21]. Further studies should identify which constituents are most active and investigate their mechanisms.

S. commixta fruit extracts reduced LPS-induced inflammatory responses in BV-2 microglial cells. Compared with the 70% ethanol extract, the aqueous extract showed stronger antineuroinflammatory activity, reducing NO production, the proinflammatory markers IL-6 and TNF-α, and COX-2 relative to LPS-treated cells. The authors attributed these effects to downregulation of MAPK and NF-κB signaling (Table 5). Caffeic acid, detected at a concentration three times higher in the aqueous than in the ethanol extract, was identified as a potential contributor to the antineuroinflammatory activity [20]. Although these in vitro

findings are promising, animal studies are needed to examine efficacy, safety, toxicity, and the mechanisms underlying the reported effects.

5.6. Antiviral Activity

Plant-derived compounds have been investigated for activity against numerous viruses, including influenza viruses. The limited availability of effective treatments for human rhinovirus 3 (HRV3) has motivated the search for new antiviral agents. Plant-derived constituents are among the candidates being investigated.

S. commixta has likewise been investigated for antiviral activity. The flavonoid phytoalexin sakuranetin, isolated from *S. commixta*, was evaluated against HRV3 using the sulforhodamine B assay. The compound was obtained from the ethyl acetate fraction and identified by NMR and low-resolution electron-impact mass spectrometry. At 100 μg/mL, sakuranetin inhibited HRV3 activity by more than 67% in human cervical carcinoma (HeLa) cells, compared with 60% inhibition by the antiviral drug ribavirin at the same concentration (Table 5). Morphological assessment showed reduced cytopathic effects after treatment with either compound, without detectable cytotoxicity in HeLa cells [30]. Further studies are needed to determine the antiviral mechanism of sakuranetin.

Another study reported inhibitory activity of aqueous and ethanolic extracts of a *S. commixta* stem-and-bark mixture against influenza A virus. Both extracts were rich in polyphenols and showed radical-scavenging activity. At 1000 μg/mL, total polyphenolic contents were 127.7 μg GAE/mL and 153.2 μg GAE/mL in the aqueous and ethanolic extracts, respectively. At noncytotoxic concentrations, both extracts reduced plaque formation and cytopathic effects. The concentrations associated with 50% inhibition of cytopathic effects (IC_{50}, μg/mL) were 768.2 and 153.0 for water and ethanol extracts, respectively. Mechanistic findings suggested effects on both early and late stages of the viral life cycle through inhibition of neuraminidase and modulation of hemagglutinin-mediated attachment and membrane fusion (Table 5). Overall, the ethanolic extract showed greater antiviral activity than the aqueous extract [51]. These cell-based results support further investigation of *S. commixta* extracts in animal models and more detailed mechanistic studies.

5.7. Cardiovascular Protection

Cardiovascular disorders, including atherosclerosis and hypertension, are associated with endothelial dysfunction and impaired NO signaling [54]. Because NO-mediated vasodilation contributes to blood pressure regulation, biomaterial platforms have been investigated for controlled, sustained NO delivery to specific tissues [55]. Natural bioactive compounds have also been reviewed for potential cardiovascular protective effects [56].

Kang et al. [57] investigated the vasorelaxant mechanism of methanolic *S. commixta* cortex extract in phenylephrine-precontracted rat aortic rings. Pretreatment with methylene blue, N^G-nitro-L-arginine methyl ester (L-NAME), and 1H-[1,2,4]-oxadiazole-[4,3-α]-quinoxalin-1-one attenuated extract-induced relaxation. The extract increased cGMP levels in human umbilical vein endothelial cells (HUVECs) and endothelium-intact carotid arteries in experiments assessing impaired vasorelaxation. The results suggested involvement of L-type Ca^{2+} channels and NO–cGMP signaling in endothelium-dependent relaxation after *S. commixta* cortex extract treatment (Table 6) [57]. Although endothelium-dependent relaxation was observed ex vivo, limited in vivo evidence and incomplete identification of active constituents constrain potential clinical applications.

Another study reported that *S. commixta* bark extract attenuated atherosclerosis-related changes in L-NAME-treated rats by reducing adhesion markers, proinflammatory cytokines, and vasoactive mediators. Aortic histopathology showed reduced intimaand media thickness after extract treatment (Table 6) [58]. Scopoletin, a bark-derived coumarin stud-

ied by Kang et al., may contribute to these antiatherosclerotic effects [22]. Scopoletin (IC_{50} = 10.2 ± 0.1 μM) was selected from four isolated compounds (lupeol, β-sitosterol, ursolic acid, and scopoletin) because it inhibited $CuSO_4$-induced low-density lipoprotein oxidation more strongly than the reference standard ascorbic acid (IC_{50} = 84.1 ± 0.3 μM). Scopoletin also reduced TNF-α-induced inflammation in EA.hy926 endothelial cells by lowering adhesion molecule expression.

Table 6. Cardiovascular protective effects of *Sorbus commixta*.

Plant Part/Compounds	Biological Activities/Model	Results	Ref.
Cortex extract (methanol)	ex vivo: SD rats (aorta), endothelial intact aortic rings, extract (PH, 3 × 10^{-6} M), pretreatment with L-NAME and ODQ (1 × 10^{-6} M), MB (1 × 10^{-5} M) HUVECs, extract (1 × 10^{-4} g/mL), L-NAME, ODQ (1 × 10^{-6} M)	Aortic ring: ↑ relaxant effect (dose-dependent), maximal relaxation = 95.3 ± 2.1% versus PH contraction Pretreatment with L-NAME and ODQ, and MB inhibited relaxing effect HUVEC and carotid artery: ↑ cGMP	[57]
Cortex extract (100% methanol)	in vivo: SD rats L-NAME (1 mg/mL, first 3 weeks): control group, extract-treated (control group, 200 mg/kg/d), L-NAME group + extract (100, 200 mg/kg/d) + L-NAME group, 6 weeks	↓ NF-κB p65, ↓ MCP-1 ↓ VCAM-1, ↓ ICAM-1, ↓ E-selectin, ↓ ACE, ↑ ecNOS (restored) ↓ ET-1	[58]
Dried bark extract (methanol, partitioned with chloroform)/Scopoletin	in vitro: EA.hy926, scopoletin pretreatment (0, 10, 20, 40 μM), 2 h; TNF-α (30 ng/mL), 4 h, 18 h (cell adhesion) TNF-α-treated THP-1 cells + BCECF-AM (10 μM) for 1 h, added to endothelial cells, 45 min	↓ ox-LDL, ↓ VCAM-1, ↓ ICAM-1, ↓ E-selectin, ↓ IκBα phosphorylation ↓ cell adhesion (dose-dependent)	[22]
Dried fruit extract (water)	in vivo: ICR mice, induced-ferric chloride, extract (1000 mg extract/kg/day), 4 weeks	↓ thrombosis	[59]
	in vitro: blood from SD rats, Washed platelets + extract (10, 25, 50, 100 μg/mL), 5 min, thrombin-induced (0.14 U/mL)	↓ platelets aggregation	

↓ = suppressed; ↑ = enhanced; SD: Sprague-Dawley; HUVEC: human umbilical vein endothelial cells; L-NAME: NG-nitro-L-arginine methyl ester; PH: phenylephrine; BCECF-AM: 2′,7′-bis-(2-Carboxyethyl)-5-(and-6)-carboxyfluorescein, acetoxymethyl ester; MB: methylene blue; ODQ: 1H-[1,2,4]-oxadiazole-[4,3-α]-quinoxalin-1-one; cGMP: cyclic guanosine monophosphate; NF-κB p65: nuclear factor kappa-light-chain-enhancer of activated B cells p65 subunit; MCP-1: monocyte chemoattractant protein-1; VCAM-1: vascular cell molecule-1; ICAM-1: intercellular adhesion molecule-1; E-selectin: endothelial leukocyte adhesion molecule 1; ACE: angiotensin-converting enzyme; ET-1: endothelin-1; ecNOS: endothelial nitric oxide synthase; ox-LDL: oxidized low-density lipoprotein; EA.hy926: human vascular endothelial cells; THP-1: human monocytic cell line; TNF-α: tumor necrosis factor-alpha; IκBα: inhibitor of kappa B alpha; ICR: Institute of Cancer Research.

Scopoletin inhibited THP-1 monocyte adhesion to endothelial cells in a concentration-dependent manner, as assessed using 2′,7′-Bis-(2-Carboxyethyl)-5-(and-6)-carboxyfluorescein fluorescence. Scopoletin suppressed vascular endothelial inflammation through inhibition of NF-κB signaling (Table 6) [22]. These findings suggest that its anti-inflammatory properties may contribute to antiatherosclerotic activity. However, further in vivo studies are required to evaluate efficacy and safety.

Antithrombotic activity of *S. commixta* fruit extract was evaluated in a mouse model of ferric chloride-induced arterial thrombosis. After 4 weeks of treatment, the extract significantly prolonged the time to thrombotic vascular occlusion from 11.6 ± 1.0 min to 18.4 ± 5.5 min, although the effect was smaller than that of the positive control, clopidogrel. The extract also inhibited aggregation of thrombin-stimulated washed rat platelets in vitro.

No effect on plasma coagulation was observed (Table 6). These findings support further investigation of *S. commixta* fruit extract for cardiovascular protection. Further work should identify the bioactive constituents and mechanisms underlying its antithrombotic effects, followed by clinical evaluation [59].

Together, these studies suggest potential cardiovascular benefits of *S. commixta* and its bioactive constituents. Additional animal studies and clinical investigations are needed to establish their relevance.

5.8. Antidiabetic Activity

Diabetes is a chronic metabolic disorder affecting millions of individuals worldwide in the 21st century. Growing evidence suggests that bioactive compounds from medicinal plants may have antidiabetic potential [60,61].

Methanolic *S. commixta* stem bark extract exhibited potential antidiabetic activity through inhibition of protein tyrosine phosphatase 1B (PTP1B), a negative regulator of insulin signaling. Fractionation identified lupeol and lupenone, both of which inhibited PTP1B in a concentration-dependent manner, with IC_{50} values of 5.6 ± 0.9 μM and 13.7 ± 2.1 μM, respectively. Their IC_{50} values were comparable to those of the positive controls, including ursolic acid (3.5 ± 0.2 μM) and RK-682 (4.5 ± 0.5 μM) (Table 7). Kinetic analysis identified both compounds as noncompetitive inhibitors, supporting further study of their potential relevance to insulin resistance. Additional studies are needed to characterize their mechanisms and in vivo effects [27].

Table 7. Antidiabetic, antiosteoporotic, antiosteoarthritic activities of *Sorbus commixta* and protection against alcohol intoxication.

Plant Part/Compounds	Biological Activities/Model	Results	Ref.
Stem bark extract (methanol) and partitioned, Lupenone and lupeol	Anti-diabetic/in vitro: PTP1B assay, *p*−nitrophenyl phosphate (2 mM), PTP1B (0.05–0.1 μg), 37 °C, 30 min Inhibition kinetics: PTP1B (0.5, 1.0, 2.0, 4.0, 8.0, 16.0 mM) in the presence or absence of lupeol (0.0, 1.0, 5.0, 10.0, 20.0 μM) and lupenone (0.0, 1.0, 5.0, 10.0, 20.0 μM)	↓ PTP1B	[27]
Leaves (methanol–water extract) and fractions: DEF; EAF, BF, water residue	α-glucosidase inhibition assay α-amylase inhibition assay Anti-glycation activity	α-glucosidase: Stronger inhibitory effect α-amylase: Weaker inhibitory effect Inhibitory potential against AGEs	[6]
S. commixta frozen berries extract (70% acetone)	α-glucosidase inhibition assay α-amylase inhibition assay	Stronger inhibitory effects	[62]
Stem bark extract (methanol) and partitioned with different solvents, Lupeol	Anti-osteoporotic/In vivo: C57BL/6 mice, three groups:1α,25-$(OH)_2D_3$ + PBS or lupeol (25 or 100 μg/kg), 3 days Other three groups: only with PBS or lupeol (5, 25, 50 or 100 μg/kg), 5 days; 8 days	Inhibited osteoclast differentiation, ↓ RANKL production, ↓ Bone loss	[28]
	Ex vivo-derived cell model: mouse Calvaria osteoblasts + lupeol (1, 5, 10, 20 μM), 2 days RT-PCR: mouse Calvaria osteoblasts + 1α,25-$(OH)_2D_3$ (0.1 μM) + lupeol (5, 10 μM), 24 h	No effect on osteoblast viability, ↓ ALP, ↓ RANKL (mRNA)	
	Osteoclast differentiation: BMM cells, RANKL + lupeol (5, 10, 20 μM), 15 min, 30 min, and 24 h	Inhibited osteoclast differentiation ↓ MAPK, ↓ NF-κBp65, ↓ AP-1, ↓ p-ERK, ↓ p-p38, ↓ c-Fos, ↓ p-NF-κB, ↓ NFATc1, ↓p-IκBα	
	Actin ring formation and resorption assay: Bone marrow cells (from tibiae of ICR male mice) + mouse calvariae osteoblasts + 1α,25-$(OH)_2D_3$ (0.1 μM) + PGE_2 (10 μM), 6 days	Inhibited pit formation (20 μM) ↓ bone resorption	

Table 7. *Cont.*

Plant Part/Compounds	Biological Activities/Model	Results	Ref.
Stem extract (30% ethanol)	Anti-osteoarthritis/In vivo: SD rats, + sodium iodoacetate (40 mg/mL), extract (100, 300 mg/kg), 24 days Writhing Response: ICR mice: control, extract (200, 600 mg/kg), or ibuprofen (200 mg/kg) 30 min, acetic acid (10 mL/kg, 0.7%)	Alleviated weight bearing, ↓ cartilage degradation, ↓ bone injury, Serum: ↓ TNF-α, ↓ IL-1β (dose-dependent) ↓ MMP-1, ↓ MMP-3, ↓ MMP-8, ↓ MMP-13, ↓ NOS2, ↓ PGE2, ↓COX-2 Inhibited writhing responses	[63]
	RAW264.7 cells + LPS (500 ng/mL) + extract (10, 30, 100, 300, 1000 μg/mL)	↓ NO production, ↓ PGE2, ↓TNF-α, ↓ IL-6, ↓ IL-1β, ↓ MMP3, ↓ MMP1, ↓ MMP-13, ↓ MMP8	
Dried cortex extract (methanol 80%) and partitioned with different solvents	Alcohol intoxication/in vivo: SD rats, extract and its fractions, methanol extract (SM, 200 and 300 mg/kg), 1–7 h; ethyl acetate fraction (SE, 50, 100, and 150 mg/kg), 2, 4, 6, 8 h; 30 min before alcohol dose (3.0 g/kg in a 30% solution with water)	SM (2 h): ↓ BAC, ↓ AUC, SE (150 mg/kg) at all time intervals ↓ BAC, SE (100, 150 mg/kg): ↓ AUC SE: No effect on alcoholic dehydrogenase activity SE (6 h): ↓ hepatic MDA, SE (2 h): ↑ catalase	[64]

↓ = suppressed; ↑ = enhanced. PTP1B: protein tyrosine phosphatase 1B; PBS: phosphate-buffered saline; RANKL: receptor activator of nuclear factor kappa-B ligand; ALP: alkaline phosphatase; BMM: bone marrow-derived macrophages; p-NF-κB: p65-phosphorylated nuclear factor kappa-light-chain-enhancer of activated B cells p65 subunit; MAPK: mitogen-activated protein kinase; p-ERK: phosphorylated extracellular signal-regulated kinase; p-p38: phospho p38; p-IκBα: phosphorylated inhibitor of kappa B alpha; c-Fos: a proto-oncogene; AP-1: activator protein 1; NFATc1: nuclear factor of activated T-cells; SD: Sprague-Dawley; ICR: Institute of Cancer Research; TNF-α: tumor necrosis factor-alpha; IL-1β: interleukin-1 beta; MMP: matrix metalloproteinase; COX-2: cyclooxygenase-2; NOS2: nitric oxide synthase-2; PGE2: prostaglandin E2; IL-6: interleukin 6; LPS: lipopolysaccharide; NO: nitric oxide; BAC: blood alcohol concentration; MDA: malondialdehyde; AUC: area under the curve; AGEs: advanced glycation end-products; DEF: diethyl ether fraction; EAF: ethyl acetate fraction; BF: *n*-butanol fraction; RAW264.7: mouse macrophage cell line.

A recent study evaluated potential antidiabetic effects of *S. commixta* leaf methanol–water extract; ethyl acetate, diethyl ether; and *n*-butanol fractions and water residue by measuring α-glucosidase and α-amylase inhibition and nonenzymatic protein glycation. The extract and fractions inhibited α-glucosidase 2- to 17-fold more strongly than acarbose, with the greatest effect observed for the *n*-butanol fraction. By contrast, α-amylase inhibition was 7- to 50-fold weaker than that of acarbose. The methanol extract and *n*-butanol fraction also showed greater overall enzyme-inhibitory activity than acarbose. The inhibition of advanced glycation end products (AGEs) formation was 5- to 26-fold greater than that achieved with aminoguanidine, with the strongest effects for the *n*-butanol fraction and methanol extract (Table 7). AGEs form through nonenzymatic reactions between reducing sugar carbonyl groups and amino groups of proteins, nucleic acids, or lipids, followed by further modifications that produce stable, irreversible products [65]. Only a limited number of AGE inhibitors have been described, and some have adverse effects [66], prompting interest in plant-derived AGE inhibitors. Accordingly, *S. commixta* leaf extracts merit further evaluation as potential AGE inhibitors. Correlation analysis identified strong positive associations between antidiabetic activity and proanthocyanidins, neochlorogenic acid, quercetin 3-*O*-β-sophoroside, rutin, quercetin *O*-dihexoside, and kaempferol *O*-dihexoside [6]. These findings highlight the potential antidiabetic activity of *S. commixta* leaf extracts. Extracts from other plant parts also warrant investigation.

A separate study evaluated α-amylase and α-glucosidase inhibition by a 70% acetone extract of frozen *S. commixta* berries. The extract had an IC_{50} approximately 38,000 times higher (1784 ± 311 μg/mL) for α-amylase and a twofold lower IC_{50} (365 ± 31 μg/mL) for α-glucosidase than the corresponding values for acarbose (IC_{50} = 0.047 ± 0.006 and 742 ± 147, respectively) (Table 7) [62]. These enzyme assay findings suggest preliminary antidiabetic potential of *S. commixta*. Further studies should evaluate these effects on animal models.

5.9. Bone-Protective Activity

Osteoporosis involves reduced bone strength, whereas osteoarthritis is characterized by progressive joint cartilage degeneration. Natural bioactive constituents have attracted interest as potential agents for bone and joint protection [67].

Bone homeostasis depends on the balance between bone-forming osteoblasts and bone-resorbing osteoclasts. Two studies have reported bone-protective effects of *S. commixta* [28,63]. Lupeol, a triterpenoid isolated from *S. commixta* stem bark, was evaluated for its effects on 1α,25-$(OH)_2D_3$-induced osteoclastogenesis and the underlying mechanisms. Lupeol inhibited osteoclast differentiation in a mouse model and in cocultures of primary mouse osteoblasts and bone marrow-derived macrophages (BMMs) stimulated with 1α,25-$(OH)_2D_3$. Mechanistically, lupeol reduced osteoclast differentiation by downregulating receptor activator of nuclear factor κB ligand (RANKL)-associated pathways involving JNK, p38, and ERK (Table 7). Lupeol reduced serum RANKL levels and bone loss in hypercalcemic mice, consistent with modulation of RANKL-related signaling [28]. These findings suggest potential antiosteoporotic activity of lupeol.

Another study found that *S. commixta* stem extract reduced *pain*-related responses and cartilage damage in a dose-dependent manner. The extract also reduced inflammatory markers in in vitro and in vivo osteoarthritis models relative to controls (Table 7). The animal experiments involved a monosodium iodoacetate-induced rat model of osteoarthritis and an acetic acid-induced mouse writhing model. Caffeic acid was identified as a major constituent of the extract. The findings suggested that anti-inflammatory activity contributed to the extract's observed effects on osteoarthritis-related outcomes. However, studies assessing ROS levels and signaling pathways are needed to better characterize the underlying mechanisms [63].

5.10. Alcohol Intoxication-Related Activity

Excessive alcohol intake has adverse health effects. Acute intoxication may be followed by a hangover involving cognitive impairment, nausea, and headache. Interest has therefore grown in food ingredients, beverages, and treatments that might protect the liver or alleviate hangover symptoms [68,69].

S. commixta extract has also been investigated for these effects. One study examined the effects of methanolic *S. commixta* cortex extract on blood alcohol concentration and hepatic lipid peroxidation in rats exposed to acute alcohol (Table 7). Pretreatment with the methanol extract (200 mg/kg for 30 min) significantly reduced blood alcohol concentration. Among the *n*-butanol, n-hexane, chloroform, ethyl acetate, and aqueous fractions, the ethyl acetate fraction (150 mg/kg) produced the greatest reduction (46%) in blood alcohol concentration relative to the control at 2 h after alcohol administration (3.0 g/kg).

The ethyl acetate fraction lowered hepatic malondialdehyde levels and restored catalase activity in treated rats. These findings suggest that *S. commixta* extract may attenuate alcohol-associated toxicity in this animal model, alongside reductions in blood alcohol concentration [64].

6. Conclusions and Future Perspectives

Sorbus commixta Hedl. has a long history of use in Korean traditional medicine. Despite accumulating in vitro and in vivo evidence, the therapeutic potential of this underexplored plant requires further investigation. Several reported activities are supported by only one animal study or by cell-based experiments. Examples include antidiabetic, anti-osteoporotic, antiosteoarthritic, and alcohol-related protective effects, for which additional research is needed. Although several studies have quantified total phenolic and flavonoid contents, more recent research has identified previously unreported phytoconstituents in different plant parts. These compounds are candidates for future study, but their translational relevance remains uncertain and requires thorough experimental validation. Variation in phytochemical composition across seasons and habitats also poses a challenge to standardization.

Despite animal studies across several disease models, data on appropriate doses and extract safety remain limited, highlighting the need for further toxicological evaluation. The lack of clinical evidence also warrants well-designed human studies. Current preclinical research also provides incomplete information about the signaling pathways modulated by extract or compound treatment. Detailed mechanistic studies are therefore needed to identify the affected pathways and downstream molecular targets.

Network pharmacology offers new approaches for investigating the complex biological activities of medicinal plant constituents. Combining this approach with metabolomics and high-throughput screening may help identify previously uncharacterized constituents and evaluate their bioactive potential. Future research priorities also include standardized formulations, molecular docking, experimental validation, and microbiome analyses.

Overall, this review summarizes the phytochemical profile and potential health-promoting properties of *S. commixta* Hedl. Further cell-based and animal research, followed by well-designed clinical studies, is needed to evaluate the therapeutic potential and safety of bioactive compounds and extracts of *S. commixta* Hedl.

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