Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Supplementary Tab. 1 Flavonoids, phenolic acids and triterpenoids identified in SB

No	Compound	Parts
Flavones aglycones		
1	Isorhamnetin[1, 2]	Leaves, fruits, seeds, pulp, roots
2	Quercetin[1–4]	Leaves, fruits, seeds, root
3	Kaempferol[1, 2]	Leaves, fruits, pulp, root
4	Myricetin[1, 2]	Seeds, leaves, pulp, fruits, roots
5	Syringetin[1]	Roots
6	Pentamethylquercetin[1]	Roots
7	Catechin[3, 5]	Leaves, branches
8	Epicatechin[6]	Fruits
9	(+)-gallocatechin[5]	Branches
10	(−)-epigallocatechin[5]	Branches
Flav-monoglycosides		
11	Isorhamnetin-7-rha[7]	Pomace
12	Isorhamnetin-3-glu[6, 7]	Pomace, fruits
13	Isorhamnetin-3-rha[4, 8]	Fruits
14	Isorhamnetin-3-galactoside[9]	Fruits
15	Quercetin-3-glu[7, 8]	Pomace, fruits
16	Quercetin-3-galactoside[2]	Seeds, leaves, pulp, fruits
17	Quercetin-3-rha[8]	Fruits
18	Kaempferol-7-rha[10]	Fruits
19	Kaempferol-3-glu[6]	Fruits
20	Syringetin-3-glu[11]	Juice concentrate
Flav-di-glycosides		
21	Isorhamnetin-3-rutinoside[4, 7]	Pomace, fruits, leaves
22	Isorhamnetin-3-neohesperidoside[4]	Fruits, leaves
23	Isorhamnetin-3-glu-7-rha[4, 7, 12]	Pomace, fruits, leaves, seeds
24	Isorhamnetin-3,7-di-glu[7]	Pomace
25	Quercetin-3-rutinoside[2, 4, 7]	Pomace, leaves, fruits, pulp
26	Quercetin-3-glu-7-rha[4, 7, 8]	Pomace, leaves, fruits
27	Quercetin-3-galactoside-7-rha[8]	Fruits
28	Kaempferol-3-rutinoside[4, 8]	Leaves, fruits
29	Kaempferol-3-neohesperidoside[4]	Leaves
30	Kaempferol-3- arabinoside-7-rha[12]	Seeds
31	Kaempferol-3-glu-7-rha[12]	Seeds
Flav-tri-glycosides		
32	Isorhamnetin-3-rutinoside-7-rha[7]	Pomace
33	Isorhamnetin-3-rutinoside-7-glu[4, 8]	Fruits, leaves
34	Isorhamnetin-3-neohesperidoside-7-glu[4]	leaves
35	Isorhamnetin-3- sophoroside-7-rha[4, 7]	Pomace, fruits, leaves
36	Isorhamnetin-3-O-(2,6-dirhamnosyl)-glu[8]	Fruits

37	Quercetin-3-rhamnosylglucoside-7-rha[4]	Fruits, leaves
38	Quercetin-3-sophoroside-7-rha[4, 7]	Pomace, fruits, leaves
39	Quercetin-3-O-(2-rutinosyl)-glu[8]	Fruits
40	Kaempferol-3-rutinoside-7-rha[7, 12]	Pomace, seeds
41	Kaempferol-3-sophoroside-7-rha[6, 7, 13]	Pomace, fruits, seeds
Flav-acylated-glycosides		
42	Isorhamnetin-3-coumaroyl-glu-glu-7-rha[7]	Pomace
43	Isorhamnetin-3-hydroxyferuloyl-glu-glu-7-rha[7, 8]	Pomace, fruits
44	Quercetin-3-coumaroyl-glu-glu-7-rha[7]	Pomace
45	Quercetin-(methyl)$_2$-3-hydroxyferuloyl-glu-glu-7-rha[7]	Pomace
46	Quercetin-(methyl)$_2$-3-caffeoyl-glu-glu-7-rha[7]	Pomace
47	Kaempferol-3-hydroxyvanilloyl-glu-glu-7-rha[7]	Pomace
48	Kaempferol-3-O-β-D-(6”-O-coumaryl) glycoside[14]	Leaves
49	Kaempferol-3-O-β-D-glu-7-O-{[(2E)-2,6-dimethyl- 6-hydroxy-2,7-octadienoyl (1→2)]}-α-L-rha[12]	Seeds
50	Isorhamnetin-(3-O-[(6-O-E-sinapoyl)-β-D-glu-(1→2)]-β-D-glu-7-O-α-L-rha)[15]	Fruits, leaves
51	Quercetin-(3-O-[(6-O-E-sinapoyl)-β-D-glu-(1→2)]-β-D-glu-7-O-α-L-rha)[15]	Fruits, leaves
52	Kaempferol-3-O-β-D-rutinosyl-7-O-{2-O-[(2E)-2,6-dimethyl-6-hydroxy-2,7-octadienoyl]}-β-D-glu[13]	Seeds
53	Isorhamnetin-3-O-β-D-rutinosyl-7-O-{2-O-[(2E))-2,6-dimethyl-6-hydroxy-2,7-octadienoyl]}-β-D-glu[13]	Seeds
54	Kaempferol-3-O-β-D-glu-7-O-{2-O-[(2E)-2,6- dimethyl-6- hydroxy-2,7-octadienoyl]}-β-D-glu[13]	Seeds
55	Kaempferol-3-O-[(2E)-2,6-dimethyl-6-hydroxy-2,7-octadienoyl (1→6)]-β-D-glu(1→2)-β-D-glu-7-O-α-L-rha[13]	Seeds
56	Kaempferol-3-O-β-D-sophoroside-7-O-{[(2E)-2,6- dimethyl-6-hydroxy-2,7-octadienoyl (1→2)]}-α-L-rha[12, 13]	Seeds
57	Kaempferol-3-O-β-D-sophoroside-7-O-{[(2E)-2,6- dimethyl-6-hydroxy-2,7-octadienoyl (1→3)]}-α-L-rha[13]	Seeds
58	Kaempferol-3-O-(6-O-3,4,5-trimethoxycinnamoyl)-β-D-glu (1→2)-β-D-glu-7-O-α-L-rha[12, 13]	Seeds
59	Kaempferol-(3-O-[(6-O-E-sinapoyl)-β-D-glu-(1→2)]- β-D-glu-7-O-α-L-rha)[13, 15]	Fruits, leaves, seeds
60	Kaempferol-3-O-(6-O-E-feruloyl)-β-D-glu(1→2)-β-D-glu-7-O-[(2E)-2,6-dimethyl-6-hydroxy -2,7-octadienoyl (1→2)]-α-L-rha[13]	Seeds
61	Kaempferol-3-O-(6-O-E-sinapoyl)-β-D-glu(1→2)-β-D-glu-7-O-[(2E)-2,6-dimethyl-6-hydroxy-2,7-octadienoyl (1→2)]-α-L-rha[13]	Seeds
62	Kaempferol-3-O-(6-O-E-feruloyl)-β-D-glu(1→2)-β-D-glu-7-O-[(2E)-2,6-dimethyl-6-hydroxy-2,7-octadienoyl (1→3)]-α-L-rha[13]	Seeds
63	Kaempferol-3-O-(6-O-E-sinapoyl)-β-D-glu(1→2)-β-D-glu-7-O-[(2E)-2,6-dimethyl-6-hydroxy-2,7-octadienoyl (1→3)]-α-L-rha[13]	Seeds
Phenolic acids		

64	Gallic acid[16, 17]	Fruits, pulp, seed kernel, seed coat and leaves
65	Protocatechuic acid[16, 17]	Fruits, pulp, seed kernel, seed coat, leaves
66	p-Hydroxybenzoic acid[17]	Pulp, seed kernel, seed coat and leaves
67	Vanillic acid[17]	Pulp, seed kernel, seed coat and leaves
68	Salicylic acid[17]	Pulp
69	Syringic acid[6]	Fruits
70	Ferulic acid[16, 17]	Fruits, pulp, seed kernel, seed coat and leaves
71	p-Coumaric acid[6, 17]	Fruits, pulp, seed kernel, leaves
72	Cinnamic acid[17]	Pulp, seed kernel, seed coat and leaves
73	Caffiec acid[17]	Pulp, seed kernel, seed coat and leaves
74	Ellagic acid[9, 18]	Fruits, leaves
75	1-Feruloyl-β-D-glu[14]	Leaves
Triterpenes		
76	Oleanolic acid[19, 20]	Fruits
77	Ursolic acid[5, 20]	Fruits, branches
78	19-α-Hydroxyursolic acid[20]	Fruits
79	3-O-[β-D-glu(1→2)-β-D-glu-(1→3)]-[α-L-rha-(1→2)]-α-L-arabinopyranosyl-13-ene-19-one-28-oic acid 28-O-β-D-glu ester[21]	Seed residue
80	3-O-[β-D-glu(1→2)-β-D-glu-(1→3)]-[α-L-rha-(1→2)]-α-L-arabinopyranosyl-13-ene-19-one-30-hydroxyolean-28-oic acid 28-O-β-D-glu ester[21]	Seed residue
81	3-O-[β-D-glu(1→2)-β-D-glu-(1→3)]-[α-L-rha-(1→2)]-β-D-glu-13-ene-19-one-28-oic acid 28-O-β-D-glu ester[21]	Seed residue
82	3-O-[β-D-glu(1→2)-β-D-glu-(1→3)]-[α-L-rha-(1→2)]-β-D-glu-13-ene-19-one-30-hydroxyolean-28-oic acid 28-O-β-D-glu ester[21]	Seed residue
83	Dulcioic acid[20]	Fruits
Others		
84	5-Hydroxymethyl-2-furancarbox-aldehyde[20]	Fruits
85	Cirsiumaldehyde[20]	Fruits
86	Ethyl 3, 4, 5-trihydroxybenzoate[22]	Leaves
87	Hydroxycoumarin[6]	Fruits
88	Nectandrin B[20]	Fruits
89	(+)-Fragransin A2[19]	Fruits
90	(−)-Saucernetindiol[19]	Fruits
91	Casuarinin[23]	Leaves
92	Hippophae cerebroside[20]	Fruits

Supplementary Tab. 2 The main pharmacological effects of SB

Parts, preparation (treatment dosage)	**Subjects**	**Pharmacological effects**	**Possible mechanism or the variation of biochemical parameters**
Anti-inflammatory effects			
Fruits, the extract (50 mg/kg p.o.)[24]	Rats	Protecting against methotrexate-induced oropharyngeal oxidative damage	Decreasing the levels of malondialdehyde (MDA), interleukin (IL)-1β and tumor necrosis factor (TNF)-α, while increasing the level of total glutathione in the oropharyngeal tissue
Dried residues (including seeds, fruit flesh and peel), the oil [40 μL (was prepared in cream form 200 μL) T.A to mice; 0~200mg/L for cells][25]	2,4-dinitrochloro-benzene (DNCB)-induced atopic dermatitis-like lesions mouse model; Human keratinocyte HaCaT cells	Improvement of atopic dermatitis-like skin lesions	Inhibiting the helper (Th)2 cell chemokines thymus and activation-regulated chemokine (TARC) and macrophage-derived chemokine (MDC) in inflamed skin
Pulp, the oil (SBKT) (Ⅰ. 1, 1.25, 2.5 and 5 μL/mL to human monocytic (THP-1) cells; Ⅱ. 100 mg/kg p.o. + 40 μL/paw T.A. to rats; Ⅲ. 100 mg/kg p.o. + 20 μL T.A and 200 mg/kg p.o. + 20μL T.A.)[26]	Human monocytic (THP -1) cells; Rat paw edema model; 12-O tetradecanoylphorbol 13- acetate (TPA)-induced psoriasis-like lesion mouse model	Anti-inflammatory and anti-psoriasis-like efficacies	Inhibiting of reactive nitrogen species, and downregulating of NF-κB protein and pro-inflammatory cytokines
Leaves, the supercritical extract (SCE200 ET) (27 μg/kg b. w. i. p.) and its active component isorhamnetin[27]	Mice	Inhibiting endotoxemia; Potential for the treatment of endotoxin induced sepsis	Reducing inflammatory cytokines and nitric oxide synthase 2 expression

Peel, seeds and whole fruits, the 70% methanol extracts; peel, the chloroform extract; (500 mg/kg, p. o.); the active component ursolic acid and oleanolic acid[19]	Compound 48/80-induced rat paw edema model	Anti-inflammatory activity; antiallergic activity	A membrane stabilizing effect caused by the inhibition of degranulation of mast cells
A mixture of SB and St. John's wort oils (2 mL/rat p. o.)[28]	Surgically-induced endometriosis rat model	Potential for the treatment of endometriosis	Decreasing the levels of TNF-α, vascular endothelial growth factor and IL-6
Immunomodulatory activity			
Leaves, the 70% ethanol extract (100 mg/kg b. w. i. p.)[29]	Young (3 month) and old (> 17 month) mice	Strengthening the immune response of aged ones	Increasing IFN-γ, IL-2 receptor alpha chain (CD25) and MHC II expression
Leaves, the supercritical extracts (SCEs 300ET and 350ET) (0.1 μg/mouse i. p.)[30]	Mice immunized with Tetanus and Diphtheria toxoids	Increasing both antibody and cellular response, as well as the generation of the secondary immune response	Increasing cytokine levels (IFN-γ, IL-4, TNF-α and IL-1β and lymphoproliferation
Fruit residue (fruit flesh, seeds and peel), the oil (5 and 10 mL/kg p.o.)[31]	Rats	Increasing NK cell cytotoxicity in chronic-stress rat model	Upregulating the expression of perforin and granzyme B
SB polysaccharide (200 μg/mL-600 μg/mL)[32]	Intestinal porcine epithelial cells (IPEC-J2 cells)	Protecting against LPS-induced IPEC-J2 cell damage	Inhibiting TLR4/NF-κB signaling pathway
Fruits, a natural high-methoxyl homogalacturonan (HRWP-A) (50 mg/kg i.g.)[33]	Mice	Enhancing viability of peritoneal macrophages from cyclophosphamide - induced immunosuppressed mice	Activating TLR4/MyD88 pathway
Fruits, the total flavonoids of SB (2.5 or 5.0 mg/L)[34]	Natural killer (NK)92-MI cells	Increasing cytotoxicity of NK92-MI cells against K562 cells	Upregulating the expressions of perforin and granzymes B
Hepatoprotective effect			
*****Fruits, the hexane extract (HRe-1) (250	Rat	Attenuating nicotine-induced oxidative	Antioxidant activity

mg/kg/day, i.g.)[35]		stress in the liver.	
*Seeds, the oil (0.26 1.30 and 2.60 mg/kg p.o.)[36]	Mice	Protecting against carbon tetrachloride (CCl_4)-induced hepatic damage	Antioxidant activity
*Leaves, the phenolic rich fraction (25~75 mg/kg p.o.)[37]	Rat	Protecting against CCl_4 induced oxidative damage in the liver.	Antioxidant activity
*Fruits, the polysaccharide extracts (50, 100, 200 mg/kg p.o.)[38]	Mice	Protecting against LPS/d-galactosamine hydrochloride (d-GalN)-induced acute liver failure	Antioxidant activity; Suppressing the TLR4-NF-κB signaling pathway
*Fruits, the polysaccharide extracts (100 and 200 mg/kg p.o.)[39]	Mice	Protecting against acetaminophen-induced hepatotoxicity	Antioxidant activity; Activating the nuclear factor erythroid-2-related factor (Nrf)-2/hemeoxygenase-(HO)-1-superoxide dismutase (SOD)-2 signaling pathway
Panax ginseng roots and SB fruits, the aqueous extract (100, 200 and 400 mg/kg)[40]	Mice	Countering acute alcohol intoxication	Increasing the levels of alcohol dehydrogenase, aldehyde dehydrogenase, decreasing microsomal ethanol oxidase activity in liver and decreasing the concentration of β-endorphin and leucine-enkephalin in brain
Fruits, the active components (20 and 40 mg/kg i.g. to rats)[9]	Rat hepatic stellate cells (HSCs); Rats	Inhibiting transforming growth factor-β induced activation of HSCs; Anti-liver fibrosis (bile duct ligation-induced in rats)	Regulating DNA damage signaling
Cardiovascular protection			
Seed residues, the total flavones (50, 100 or 150 mg/kg/day)[41]	Sucrose-fed rats	Suppressing the elevated hypertension, hyperinsulinemia and dyslipidemia	Improving insulin sensitivity and blocking angiotensin II signal pathway
Seed residues, the total flavonoids (50, 100 and 150 mg/kg b.w. p.o.)[42]	High-fat diet fed mice	Hypolipidaemic and hypoglycaemic effects	Not clear
Extraction residues[43]	Healthy normal-weight male volunteers	Delay postprandial lipemia	Not clear

Pulp, the oil (5, 10, and 20 mL/kg/day p.o.) [44]	Rats	Protecting against myocardial ischemia-reperfusion injury	Activating protein kinase B-endothelial nitric oxide synthase (Akt/eNOS) signaling pathway; inhibiting TNF-α/ IKKβ/NF-κB
SB oil (20 mL/kg/day)[45]	Rats	Protecting against isoproterenol-induced myocardial damage	Antioxidant activity
Fruits, the total flavones (300 µg/kg, intravenously)[46]	Mouse femoral artery thrombosis model	Preventing in-vivo thrombogenesis	Inhibiting platelet aggregation
*Fruits, the phenolic fraction (0.5-50 µg/mL)[47]	Human plasma and blood platelet	Antioxidant and antiplatelet activity	Inhibiting H_2O_2 or H_2O_2/Fe induced plasma lipid peroxidation and protein carbonylation; reducing the production of TBARS and superoxide anion in resting and thrombin-stimulated platelets.
Fruits, the phenolic fraction (0.5-50 µg/mL)[48]	Human blood platelet	Inhibiting blood platelets adhesion to collagen and fibrinogen	Not clear
Fruits and leaves, the flavone (75 mg/kg p.o. to mice; 0.2 mg/mL, 1.0 mg/mL to Mouse PBMC)[49]	Mouse PBMC; The apoE ($apoE^{-/-}$) deficient mice	Inhibiting macrophage foaming, inflamma - tion and vascular plaque formation	Upregulating the expression level of C1q/tumor necrosis factor-related proteins 6 (CTRP6)
Seeds, the oil (1 mL, p.o.)[50]	Rabbits	Anti-atherogenic activity	Decreasing plasma cholesterol, LDL-cholesterol levels and increasing HDL-cholesterol levels
Effect on diabetes and glycometabolism			
Seed residues, the aqueous extract (400 mg/kg/day b.w. p.o.)[51]	Streptozotocin-induced diabetic rats	Hypoglycemic, hypotriglyceridemic and antioxidant effects	Not clear
Whole fruits and the 70% ethanol soluble fraction[52]	Healthy normal-weight male volunteers (n=10)	Improving postprandial glycemic control	Not clear
Leaves, the n-butanol fraction, the methanolic extract, the hexane fraction ect. (5 µg/ mL)[14]	In vitro assay	α-glucosidase inhibitory effect	Not clear
Seeds, the 70% ethanol elution fraction,	In vitro assay	α-glucosidase inhibitory activity	Not clear

kaempferol ect.[13]			
Anti-cancer effect			
Fruit pulp, the 80% ethanol extract (150 and 300 mg/kg, b.w. p.o.)[53]	Mice	Inhibiting benzo(a)pyrene-induced forestomach and 7,12-dimethyl benzanthracene (DMBA)-induced skin papillomagenesis in mouse	Up-regulating phase II and antioxidant enzymes as well as DNA-binding activity of interferon regulatory factor-1
Quercetin (2.5-40μM), pentamethyl-quercetin (2.5-20μM), kaempherol, myricetin, syringetin, isorhamnetin (10-40μM) from roots[1]	Human promyelotic leukemia HL-60 cells	Antiproliferative activity	Quercetin, kaempherol and myricetin: the induction of apoptosis; other 3 flavonols: without induction of apoptosis, different from above 3 flavonols
Isorhamnetin (25-300 μg/mL for 12, 24, 48 and 72 h)[54]	Human hepatocellular carcinoma cells (BEL-7402)	The cytotoxic effects against human hepatocellular carcinoma cells BEL-7402 cells	Appearance of a hypodiploid peak (sub-G_0/G_1 peak), probably related to apoptosis
Branches, the 70% ethanol extract (1.0 mg/mouse T.A.)[5]	Mice	Inhibiting skin papillomas promoted by TPA following initiated by DMBA in mice	Not clear
Leaves, the 50% ethanol extract (25, 50, and 100 μg/mL)[55]	Human acute myeloid leukemia cells (KG-1a, HL60, and U937)	Antiproliferative effect (all doses for HL60, 100 μg/mL for KG-1a and U937)	Activating the S phase checkpoint, which probably led to deceleration of the cell cycle and apoptosis induction
Fruits, a watersoluble homogenous poly-saccharide (HRWP-A) (50, 100 and 200 mg/kg, i.g.)[56]	Mice	Inhibiting the lewis lung carcinoma growth	Related to immunostimulating activity (enhancing the lymphocyte proliferation, the macrophage activities, NK cell activity and cytotoxic T lymphocyte cytotoxicity in tumor-bearing mice
*Leaves, the aqueous extract (0.62, 6.2, and 62 μg/mL)[57]	Rat C6 glioma cells	Antiproliferative activity	Reducing reactive oxygen species (ROS) levels, inducing the early events of apoptosis
*Fruits, the chemical extraction and in	Human liver cancer cells	Antiproliferative activity	The cellular antioxidant capacity

vitro digested samples[6]	(HepG2), human breast cancer cells (MCF-7, MDA-MB-231) and human colon cancer cells (Caco-2)		
Fruits, the extract and some phenolic acids and flavonoids[16]	Human liver cancer cells HepG2	Antiproliferative activity	Related to phenolic acids and flavonoid aglycones, but precise mechanisms was not studied.
Neuroprotective effect			
Fruits, SB juice (20% and 40%) (1mL/10 g b.w. p.o.)[58]	Mice	Protecting against lead-induced neurotoxicity	Decreasing MDA Levels, acetyl-cholinesterase (AchE) and monoamine oxidase (MAO)-A and -B Activity; Increasing the level of 5-HT in cerebral tissue
Fruits, the aqueous extract (40 mg/kg b. w. p. o.)[59]	Rats	Protecting against haloperidol-induced orofacial dyskinesia	Increasing release of dopamine or decreasing dopamine turnover in rat striatum
Leaves, the 75% alcoholic extract (100 and 200 mg/kg)[60]	Rats	Protecting against scopolamine-induced cognitive impairment	Reducing the increased AChE activity and MDA level in the brain
*Leaves, the 70% ethanol extract (200 µg/mL)[61]	C-6 glioma cells	Protecting against hypoxia-induced oxidative injury in glial cells	Inhibiting hypoxia induced cytotoxicity, mitochondrial integrity, ROS production and DNA damage
*Leaves, the aqueous extract (25, 50 and 100 µg/mL) [62]	HT22 cells, hippocampus neurons	Inhibiting hypoxia induced oxidative stress	Relating to Janus kinase-signal transducers and activators of transcription (JAK/STAT) signaling
*Fruits and leaves, the 70% ethanol extract (3.2-100 µg/mL)[63]	Human neuroblastoma cell line-IMR32	Protecting against hydrogen peroxide-induced cell cytotoxicity in a dose dependent manner	Antioxidant activity
*Leaves, the 80% aqueous methanol extract, the ethyl acetate fraction (5, 10, and 20 µg/mL)[18]	Neuronal PC-12 cells	Protecting against H_2O_2-induced oxidative stress in PC-12 cells; enhancing cellular survival response to hypoxia	Blocking mitochondrial dysfunction against oxidative stress; a decrease in intracellular oxidative stress
Effects on the skin			
Seed residues, the 80% ethanol extract	B16F10 mouse melanoma	Anti-melanogenesis properties	Decreasing the tyrosinase activity and down-regulating the

(45.45 μg/mL and 4.55 μg/mL)[64]	cells		expression of tyrosinase and tyrosinase-related protein (TRP)-1
Emulsion formulations containing plant extracts (SB and *Cassia fistula*) (500 mg, twice daily, T.A.)[65]	Patients with grade I and grade II acne vulgaris	Reducing skin sebum contents (anti-acne effects)	Not clear
SB fruit blend [containing SB fruit extract (31.1%), blueberry extract and collagen] (30 and 50%, p. o.)[66]	hairless mice	Against ultraviolet (UV) radiation-induced skin aging	Regulating the moisture content, matrix metalloproteinase (MMP) expression levels and SOD activity
Seeds, the oil (500 ng/mL)[67]	Human keratinocytes and fibroblasts	Skin photo-protection	Against UV-induced disturbances in redox balance as well as lipid metabolism in skin fibroblasts and keratinocytes
Seeds, the oil (20 mL, T.A. respectively in recipient and donor sites)[68]	Ovine burn wound model	Wound healing activity (full-thickness burns and split-thickness harvested wounds)	Not clear
Leaves, polyvinyl alcohol-blended pectin hydrogel containing the leaves extract (T.A.)[69]	Rat acute wound models	Enhancing wound healing	Not clear
Effects on eye disease			
Seeds and pulp, the oil (2 g/day, p. o.)[70]	Patients with dry eyes	Alleviating dry eye symptoms and the increase in tear film osmolarity during the cold season	Not clear
Pulp, the oil (0.5 and 2.5 mL/kg, p. o.) and palmitoleate[71]	Murine dry eye model	Restoring aqueous tear secretion to its normal value	Suppressing inflammatory cytokines and chemokines in the lacrimal gland
*Proanthocyanidins from seeds (50 and 100 mg/kg/day, p.o.)[72]	Pigmented rabbits	Protecting against visible light-induced retinal degeneration	Antioxidant, anti-inflammatory and antiapoptotic mechanisms
*Total flavones from SB (250 and 500 mg/kg i.g.)[73]	Pigmented rabbits	Protecting against visible light-induced retinal degeneration	Antioxidant, anti-inflammatory and antiapoptotic mechanisms
*Seeds, the oil (0.5 mL/day p. o.)[74]	Rats	Protecting against hypertensive retinopathy induced retina damage	Neuroprotective and antioxidant properties

*Leaves, the aqueous extract (100, 200, 500, and 1000 µg/mL)[75]	Isolated goat lenses	Delaying onset and/or progression of cataract	Restoring the decreased levels of SOD and glutathione (GSH) in 500 and 1000 µg/mL dose and reducing MDA level in all the doses
Effects on gastrointestinal disease			
Ripe fruits, the hexane extract (HRe-1) (1 mL/kg p. o.)[76]	Rats	Preventing stress-, indomethacin-induced gastric injury	Not clear
Seeds, the oil; pulp, the oil (3.5 and 7 mL/kg /day, p. o.)[77]	Rats	Protecting against water immersion, reserpine, pylorus ligation, acetic acid induced gastric ulcers	Not clear
Fruits and pulp, a commercially available formulation (4 ounces [35.6 g fruits and pulp], twice daily)[78]	Horses, stall-confined and intermittently fed	Preventing glandular ulcers, without a significant increase in gastric juice pH	Not clear
Fruits juice, polyphenolics[79]	In vitro simulated model	Promoting the proliferation of bacteroides/ prevotella group, lactic acid bacteria and bifidobacteria	Not clear
Other pharmacological effects			
Fruits, the water-soluble polysaccharide (50, 100 and 200 mg/kg p. o.)[80]	Mice	Anti-fatigue activity	Involving triglyceride (or fat) mobilization during exercise and protecting corpuscular membrane by preventing lipid oxidation via modifying several enzyme activities
*Leaves, the aqueous extracts (200 and 800 mg kg b. w. p. o.)[81]	Rats	Anti-fatigue; Protecting against the exhau-stive exercise-induced oxidative damage	Countering the increases of MDA levels, the increases of the activities of glutathione peroxidase (GPx), alanine aminotransferase and creatine kinase ctivities in the heart tissue induced by the exhaustive exercise
*Seeds, the oil (2.5 mL/kg b. w. p. o.)[82]	Rats	Protecting against hypobaric hypoxia-induced cerebral vascular injury	Countering the increases of the free radicals and MDA levels and the decrease in the glutathione reductase (GR), GPx and SOD enzyme activities induced by hypoxia in the brain tissue

*Leaves, the ethanol extract (50, 100 and 200 mg/kg b. w. p. o.)[83]	Rats	Protecting against hypoxia-induced pulmonary vascular leakage	Countering the increases of the free radicals and MDA levels and decrease in the GR, GPx and GSH levels induced by hypoxia in the lung homogenates
Total flavonoids (70, 140 mg/kg, i. g.)[84]	Rats	Preventing cobalt chloride- and hypobaric chamber-induced high-altitude polycythemia	Not clear
*Leaves, the aqueous extracts (100 mg/kg b. w. p. o.)[85]	Rats	The resistance effect to cold-hypoxia - restraint-induced hypothermia	Countering the increases of ROS, SOD, catalase and MDA levels and the decrease of ratio of GSH/oxidized glutathione during cold-hypoxia-restraint exposure

*: Antioxidant activity

References

1 H. Hibasami, A. Mitani, H. Katsuzaki, K. Imai, K. Yoshioka and T. Komiya, *Int. J. Mol. Med.*, 2005, **15**, 805-809.

2 U.K. Sharma, K. Sharma, N. Sharma, A. Sharma, H.P. Singh and A.K. Sinha, *J. Agr. Food Chem.*, 2008, **56**, 374-379.

3 Y. Zu, C. Li, Y. Fu and C. Zhao, *J. Pharmaceut. Biomed.*, 2006, **41**, 714-719.

4 R.M. Pop, C. Socaciu, A. Pintea, A.D. Buzoianu, M.G. Sanders, H. Gruppen and J.P. Vincken, *Phytochem. Anal.*, 2013, **24**, 484-492.

5 K. Yasukawa, S. Kitanaka, K. Kawata and K. Goto, *Fitoterapia*, 2009, **80**, 164-167.

6 R. Guo, X. Chang, X. Guo, C.S. Brennan, T. Li, X. Fu and R.H. Liu, *Food Funct.*, 2017, **8**, 4229-4240.

7 D. Rosch, A. Krumbein, C. Mugge and L.W. Kroh, *J. Agr. Food Chem.*, 2004, **52**, 4039-4046.

8 K. Tkacz, A. Wojdylo, I.P. Turkiewicz, F. Ferreres, D.A. Moreno and P. Nowicka, *Food Chem.*, 2020, **309**, 125766.

9 G. Zhang, Y. Liu and P. Liu, *J Agric Food Chem*, 2018, **66**, 12257-12264.

10 C. Chen, H. Zhang, W. Xiao, Z. Yong and N. Bai, *J. Chromatogr. A*, 2007, **1154**, 250-259.

11 D. Gutzeit, P. Winterhalter and G. Jerz, *J. Chromatogr. A*, 2007, **1172**, 40-46.

12 J. Zhang, W. Gao, M. Cao and D. Kong, *J. Asian Nat. Prod. Res.*, 2012, **14**, 1122-1129.

13 R. Li, Q. Wang, M. Zhao, P. Yang, X. Hu and D. Ouyang, *Fitoterapia*, 2019, **137**, 104248.

14 J.S. Kim, Y.S. Kwon, Y.J. Sa and M.J. Kim, *J Agric Food Chem*, 2011, **59**, 138-144.

15 C. Chen, X. Xu, Y. Chen, M. Yu, F. Wen and H. Zhang, *Food Chem.*, 2013, **141**, 1573-1579.

16 R.X. Guo, X. Guo, T. Li, X. Fu and R.H. Liu, *Food Chem.*, 2017, **221**, 997-1003.

17 R. Arimboor, K.S. Kumar and C. Arumughan, *J. Pharmaceut. Biomed.*, 2008, **47**, 31-38.

18 C.H. Cho, H. Jang, M. Lee, H. Kang, H.J. Heo and D.O. Kim, *J Microbiol Biotechnol*, 2017, **27**, 1257-1265.

19 D. Redei, N. Kusz, N. Jedlinszki, G. Blazso, I. Zupko and J. Hohmann, *Planta Med.*, 2018, **84**, 26-33.

20 R. Zheng, X. Xu, Z. Tian and J. Yang, *Nat. Prod. Res.*, 2009, **23**, 1451-1456.

21 C. Chen, W. Gao, L. Cheng, Y. Shao and D. Kong, *J. Asian Nat. Prod. Res.*, 2014, **16**, 231-239.

22 P.K. Pandey, B. Ahmed, J. Prasad, M. Bala and H.A. Khan, *Sci Rep*, 2019, **9**, 18873.

23 D.J. Kwon, Y.S. Bae, S.M. Ju, A.R. Goh, G.S. Youn, S.Y. Choi and J. Park, *Biochem. Bioph. Res. Co.*, 2012, **417**, 1254-1259.

24 E. Erhan, S. Terzi, M. Celiker, O. Yarali, M. Cankaya, F.K. Cimen, I. Malkoc and B. Suleyman, *Clin. Exp. Otorhinolar.*, 2017, **10**, 181-187.

25 D.D. Hou, Di ZH, R.Q. Qi, H.X. Wang, S. Zheng, Y.X. Hong, H. Guo, H.D. Chen and X.H. Gao, *Skin Pharmacol. Phys.*, 2017, **30**, 268-276.

26 A. Balkrishna, S.S. Sakat, K. Joshi, K. Joshi, V. Sharma, R. Ranjan, K. Bhattacharya and A. Varshney, *Front Pharmacol*, 2019, **10**, 1186.

27 B. Jayashankar, K.P. Mishra, L. Ganju and S.B. Singh, *Int. Immunopharmacol.*, 2014, **20**, 89-94.

28 M. Ilhan, I. Suntar, M.A. Demirel, E. Yesilada, H. Keles and A.E. Kupeli, *Taiwan. J. Obstet. Gyne.*, 2016, **55**, 786-790.

29 K.P. Mishra, R. Mishra, A.P. Yadav, B. Jayashankar, S. Chanda and L. Ganju, *Biomedicine & Aging Pathology*, 2011, **1**, 61-64.

30 B. Jayashankar, D. Singh, H. Tanwar, K.P. Mishra, S. Murthy, S. Chanda, J. Mishra, R. Tulswani, K.

Misra, S.B. Singh and L. Ganju, *Int. Immunopharmacol.*, 2017, **44**, 123-136.
31 H. Diandong, G. Feng, L. Zaifu, T. Helland, F. Weixin and C. Liping, *Int J Immunopathol Pharmacol*, 2016, **29**, 76-83.
32 L. Zhao, M. Li, K. Sun, S. Su, T. Geng and H. Sun, *Int. J. Biol. Macromol.*, 2020, **155**, 1202-1215.
33 H. Wang, H. Bi, T. Gao, B. Zhao, W. Ni and J. Liu, *Int. J. Biol. Macromol.*, 2018, **107**, 1039-1045.
34 D. Hou, D. Wang, X. Ma, W. Chen, S. Guo and H. Guan, *Int. J. Immunopath. Ph.*, 2017, **30**, 353-361.
35 S. Taysi, K. Gumustekin, B. Demircan, O. Aktas, N. Oztasan, F. Akcay, H. Suleyman, S. Akar, S. Dane and M. Gul, *Pharm. Biol.*, 2010, **48**, 488-493.
36 Y. Hsu, C. Tsai, W. Chen and F. Lu, *Food Chem. Toxicol.*, 2009, **47**, 2281-2288.
37 D.T. Maheshwari, K.M. Yogendra, S.K. Verma, V.K. Singh and S.N. Singh, *Food Chem. Toxicol.*, 2011, **49**, 2422-2428.
38 H. Liu, W. Zhang, S. Dong, L. Song, S. Zhao, C. Wu, X. Wang, F. Liu, J. Xie, J. Wang and Y. Wang, *J. Ethnopharmacol.*, 2015, **176**, 69-78.
39 X. Wang, J. Liu, X. Zhang, S. Zhao, K. Zou, J. Xie, X. Wang, C. Liu, J. Wang and Y. Wang, *Phytomedicine*, 2018, **38**, 90-97.
40 D.C. Wen, X.Y. Hu, Y.Y. Wang, J.X. Luo, W. Lin, L.Y. Jia and X.Y. Gong, *J. Ethnopharmacol.*, 2016, **192**, 67-73.
41 X. Pang, J. Zhao, W. Zhang, X. Zhuang, J. Wang, R. Xu, Z. Xu and W. Qu, *J. Ethnopharmacol.*, 2008, **117**, 325-331.
42 J. Wang, W. Zhang, D. Zhu, X. Zhu, X. Pang and W. Qu, *J. Sci. Food Agr.*, 2011, **91**, 1446-1451.
43 K.M. Linderborg, H.M. Lehtonen, R. Jarvinen, M. Viitanen and H. Kallio, *Int. J. Food Sci. Nutr.*, 2012, **63**, 483-490.
44 K. Suchal, J. Bhatia, S. Malik, R.K. Malhotra, N. Gamad, S. Goyal, T.C. Nag, D.S. Arya and S. Ojha, *Front. Pharmacol.*, 2016, **7**, 155.
45 S. Malik, S. Goyal, S.K. Ojha, S. Bharti, S. Nepali, S. Kumari, V. Singh and D.S. Arya, *Int. J. Toxicol.*, 2011, **30**, 671-680.
46 J. Cheng, K. Kondo, Y. Suzuki, Y. Ikeda, X. Meng and K. Umemura, *Life Sci.*, 2003, **72**, 2263-2271.
47 B. Olas, B. Kontek, P. Malinowska, J. Zuchowski and A. Stochmal, *Oxid. Med. Cell. Longev.*, 2016, **2016**, 4692486.
48 B. Olas, B. Kontek, M. Szczesna, L. Grabarczyk, A. Stochmal and J. Zuchowski, *J. Physiol. Pharmacol.*, 2017, **68**, 223-229.
49 X. Zhuo, Y. Tian, Y. Wei, Y. Deng, Y. Wu and T. Chen, *Biosci Biotechnol Biochem*, 2019, **83**, 2000-2007.
50 M. Basu, R. Prasad, P. Jayamurthy, K. Pal, C. Arumughan and R.C. Sawhney, *Phytomedicine*, 2007, **14**, 770-777.
51 W. Zhang, J. Zhao, J. Wang, X. Pang, X. Zhuang, X. Zhu and W. Qu, *Phytother. Res.*, 2010, **24**, 228-232.
52 H.M. Lehtonen, R. Jarvinen, K. Linderborg, M. Viitanen, M. Venojarvi, H. Alanko and H. Kallio, *Eur. J. Clin. Nutr.*, 2010, **64**, 1465-1471.
53 B. Padmavathi, M. Upreti, V. Singh, A.R. Rao, R.P. Singh and P.C. Rath, *Nutr. Cancer*, 2005, **51**, 59-67.
54 B.S. Teng, Y.H. Lu, Z.T. Wang, X.Y. Tao and D.Z. Wei, *Pharmacol. Res.*, 2006, **54**, 186-194.
55 G.T. Zhamanbaeva, M.K. Murzakhmetova, S.T. Tuleukhanov and M.P. Danilenko, *Bull Exp Biol*

Med, 2014, **158**, 252-255.
56 H. Wang, T. Gao, Du Y, H. Yang, L. Wei, H. Bi and W. Ni, *Carbohyd. Polym.*, 2015, **131**, 288-296.
57 S.J. Kim, E. Hwang, S.S. Yi, K.D. Song, H.K. Lee, T.H. Heo, S.K. Park, Y.J. Jung and H.S. Jun, *Appl. Biochem. Biotech.*, 2017, **182**, 1663-1674.
58 Y. Xu, G. Li, C. Han, L. Sun, R. Zhao and S. Cui, *Biol. Pharm. Bull.*, 2005, **28**, 490-494.
59 F. Batool, A.H. Shah, S.D. Ahmed, Z.S. Saify and D.J. Haleem, *Med Sci Monit*, 2010, **16**, R285-R292.
60 D.P. Attrey, A.K. Singh, T. Naved and B. Roy, *Indian journal of experimental biology*, 2012, **50**, 690-695.
61 S. Narayanan, D. Ruma, B. Gitika, S.K. Sharma, T. Pauline, M.S. Ram, G. Ilavazhagan, R.C. Sawhney, D. Kumar and P.K. Banerjee, *Mol. Cell. Biochem.*, 2005, **278**, 9-14.
62 M. Manickam and R. Tulsawani, *PLoS One*, 2014, **9**, e87694.
63 S. Shivapriya, K. Ilango and G.P. Dubey, *Saudi J. Biol. Sci.*, 2015, **22**, 645-650.
64 J. Zhang, C. Wang, C. Wang, B. Sun and C. Qi, *Food Funct.*, 2018, **9**, 5402-5416.
65 B.A. Khan and N. Akhtar, *Postepy dermatologii i alergologii*, 2014, **31**, 229-234.
66 I.S. Hwang, J.E. Kim, S.I. Choi, H.R. Lee, Y.J. Lee, M.J. Jang, H.J. Son, H.S. Lee, C.H. Oh, B.H. Kim, S.H. Lee and D.Y. Hwang, *Int. J. Mol. Med.*, 2012, **30**, 392-400.
67 A. Gegotek, A. Jastrzab, I. Jarocka-Karpowicz, M. Muszynska and E. Skrzydlewska, *Antioxidants*, 2018, **7**, 110.
68 H. Ito, S. Asmussen, D.L. Traber, R.A. Cox, H.K. Hawkins, R. Connelly, L.D. Traber, T.W. Walker, E. Malgerud, H. Sakurai and P. Enkhbaatar, *Burns*, 2014, **40**, 511-519.
69 J. Kim and C.M. Lee, *Int. J. Biol. Macromol.*, 2017, **99**, 586-593.
70 P.S. Larmo, R.L. Järvinen, N.L. Setälä, B. Yang, M.H. Viitanen, J.R.K. Engblom, R.L. Tahvonen and H.P. Kallio, *The Journal of Nutrition*, 2010, **140**, 1462-1468.
71 Y. Kimura, D. Mori, T. Imada, Y. Izuta, M. Shibuya, H. Sakaguchi, E. Oonishi, N. Okada, K. Matsumoto and K. Tsubota, *Nutrients*, 2017, **9**, 364.
72 Y. Wang, L. Zhao, Y. Huo, F. Zhou, W. Wu, F. Lu, X. Yang, X. Guo, P. Chen, Q. Deng and B. Ji, *Nutrients*, 2016, **8**, 245.
73 Y. Wang, F. Huang, L. Zhao, D. Zhang, O. Wang, X. Guo, F. Lu, X. Yang, B. Ji and Q. Deng, *J Agric Food Chem*, 2016, **64**, 161-170.
74 K. Bouras, K. Kopsidas, M. Bariotakis, P. Kitsiou, K. Kapodistria, G. Agrogiannis, I. Vergados, P. Theodossiadis and D. Perrea, *Biomedicine hub*, 2017, **2**, 1-12.
75 S. Dubey, P. Deep and A.K. Singh, *Vet. Ophthalmol.*, 2016, **19**, 144-148.
76 H. Suleyman, L.O. Demirezer, M.E. Buyukokuroglu, M.F. Akcay, A. Gepdiremen, Z.N. Banoglu and F. Gocer, *Phytotherapy research*, 2001, **15**, 625-627.
77 J. Xing, B. Yang, Y. Dong, B. Wang, J. Wang and H.P. Kallio, *Fitoterapia*, 2002, **73**, 644-650.
78 N.K. Huff, A.D. Auer, F.J. Garza, M.L. Keowen, M.T. Kearney, R.B. McMullin and F.M. Andrews, *J Vet Intern Med*, 2012, **26**, 1186-1191.
79 S. Attri, K. Sharma, P. Raigond and G. Goel, *Food Res. Int.*, 2018, **105**, 324-332.
80 W. Ni, T. Gao, H. Wang, Du Y, J. Li, C. Li, L. Wei and H. Bi, *J. Ethnopharmacol.*, 2013, **150**, 529-535.
81 X. Zheng, W. Long, G. Liu, X. Zhang and X. Yang, *J. Sci. Food Agr.*, 2012, **92**, 736-742.
82 J. Purushothaman, G. Suryakumar, D. Shukla, A.S. Malhotra, H. Kasiganesan, R. Kumar, R.C. Sawhney and A. Chami, *Brain Res. Bull.*, 2008, **77**, 246-252.

83 J. Purushothaman, G. Suryakumar, D. Shukla, H. Jayamurthy, H. Kasiganesan, R. Kumar and R.C. Sawhney, *Evid.-Based Compl. Alt.*, 2011, **2011**, 574524.

84 J.Y. Zhou, S.W. Zhou, Du XH and S.Y. Zeng, *Molecules*, 2012, **17**, 11585-11597.

85 P. Sharma, G. Suryakumar, V. Singh, K. Misra and S.B. Singh, *Int. J. Biometeorol.*, 2015, **59**, 1115-1126.