Supplementary Materials

A Review of the Pharmacological Potential of *Spatholobus suberectus* Dunn on Cancer

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Table S1. *In vitro* pharmacological properties of *Spatholobi Caulis* Dunn

Active constituents of SSD	Dose	Positive control	Mechanism of action	Activity	References
Methanol extracts	200 μg/mL	-	HIV-1 PR inhibition	Antimicrobial activity	[1]
Aqueous extracts	14.8-60.8 μg/mL	-	-		[2]
	5, 10 μg/mL	-	-		[3]
Ethanol (0-75% (v/v) in water) extracts	0.45-1.13 μg/mL (EC50)	-	HCV replication suppression		[4]
ECG, EGCG	~68 μM (EC50)	-	HCV replication suppression		[4]
7-hydroxy-6-methoxy-flavanone	96,1 μM (IC50)	-	Sortase A (SrtA) activity inhibition		[5]
Formononetin	74.9 μM (IC50)	-	Sortase A (SrtA) activity inhibition		[5]

Ethanol (80% (v/v) in water) extracts	0.195-1.56 mg/mL (MIC)	Oxacillin (32 μg/mL) and ampicillin (4 μg/mL)	-		[6]
Ethanol (95% (v/v) in water) extracts	83.9 μg/mL (IC50)	-	Inhibitory effects on tyrosinase		[7]
	98.14 μM ascorbate equivalent /g	Ascorbic acid	DPPH scavenging activity		[8]
Methanol extracts	3.3 μg/mL (IC50)	Ascorbic acid and trolox	Hydrogen peroxide inhibition		[9]
Formononetin	10 μM	-	Inhibition of early-phase apoptosis		[10]
Aqueous extracts	1990 mM Trolox equivalent /g	Trolox	-	Antioxidant activity	[11]
	184.4 μM ascorbate equivalent /g	Ascorbic acid	DPPH scavenging activity		[8]
	-	Deferoxamine (10 mM)	ROS scavenging		[12]
	6.42 μg/mL, IC50	Ascorbic acid, acarbose	ROS scavenging; Down regulation of PI3K/AKT and AMPK Pathways		[13,14]
	30-100 μg/mL	EGCG	The inhibition of elastase enzyme activity		[15]

	25-100 μg/mL	Ascorbic acid	ROS scavenging	[16]
	2.81 μg/mL, IC50	Ascorbic acid, acarbose	ROS scavenging; Down regulation of PI3K/AKT and AMPK Pathways	[14,17]
Ethanol extracts	6-40 μg/ml	Amifostine (45 mg/kg)	Decreased levels of ROS and MDA: Increased levels of SOD, GPX, and G-CSFR	[18]
	30-100 μg/mL	EGCG	Decreased signaling of MMPs, TIMP-1, COL1A1, elastin, and HAS2; MAPK/AP-1; NF-κB and c-Jun	[15]
Ethanol (70% (v/v) in water) extracts	10-100 μg/mL	-	Increase Nrf2/ARE the stress-response system	[19]
Combined actions of epicatechin, syringic acid, and vanillic acid	2:1:1 (ratio of syringic acid, vanillic acid, and epicatechin)	-	The synergistic inhibition effect on elastase activity	[15]
Catechin	10 μM	-	-	[20]

Daidzein, formononetin, and procyanidin B2	-	-	-	Stimulation of hematopoiesis	[20]
Sub-fractions of ethanol extracts	31-631 μg/mL (IC50)	P. kadsura	Inhibition of cyclooxygenase-1/2, phospholipase A2, 5-lipoxygenase and 12-lipoxygenase	Anti-inflammatory activity	[21]
Aqueous extracts	60 μg/mL (IC50)	-	Inhibition of NO and TNF-α production		[8,22]
Total phenolics	1.33 μg/mL (IC50)	Sivelestat	-		[23]
Catechin, gallocatechin, liquiritigenin, , butin, 3',4',7-trihydroxyflavone, and plathymenin	-	-	5-Lipoxygenase inhibition		[24]
2,6-dimethoxy-1,4-benzoquinone, isoliquiritigenin	5.69-6.78 μM	l-N6-(1-iminoethyl)-lysine), indomethacin	Inhibition of NO; Pro-inflammatory cytokine inhibition		[25]
Spasuberol C, formononetin sodium, liquiritigenin, genistein, formononetin	16.34-28.33 μM	l-N6-(1-iminoethyl)-lysine), indomethacin	Inhibition of NO; Pro-inflammatory cytokine inhibition		[25]

Spasuberol A and B, daidzein, genistin, 4,7,2-trihydroxy-4-methoxy-isoflavanol, and homovanillyl-4-oxo-nonanoate	36.43-46.26 μM	l-N6-(1-iminoethyl)-lysine), indomethacin	Inhibition of NO; Pro-inflammatory cytokine inhibition		[25]
Spasuberoside A, spasuberoside B	> 100 μM	l-N6-(1-iminoethyl)-lysine), indomethacin	Inhibition of NO; Pro-inflammatory cytokine inhibition		[25]
8-O-methylretusin, biochanin A, formononetin, genistin, homovanillyl-4-oxo-nonanoate, odoratin, and Spasuberol A	21.1-51.1 μM	l-N6-(1-iminoethyl)-lysine), indomethacin	Inhibition of NO		[26]
(+)-epipinoresinol, (+)-pinoresinol, 3-methoxydaidzein, 4-hydroxy-3-methoxy cinnamic acid, methyl ester, biochanin A, butesuperin A, calycosin, daidzin, isolariciresinol, maackiain, ononin, and Salicylic acid	57.8-197.4 μM	l-N6-(1-iminoethyl)-lysine), indomethacin	Inhibition of NO		[26]
4,8-dimethoxy7-O-β-d-glucopyranosyl isoflavone, 6,9-dihydroxy megastigma-4,7-	> 200 μM	l-N6-(1-iminoethyl)-lysine), indomethacin	Inhibition of NO		[26]

dien-3-one, 8,9-dihydroxy megastigma-4,6-dien-3-one, nicotinic acid, phydroxybenzoic acid, and protocatechuate					
Procyanidin B4	22.5 nM (IC50)	Etoposide (IC50 = 78.4 μM)	-	Topoisomerase-II-inhibitory activity	[27]
(+)-catechin-(4→8)-(+)-catechin-(4→8)-(-)-epicatechin	21.9 nM (IC50)	Etoposide (IC50 = 78.4 μM)	-		[27]
Methanol extract	100-500 μg/mL	Ketoconazole (10 μM)	Cyt P450 inhibition	Cyt P450 3A4 enzyme inhibition *activity*	[28]
Aqueous extract	100-1000 μg/mL	Ketoconazole (10 μM)	Cyt P450 inhibition		[28]
Aqueous extracts	10-100 μg/mL	-	Suppression of c-Fos, NFATc1; The block of receptor activator of NF-κB ligand-induced early signaling pathways	Inhibition of osteoclast differentiation and bone resorption	[29]
Ethanol (70% (v/v) in water) extracts	12.5-200 μg/mL	Baicalein (10-20 μM)	-		[30]
Aqueous and ethanolic extracts	3, 10, 30 μg/mL	Acarbose (125-500 μg/mL)	Inhibition of *α*-glucosidase activity	Anti-diabetic activity	[14]
	10, 50, 100 μg/mL	Glucose and fructose (25 mM)	Inhibition of *AGEs formation*		[19]

Abbreviation: AGEs- advanced glycation end products; AKT- *protein* kinase B; AMPK- AMP-activated protein kinase; AP-1- activator protein 1; ARE- antioxidant responsive element; b.w. body weight; BPA- production of erythroid burst-promoting activity; c-Jun-transcription factor Jun; COL1A1- type I collagen; Cyt P450- cytochrome P450; DPPH- 2,2-diphenyl-1-picrylhydrazyl; EC50- Half maximal effective concentration; EGC- epigallocatechin; EGCG-epigallocatechin gallate; G-CSFR- granulocyte colony-stimulating factor receptor; GM-CSA- granulocyte-monocyte colony-stimulating activity; GM-CSF- granulocyte-macrophage colony-stimulating factor; GPX- glutathione peroxidase; HAMP- hepcidin Antimicrobial Peptide; HAS2- hyaluronan synthase 2; HCV- hepatitis C virus; HIV 1 PR- human immune deficiency virus-1 protease; i.p. intraperitoneal; IL-6 –interleukin 6; MAPK- *mitogen-activated protein kinase;* MDA- malondialdehyde; MIC- minimum inhibitory concentration; MK-CSA- megakaryocyte colony-stimulating activity; MMPs- matrix metalloproteinases; NFATc1- nuclear factor of activated T-cells; NF-κB - nuclear factor kappa B; NO- nitric oxide; Nrf2- nuclear factor erythroid 2-related factor 2; p.o. per oral; PI3K- phosphoinositide 3-kinases; ROS- reactive oxygen species; SOD- superoxide dismutase; TIMP-1- tissue inhibitor matrix metalloproteinase 1; TNF-α- tumor necrosis factor-alpha

Table S2. *In vivo* pharmacological properties of *Spatholobi Caulis* Dunn

Active constituents of SSD	Model	Doses and route of administration	Positive control	Mechanism of action	Activity	References
Aqueous extracts	BALB/c mice	50, 100 mg/kg b.w., p.o.	-	-	Antimicrobial activity	[3]
Aqueous extracts	Wistar albino rats	100, 200 mg/kg, p.o.	-	Decrease NO, MDA, TNF-α, caspase-3, and NF-κB; Increase GPX, SOD, and IL-10 expressions	Antioxidant activity	[31]
	C57BL/6J mice	200 mg/kg b.w. p.o.	Ascorbic acid, acarbose	ROS scavenging; Down regulation of PI3K/AKT and AMPK Pathways		[13,14]
Ethanol extracts	C57BL/6J mice	200 mg/kg b.w. p.o.	Ascorbic acid, acarbose	ROS scavenging; Down regulation of PI3K/AKT and AMPK Pathways		[14,17]
	Kun Ming mice	40 g/kg b.w, p.o.	Amifostine (45 mg/kg)	Decreased levels of ROS and MDA: Increased levels of SOD, GPX, and G-CSFR		[18]
Ethanol (70% (v/v) in water) extracts	db/db, C57BL/KsJ and db/m mice	200 mg/kg b.w., p.o.	-	Increase Nrf2/ARE the stress-response system		[19]
Catechin	Kun Ming mice	1 mg/day, i.p.	-	GM-CSF; IL-6	Stimulation of hematopoiesis	[32]
	NIH strain mice	0.01, 0.05 g/kg b.w, i.p.	-	GM-CSA, BPA and MK-CSA		[33]

Decoction of SSD	Kun Ming mice	-	-	-		[34]
Aqueous extracts	C57BL/6 female mice	108 g dried CS/kg b.w., i.p.	-	HAMP expression inhibition; Decrease in hepatic iron concentration; Increase in serum iron concentration		[35]
Aqueous extracts	Wistar albino rats	100, 200 mg/kg b.w., p.o.	Heparin	Decreased IL-Iβ and amylase and lipase	Anti-inflammatory activity	[36]
Liquiritigenin	BALB/c mice	1 mg/mL	-	Blocked T Cell Activation; Downregulation of PI3K/Akt pathways		[37]
Ethanol (95% (v/v) in water) extracts	ICR mice	100 and 200 mg/kg b.w., p.o.	Aspirin (1 mM), nitroprusside 30 (μg/ml)	Prevention of fibrinogen binding to GP IIb/IIIa receptor	Antiplatelet effects	[38]
Aqueous extracts	SD rats	10 mg/kg b.w., p.o.	Ketoconazole (0.25 and 1 μM)	Cyt P450 inhibition	Hepatoprotective activity	[39]
Aqueous and ethanolic extracts	C57BL/6J mice	100 and 200 mg/kg b.w., p.o	STZ-induced diabetic plus acarbose (200 mg/kg bw., p.o.)	Reduced blood glucose, oral glucose tolerance test, Phosphoenol pyruvate carboxykinase, and glucose-6-phosphatase, enhances glucose uptake and GLUT4 activation via PI3K/AKT and AMPK pathway	Anti-diabetic activity	[14]

	C57BL/KsJ db/db mice and db/m mice	50 mg/kg b.w., p.o	Metformin (200 mg/kg, p.o.)	Reduced body weight, blood glucose, HbA1c, triglyceride, total cholesterol, low-density lipoprotein cholesterol, and free fatty acid	[19]

Abbreviation: AKT- *protein* kinase B; AMPK- AMP-activated protein kinase; AP-1- activator protein 1; ARE- antioxidant responsive element; b.w. body weight; BPA- production of erythroid burst-promoting activity; c-Jun-transcription factor Jun; COL1A1- type I collagen; Cyt P450- cytochrome P450; DPPH- 2,2-diphenyl-1-picrylhydrazyl; EC50- Half maximal effective concentration; EGC- epigallocatechin; EGCG-epigallocatechin gallate; G-CSFR- granulocyte colony-stimulating factor receptor; GM-CSA- granulocyte-monocyte colony-stimulating activity; GM-CSF- granulocyte-macrophage colony-stimulating factor; GPX- glutathione peroxidase; HAMP- hepcidin Antimicrobial Peptide; HAS2- hyaluronan synthase 2; HCV- hepatitis C virus; HIV 1 PR- human immune deficiency virus-1 protease; i.p. intraperitoneal; IL-6 –interleukin 6; MAPK-*mitogen-activated protein kinase;* MDA- malondialdehyde; MIC- minimum inhibitory concentration; MK-CSA- megakaryocyte colony-stimulating activity; MMPs- matrix metalloproteinases; NFATc1- nuclear factor of activated T-cells; NF-κB - nuclear factor kappa B; NO- nitric oxide; Nrf2- nuclear factor erythroid 2-related factor 2; p.o. per oral; PI3K- phosphoinositide 3-kinases; ROS- reactive oxygen species; SOD- superoxide dismutase; TIMP-1- tissue inhibitor matrix metalloproteinase 1; TNF-α- tumor necrosis factor-alpha

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