

Supplementary Table III

Anti-cancer effects of *Peganum harmala* and the related mechanisms

Extracts/compounds	Cancer models	Activities (IC ₅₀) (µg/mL)	Mechanisms	References
Methanolic extract	HT-29 cell line	49.05 ± 3.2		Elansary et al., 2020
	HeLa cell line	43.86 ± 2.7		
	MCF-7 cell line	58.64 ± 4.2		
	Jurkat cell line	59.53 ± 4.2		
Total alkaloid	MDA-MB-231 cell line		Apoptosis triggered by both intrinsic and extrinsic pathways	Shabani et al., 2015
Total alkaloid of aerial parts	MCF7 cell line	15.5 ± 4.1		Bournine et al., 2017
	Hs683 cell line	52.7 ± 7.0		
	SKMEL-28 cell line	80.2 ± 3.7		
	U373 cell line	46.6 ± 5.5		
	A549 cell line	55.5 ± 7.5		
	B16F10 cell line	20.0 ± 0.8		
Total alkaloid of fruits	MCF7 cell line	8.1 ± 1.4		
	Hs683 cell line	12.1 ± 2.6		
	SKMEL-28 cell line	7.9 ± 1.7		
	U373 cell line	15.6 ± 1.6		
	A549 cell line	18.1 ± 1.2		
	B16F10 cell line	3.4 ± 0.4		
Total alkaloid of seeds	MCF7 cell line	6.6 ± 0.5		
	Hs683 cell line	4.4 ± 0.8		
	SKMEL-28 cell line	11.7 ± 1.4		
	U373 cell line	5.4 ± 0.3		
	A549 cell line	8.7 ± 1.5		
	B16F10 cell line	4.1 ± 0.2		
Total alkaloid of roots	MCF7 cell line	3.7 ± 0.4		
	Hs683 cell line	4.6 ± 0.5		
	SKMEL-28 cell line	6.2 ± 0.5		
	U373 cell line	2.6 ± 0.3		
	A549 cell line	3.8 ± 0.4		
	B16F10 cell line	1.0 ± 0.1		
Total alkaloid extract	MDA-MB-231 cell line	30		Seyed Hassan Tehrani et al., 2014
	MCF-7 cell line	40 (48 h)		
Harmaline	ESCC patient-derived xenograft mice	About 50% reduction of tumor volume (100 mg/kg p.o. for 62 days)	Cell cycle arrest through p27 regulation and act as a mTOR inhibitor	Zhang et al., 2021
	SGC-7901 cell line	4.1 ± 0.9 µM	Cell cycle arrest and apoptosis by up-regulating Fas/FasL	Wang et al., 2015c
	SGC-7901 xenograft mice	About 30% reduction of tumor volume (15 mg/kg p.o. for 10 days)		
Pegaharmol A	HL-60 cell line	39.0		Li et al., 2020b
	A549 cell line	55.7		
Peganumine A	HL-60 cell line	5.8		Wang et al., 2014b
	PC-3 cell line	40.2		
	HepG 2 cell line	55.4		
	MCF-7 cell line	38.5		
Peganumine G	ZR-75-1 cell line	6.2 ± 2.7	As a G-quadruplex ligand	Yang et al., 2016
Peganumine H		2.4 ± 0.8		
Pegaharmine D	HL-60 cell line	3.8 ± 0.3		
	PC-3 cell line	11.5 ± 0.6		
	SGC-7901 cell line	15.2 ± 0.4		
Pegaharmine E	HL-60 cell line	25.1		Wang et al., 2018a
Peganumaline B		21.5		
Peganumaline F		24.6		
Pegaharmine J		4.4		
				Wang et al., 2017a

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PH-HM-16 (alkaloid)	HL-60 cell line	68.8		Sadaf et al., 2021
	PC-3 cell line	17.6		
	SGC-7901 cell line	111.9		
	MCF-7 cell line	41.8		
	HCT116 cell line	71.5		
	A549 cell line	176.0		
Harmine	SW620 cell line	5.1	Cell cycle arrest and apoptosis via Akt/ERK pathway	Liu et al., 2016
	B16F-10 cell line	26.3% Viability under 50 µg/mL treatment	Both intrinsic and extrinsic pathways of apoptosis through regulation of transcription factors and pro-inflammatory cytokines	Hamsa and Kuttan, 2011a
	B16F-10 melanoma bearing mice	51.6-83.6% Reductions in tumor nodule formation	regulation of pro- and anti-metastatic genes including ERK, VEGF and MMPs	Hamsa and Kuttan, 2011b
	MGC-803 cell line	58.8 ± 11.3	Apoptosis and autophagy induced through PI3K/ Akt/mTOR signaling pathway; autophagy induced through AMPK signaling pathway	Li et al., 2017
	SGC-7901 cell line	40.9 ± 5.7		
	A549 cell line	10.1	Activation of RECK signaling pathway	Shen et al., 2018
	A549 NSCLC bearing mice	Significantly blocked tumor growth and decreased metastatic nodes numbers		
	H460 cell line	19.5		
	PC9 cell line	32.7		
	HBL-100 cell line	32.6 ± 0.7		Ayoob et al., 2017
	A549 cell line	106.7 ± 2.5		
	HT-29 cell line	45.6 ± 0.9		
	HELA cell line	61.8 ± 0.7		
	HCT-116 cell line	34.0 ± 0.2		
	U-937 cell line	23.1 ± 0.9		Wang et al., 2015b
	HL-60 cell line	71.2 ± 3.3		
	KG1 cell line	62.7 ± 2.8		
	HEL cell line	20.3 ± 1.1		
	Med-mek carcinoma cell line	14.4 ± 0.0		
	UCP-med carcinoma cell line	18.4 ± 0.0		Lamchouri et al., 2013
	UCP-med sarcoma cell line	6.5 ± 0.0		
	Sp2/O-Ag14 cell line	2.4 ± 0.1		
	1-Ethyl-7-methoxy-9H-pyrido[3,4-b]	HL-60 cell line	7.6	
HL-60 cell line		9.1		
Harmalanine		9.3		Wang et al., 2017b
	Peharmaline A	9.2		
Pegaharmaline A	PC-3 cell line	21.6		Wang et al., 2014a
	SGC-7901 cell line	25.4		
	HL-60 cell line	9.4		
	PC-3 cell line	66.7		
Pegaharmaline B	HepG 2 cell line	74.7		Wang et al., 2014a
	MCF-7 cell line	51.9		
	A549 cell line	82.3		
	HL-60 cell line	13.6		

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Extracts/compounds	Cancer models	Activities (IC ₅₀) μ M	Mechanisms	References	
Pegaharmaline B	PC-3 cell line	28.9		Wang et al., 2014a	
	HepG 2 cell line	45.3			
	MCF-7 cell line	66.6			
	A549 cell line	70.9			
3-(4-Hydroxyphenyl)quinoline	A549 cell line	18.9 \pm 1.4		Zhang et al., 2022	
	HepG2 cell line	3.1 \pm 0.1			
	MCF-7 cell line	54.9 \pm 1.1			
Norharmane	A549 cell line	16.5 \pm 1.1			
	HepG2 cell line	17.3 \pm 3.0			
	MCF-7 cell line	32.1 \pm 0.8			
Perlolryine	A549 cell line	42.5 \pm 3.6			
(S)-Vasicinone-1-O- β -D-glucopyranoside	MCG-803 cell line	84.1 \pm 3.7			Wang et al., 2015a
(S)-Vasicinone		94.5 \pm 10.5			
3 α -Acetoxy-27-hydroxyolean-12-en-28-oic acid methyl ester	A549 cell line	8.0 \pm 0.8		Wang et al., 2016b	
	H460 cell line	36.1 \pm 1.8			
	U-937 cell line	41.3 \pm 2.3			
	KG-1	27.3 \pm 1.6			
3-Oxotirucalla-7,24-dien-21-oic acid	A549 cell line	36.2 \pm 2.0			
	H460 cell line	40.0 \pm 2.3			
	U-937 cell line	31.2 \pm 1.5			
	KG-1	27.4 \pm 1.4			
3 α ,27-Dihydroxylup-20(29)-en-28-oic acid methyl ester	A549 cell line	51.3 \pm 2.1			
	H460 cell line	65.3 \pm 3.4			
	U-937 cell line	26.1 \pm 1.3			
	KG-1 cell line	16.4 \pm 1.2			
3 α -Acetoxy-27-hydroxylup-20(29)-en-28-oic acid methyl ester	A549 cell line	46.3 \pm 1.6			
	H460 cell line	42.6 \pm 2.1			
	U-937 cell line	18.6 \pm 1.0			
	KG-1 cell line	24.6 \pm 1.1			
(E)-Caffeyl alcohol 4-O- β -D-glucopyranoside	H460 cell line	61.0 \pm 3.2			
	U-937 cell line	44.6 \pm 2.6			
	KG-1 cell line	29.9 \pm 1.3			
	3T3 cell line	78.6 \pm 2.6			
Coniferin	A549 cell line	16.3 \pm 0.6			
	U-937 cell line	52.6 \pm 2.1			
Syringin	A549 cell line	55.7 \pm 2.2			
	U-937 cell line	22.8 \pm 1.3			
	KG-1 cell line	57.1 \pm 2.7			
	3T3 cell line	64.1 \pm 3.2			
Syringinocide	U-937 cell line	55.3 \pm 1.7			
N-Acetyl-9-syringinocide	U-937 cell line	30.7 \pm 1.2			
	KG-1 cell line	41.4 \pm 1.7			
	3T3 cell line	85.2 \pm 6.8			
2-(Indol-3-yl)ethyl- β -D-glucopyranoside	U-937 cell line	52.1 \pm 2.6	Wang et al., 2015b		
	HL-60 cell line	78.9 \pm 3.8			
	KG1 cell line	23.1 \pm 1.4			
	HEL cell line	121.3 \pm 5.5			

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2-(Indol-3-yl)ethyl-α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside	U-937 cell line	80.2 ± 4.5	Apoptosis through Ras/Raf/ERK pathway	
	HL-60 cell line	55.3 ± 3.4		
	KG1 cell line	60.2 ± 2.7		
	HEL cell line	131.0 ± 4.9		
(S)-3-Hydroxy-3-(N-acetyl-2-aminoethyl)-6-methoxyindol-2-one	U-937 cell line	75.3 ± 2.8		
	HL-60 cell line	36.2 ± 1.1		
	HEL cell line	55.3 ± 3.2		
Harmol	U-937 cell line	46.1 ± 2.0		
	HL-60 cell line	62.0 ± 2.8		
	KG1 cell line	47.7 ± 2.3		
	HEL cell line	54.6 ± 2.3		
Ruine	U-937 cell line	30.6 ± 1.2		
	HL-60 cell line	60.7 ± 2.9		
	KG1 cell line	44.5 ± 2.1		
	HEL cell line	71.6 ± 2.7		
Harmic acid methyl ester	U-937 cell line	22.3 ± 1.4		
	HL-60 cell line	44.3 ± 2.1		
	KG1 cell line	56.8 ± 2.5		
	HEL cell line	35.2 ± 2.8		
Harmalacidine	U-937 cell line	3.1 ± 0.2		
	HL-60 cell line	61.3 ± 2.8		
	KG1 cell line	32.6 ± 1.7		
	HEL cell line	25.7 ± 1.1		
Harmaline	U-937 cell line	10.6 ± 0.7		
	HL-60 cell line	55.3 ± 2.4		
	KG1 cell line	46.8 ± 1.9		
	HEL cell line	20.1 ± 1.2		
Protonated harmaline	U-937 cell line	15.3 ± 0.7		
	HL-60 cell line	45.7 ± 2.1		
	KG1 cell line	56.9 ± 2.3		
	HEL cell line	21.2 ± 1.1		
luotonin C	U-937 cell line	49.6 ± 1.9		
	HL-60 cell line	87.3 ± 3.7		
	KG1 cell line	113.2 ± 5.6		
	HEL cell line	68.3 ± 3.0		
11-Methoxyyl-rutaecarpine	U-937 cell line	55.3 ± 1.7		
	HL-60 cell line	93.8 ± 6.8		
	KG1 cell line	88.1 ± 3.7		
	HEL cell line	120.9 ± 5.5		
Vasicine	PC-3 cell line	15.4	Li et al., 2018a	
(S)-1-(2-Aminobenzyl)-3-hydroxypyrrro-lidin-2-one β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside	HL-60 cell line	42.8		
Vasicinone		67.8		
1-(2-Aminobenzyl)-3-hydroxypyrrrolidin-2-one		42.3		
Harmalacidine	Med-mek carcinoma cell line	17.72 ± 0.02 μg/mL		Lamchouri et al., 2013
	UCP-med carcinoma cell line	28.93 ± 0.01 μg/mL		
	UCP-med sarcoma cell line	17.60 ± 0.01 μg/mL		
	Sp2/O-Ag14 cell line	7.96 ± 0.02 μg/mL		

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Extracts/compounds	Cancer models	Activities (IC ₅₀) (µM)	Mechanisms	References
Vasicine	Med-mek carcinoma cell line	52.24 ± 0.02 µg/mL		
	UCP-med sarcoma cell line	52.36 ± 0.02 µg/mL		
Vasicinone	Med-mek carcinoma cell line	25.32 ± 0.04 µg/mL		
	UCP-med carcinoma cell line	59.97 ± 0.02 µg/mL		
	UCP-med sarcoma cell line	64.79 ± 0.02 µg/mL		
	Sp2/O-Ag14 cell line	19.20 ± 0.02 µg/mL		
3β-Acetoxy-27-hydroxy-lup-20 (29)-en-28-oic acid	HeLa cell line	11.5 ± 3.4		Li et al., 2020a
	HepG2 cell line	15.4 ± 1.2		
	SGC-7901 cell line	14.6 ± 0.8		
3α-Acetoxy-27-hydroxy-olean-12-en-11-oxo-28-oic acid methyl ester	HepG2 cell line	74.7 ± 1.8		
3α-Hydroxy-olean-27-(4-hydroxy-3-methoxy-E-cinnamoyloxy)-12-en-28-oic acid methyl ester	HeLa cell line	39.6 ± 1.0		
	HepG2 cell line	34.5 ± 0.6		
	SGC-7901 cell line	34.8 ± 0.9		
3α-Acetoxy-27-hydroxyolean-12-en-28-oic acid	HeLa cell line	23.1 ± 1.7		
	HepG2 cell line	32.6 ± 1.5		
	SGC-7901 cell line	24.3 ± 4.5		
3α-Acetoxy oleanolic acid	HeLa cell line	12.3 ± 0.5		
	HepG2 cell line	17.6 ± 3.6		
	SGC-7901 cell line	16.6 ± 2.2		
Urs-12-ene-28-carboxy-3α-tetradecanoate	HeLa cell line	15.1 ± 1.0		
	HepG2 cell line	21.4 ± 1.4		
	SGC-7901 cell line	37.8 ± 0.7		
Methyl-lup-20 (29)-en-3-on-28-oate	HeLa cell line	45.3 ± 1.9		
	HepG2 cell line	56.6 ± 2.2		
	SGC-7901 cell line	63.0 ± 5.2		
Betulonic acid	HeLa cell line	54.0 ± 3.6		
lup-20 (29)-en-3-on-28-oic acid	HeLa cell line	54.3 ± 9.1		
	SGC-7901 cell line	39.5 ± 3.2		
3-Oxo-27-hydroxylup-20 (29)-en-28-acid methyl ester	HeLa cell line	22.2 ± 1.5		
	HepG2 cell line	20.4 ± 5.2		
	SGC-7901 cell line	15.0 ± 0.9		
3α-Acetoxy-27-hydroxylup-20 (29)-en-28-oic acid methyl ester	HeLa cell line	22.9 ± 2.5		
	HepG2 cell line	21.0 ± 2.0		
	SGC-7901 cell line	27.4 ± 10.1		
3β-Acetoxy-27-hydroxylup-20 (29)-en-28-oic acid methyl ester	HeLa cell line	8.3 ± 1.4		
	HepG2 cell line	11.0 ± 0.7		
	SGC-7901 cell line	15.6 ± 0.9		
3α, 27-Dihydroxylup-20 (29)-en-28-oic acid methyl ester	HeLa cell line	24.7 ± 0.6		
	HepG2 cell line	30.6 ± 3.5		
	SGC-7901 cell line	15.8 ± 1.6		