A Novel Therapy of Chinese Herbs: Danshen (*Savia miltiorrhiza*) Extracts Against Apicidin-resistant HA22T Hepatocellular Carcinoma Cells

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Abstract

Worldwide, Human hepatocellular carcinoma (HCC) is the now fifth most common cancer and third leading cause of cancer death. HCC can be treat by surgical resection, chemotherapy or radiotherapy, but in HCC, the 5-year survival rate of less than 5% due to high recurrence after surgical resection and resistance to chemotherapy, therefore, chemoresistance is a major obstacle in the treatment of HCC. The Apicidin is a novel HDAC inhibitor derived from a fungal metabolite, and it's a treatment resistant in HCC remains to be elucidated. In Our previous study, we successfully established the stable HA22T cancer cell lines which chronically resisted to the histone deacetylase (HDAC) inhibitor, apicidin. Moreover, we found Apicidin-R HA22T cells could enhance pro-survival capability and cell metastasis via activating the IGF-IR/PI3K/Akt signaling pathway, and also could activate the IKK α β /NF- κ B pathway to promote the EMT effect. In this study, we intend to use this model to identify 30 compounds of Danshen (*Savia miltiorrhiza*) extracts could inhibit chemoresistant effects induced by Apicidin in HA22T cells. Our preliminary result showed 12 compounds of Danshen extracts could suppress the cell viability of Apicidin-R HA22T cells in a dose-dependent manner. The possible mechanism of Danshen extracts to overcome behavior of EMT and metastasis in Apicidin-R HA22T cell will be further identified in the near future.

Result

Table 1 . Effect of 30 compounds of Danshen (*Savia miltiorrhiza*) extracts to inhibit cell viability in Apicidin-resistant HA22T Hepatocellular Carcinoma Cells

	Number of Danshen Extract	Molecular Weight	Chemical Formula
Inhibit Cell viability (dose-dependent manner)			
	Dsh-003	269.14	$C_{19}H_{20}O_3$
	Dsh-431	411.18	$C_{27}H_{25}NO_3$
	Dsh-451	316.16	$C_{21}H_{22}N_{20}$
	Dsh-311	307.17	$C_{20}H_{21}NO_2$
	Dsh-411	388.17	$C_{26}H_{23}NO_2$
	Dsh-452	320.15	$C_{20}H_{20}N_2O_2$
	Dsh-412	385.17	$C_{25}H_{23}NO_3$
	Dsh-432	415.18	$C_{26}H_{25}NO_4$
	Dsh-261	377.16	$C_{23}H_{23}NO_4$
	Dsh-271	391.18	$C_{24}H_{25}NO_4$
	Dsh-211	305.14	$C_{20}H_{19}NO_2$
	Dsh-221	319.16	$C_{21}H_{21}NO_2$
Inhibit Cell viability (In High dose)			
	Dsh-111	287.09	$C_{19}H_{12}NO_2$
	Dsh-242	351.18	$C_{22}H_{25}NO_3$
	Dsh-121	301.11	$C_{20}H_{15}NO_3$
	Dsh-421	395.19	$C_{27}H_{25}NO_2$
	Dsh-222	323.15	$C_{20}H_{21}NO_3$
	Dsh-441	434.20	$C_{29}H_{26}N_2O_2$
	Dsh-132	359.12	$C_{22}H_{17}NO_4$
	Dsh-124	305.11	$C_{19}H_{15}NO_3$
	Dsh-002	294.13	$C_{19}H_{18}O_3$
	Dsh-112	287.09	$C_{19}H_{12}NO_2$
	Dsh-114	291.09	$C_{18}H_{13}NO_3$
	Dsh-001	276.08	$C_{18}H_{12}O_3$
	Dsh-122	301.11	$C_{20}H_{15}NO_3$
No Effect			
	Dsh-232	337.17	$C_{21}H_{23}NO_3$
	Dsh-281	335.15	$C_{21}H_{21}NO_3$
	Dsh-231	333.17	$C_{22}H_{23}NO_2$
	Dsh-321	321.17	$C_{21}H_{23}NO_2$
	Dsh-272	395.17	$C_{22}H_{25}NO_3$

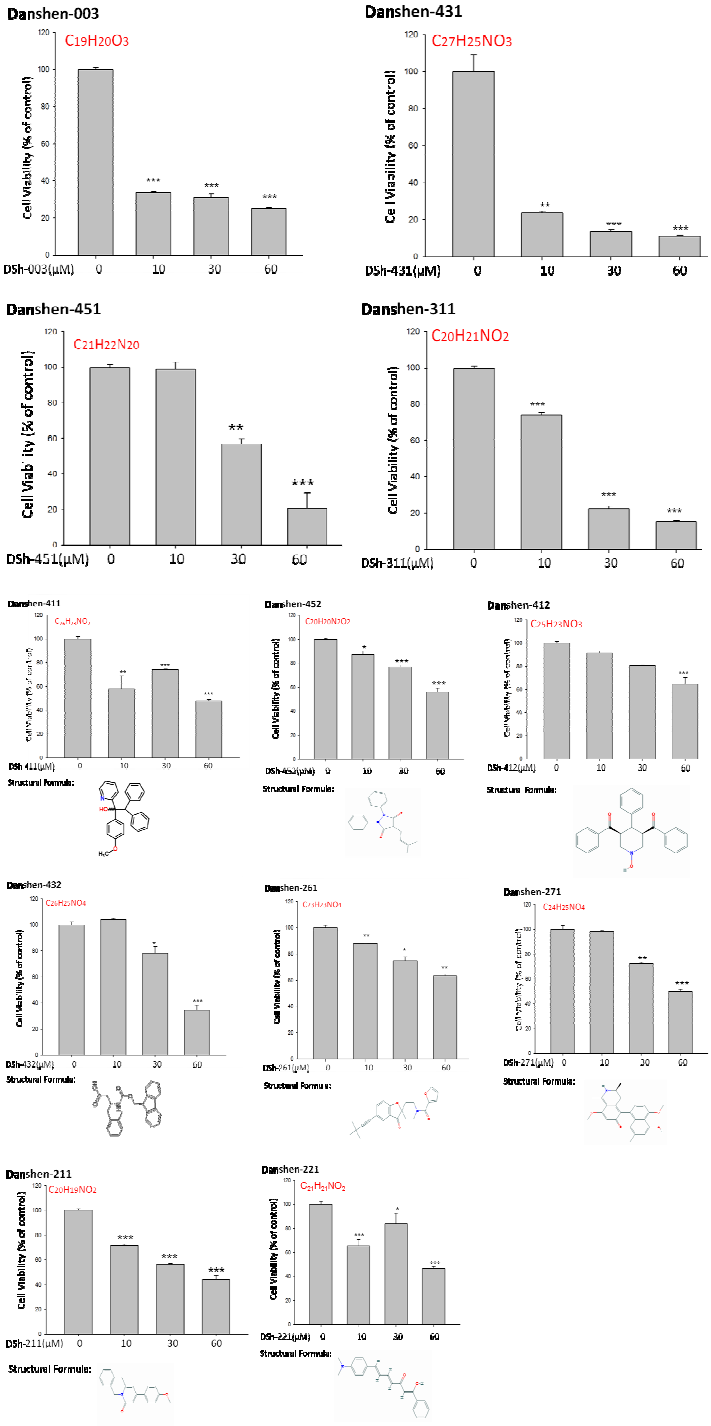

Figure 1. The 12 compounds (Dsh-003, Dsh-431, Dsh-451, Dsh-311, Dsh-411, Dsh-452, Dsh-412, Dsh-432, Dsh-261, Dsh-271, Dsh-211, Dsh-221) of Danshen (*Savia miltiorrhiza*) extracts could inhibit chemoresistant effects induced by Apicidin in HA22T Hepatocellular Carcinoma Cells