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Thymoquinone synergizes the anticancer properties of cisplatin against head and neck squamous cell carcinoma and protects normal oral epithelial cells

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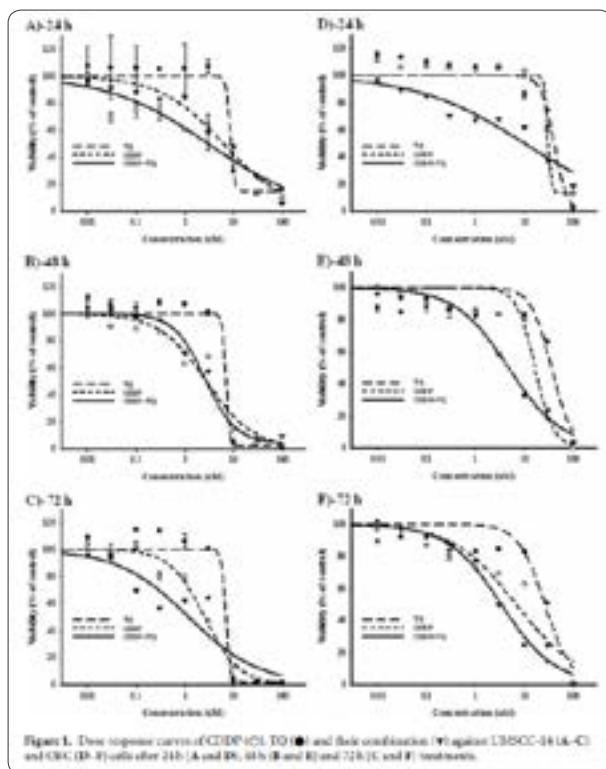
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Cisplatin (CDDP) is a potent anticancer agent used for several tumor types. Thymoquinone (TQ) is naturally occurring compound drawing great attention as anticancer and chemomodulator for chemotherapies. Herein, we studied the potential cytotoxicity of thymoquinone, CDDP and their combination against human oral squamous cell carcinoma cell in contrast to normal oral epithelial cells. CDDP similarly killed both head and neck squamous cell carcinoma cells (UMSCC-14C) and normal oral epithelial cells (OEC). TQ alone exerted considerable cytotoxicity against UMSCC-14C cells; while it induced weaker killing effect against normal oral epithelial cells (OEC). Equitoxic combination of TQ and CDDP showed additive to synergistic interaction against both UMSCC-14C and OEC cells. TQ alone increased apoptotic cell fraction in UMSCC-14C cells, as early as after 6 hours. In addition, prolonged exposure of UMSCC-14C to TQ alone resulted in $96.7 \pm 1.6\%$ total apoptosis which was increased after combination with CDDP to $99.3 \pm 1.2\%$ in UMSCC-14C cells. On the other hand, TQ induced marginal increase in the apoptosis in OEC and even decreased the apoptosis induced by CDDP alone. Finally, apoptosis induction results were confirmed by the change in the expression levels of p53, Bcl-2 and Caspase-9 proteins in both UMSCC-14c and OEC cells.



CDDP exposure	UMSCC-14		OEC	
	IC ₅₀	S index (%)	IC ₅₀	S index (%)
CDDP	6.2 ± 0.4	100 ± 0.0	10.0 ± 2.4	100 ± 0.0
TQ	5.8 ± 0.8	100 ± 0.0	40.8 ± 2.8	27 ± 0.2
CDDP + TQ	1.4 ± 0.3	100 ± 0.0	10.0 ± 0.7	20 ± 0.4
OEC value (24h)				
CDDP exposure	Additive (S)		Synergistic (S)	
	IC ₅₀	S index (%)	IC ₅₀	S index (%)
CDDP	12 ± 1.0	100 ± 0.0	10.0 ± 2.0	27 ± 0.2
TQ	7.4 ± 1.0	100 ± 0.0	10.0 ± 1.0	1.0 ± 0.2
CDDP + TQ	2 ± 0.2	100 ± 0.0	4.0 ± 0.0	0.0 ± 0.1
OEC value (72h)				
CDDP exposure	Additive (S)		Synergistic (S)	
	IC ₅₀	S index (%)	IC ₅₀	S index (%)
CDDP	1.2 ± 0.0	100 ± 0.0	4.0 ± 0.7	27 ± 0.2
TQ	1.0 ± 0.1	100 ± 0.0	10.0 ± 0.4	0.0 ± 0.0
CDDP + TQ	1.2 ± 0.0	100 ± 0.0	5.0 ± 0.0	0.0 ± 0.1
OEC value (48h)				
CDDP exposure	Additive (S)		Synergistic (S)	
	IC ₅₀	S index (%)	IC ₅₀	S index (%)
CDDP	1.2 ± 0.0	100 ± 0.0	4.0 ± 0.7	27 ± 0.2
TQ	1.0 ± 0.1	100 ± 0.0	10.0 ± 0.4	0.0 ± 0.0
CDDP + TQ	1.2 ± 0.0	100 ± 0.0	5.0 ± 0.0	0.0 ± 0.1

Table 1. Temporal effects of TQ on the cytotoxicity parameters of CDDP in UMSCC-14 and OEC cell lines.

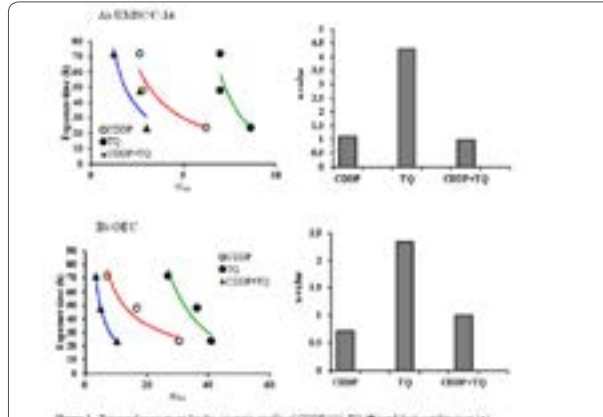
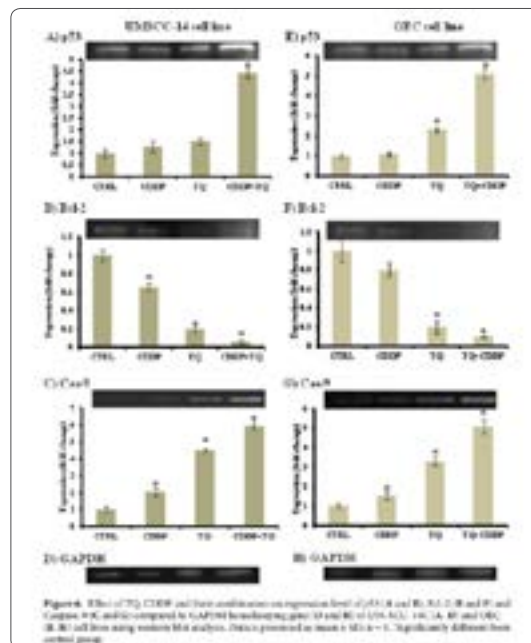
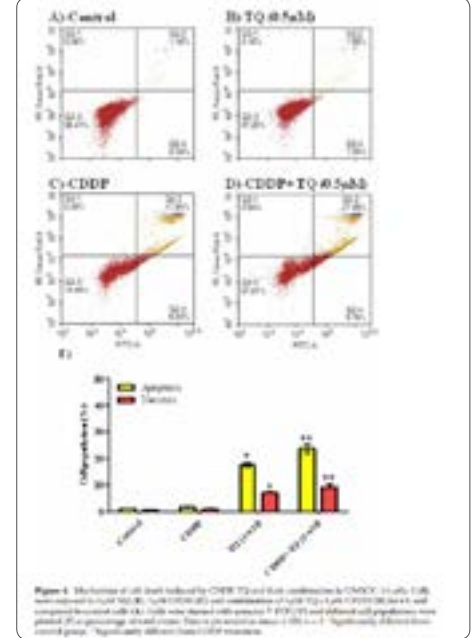
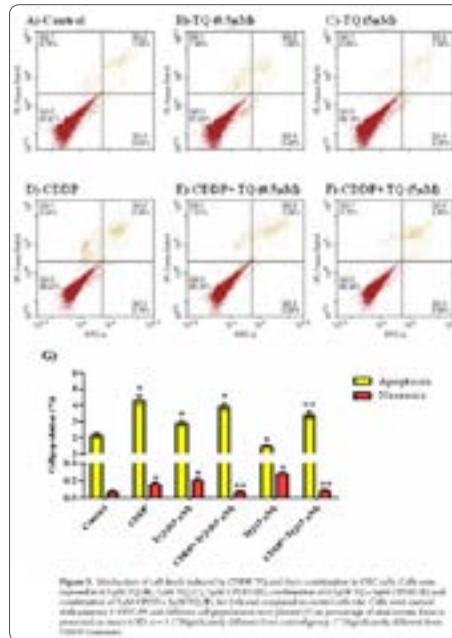
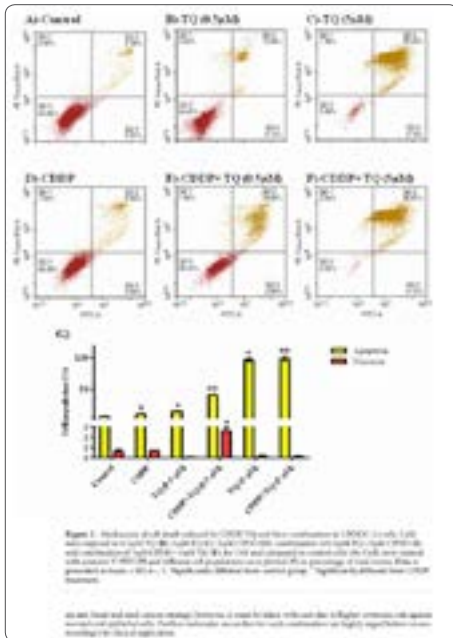


Figure 2. Temporal parameters for the cytotoxic profile of CDDP (●), TQ (■) and their combination (▲) against UMSCC-14 (A and B) and OEC (C and D) cells.



Biography

Omar Al Afi has completed his Master's Degree from College of Medicine, King Abdulaziz University (KAU), Kingdom of Saudi Arabia in Clinical Biochemistry. He is the Head of the Department of Laboratory in Comprehensive Specialized Polyclinic for Security Forces in Medina, Kingdom of Saudi Arabia. He also works at King Fahad Research Center in KAU in Jeddah as a Researcher. He has many oral presentation in his field and has published a paper in *Nature* journal. His research interest include: clinical biochemistry, cancer research and cell culture.

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