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Succinyltanshinone IIA Displays Stronger Inhibition than Tanshinone IIA In Breast Cancer Cell by Mitochondria-Dependent Apoptosis

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***SUMMARY*. A novel compound, succinyltanshinone IIA (STA), modified from the natural product tanshinone IIA (TA), was recently reported to exhibit higher potency than amphotericin B against fungi. However, related cytotoxicity in breast cancer between STA and TA remains unclear. In this study, STA showed stronger inhibitory activity on breast cancer cell growth than TA in both human epidermal growth factor receptor 2 (HER2) and estrogen receptor (ER) positive breast cancer. Similarly, STA and TA displayed higher apoptotic effect in ER positive cells than HER2 positive breast cancer cells by detecting DNA fragmentation level. Furthermore, we determined that STA significantly reduced Bcl-2 protein in HER2 positive cancer cells as compared to TA. In both STA and TA treated ER positive cancer cells, Akt phosphorylation levels were up-regulated. Taken together, STA is a novel potential anticancer compound *in vitro,* and its higher potency against breast cancer as compared TA may lead to promising bioavailability in clinical studies.**

RESUMEN. Recientemente se informó que un nuevo compuesto, succiniltanshinona IIA (STA), modificado a partir del producto natural tanshinona IIA (TA), exhibe una mayor potencia que la anfotericina B contra hongos. Sin embargo, la citotoxicidad relacionada en el cáncer de mama entre STA y TA sigue sin estar clara. En este estudio, STA mostró una actividad inhibitoria más fuerte en el crecimiento de células de cáncer de seno que la TA para el receptor 2 del factor de crecimiento epidérmico humano (HER2) y el receptor de estrógeno (ER) positivo. Del mismo modo, STA y TA mostraron un mayor efecto apoptótico en las células ER positivas que las células de cáncer de mama HER2 positivas al detectar el nivel de fragmentación del ADN. Además, determinamos que STA redujo significativamente la proteína Bcl-2 en células cancerosas positivas para HER2 en comparación con TA. Tanto en las células cancerosas ER positivas tratadas con STA como con TA, los niveles de fosforilación de Akt estaban regulados por aumento. Tomados en conjunto, STA es un nuevo compuesto potencial contra el cáncer *in vitro,* y su mayor potencia contra el cáncer de mama en comparación con TA puede conducir a una biodisponibilidad prometedora en estudios clínicos.

KEY WORDS: apoptosis, Bcl-2, breast cancer, succinyltanshinone IIA.

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