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Combining naturally occurring polyphenols with TNF-related apoptosis-inducing ligand: a promising approach to kill resistant cancer cells?

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Fig. 1 Schematic diagram of the TRAIL-induced apoptotic signaling. TRAIL binding on DR4 and/or DR5 triggers the recruitment of the adaptor protein FADD and the subsequent recruitment of the initiator Caspase-8 and/or -10, forming the DISC. The effector Caspase-3 is activated either directly by the initiator caspases (extrinsic pathway), or through the mitochondrial activation of Caspase-9 within the apoptosome (intrinsic pathway). The decoy receptors DcR1 and DcR2, as well as various anti-apoptotic proteins (in red), are involved in the regulation of the TRAIL signaling.

Fig. 2 Chemical structures of polyphenols that exhibit a synergistic effect with TRAIL.

Fig. 3 Chemical structure of the synthetic flavonoid flavopiridol.

Fig. 4 Schematic model of action of polyphenols on the TRAIL signaling pathway. Polyphenols modulate both the extrinsic and intrinsic pathways, and also tumor suppressors such as P53 and survival proteins such as Akt. The molecular targets vary depending on the structure of the polyphenolic compound and the cell type. This model reports only the main molecular targets of polyphenols.