
P. De Cicco, E. Panza, C. Armogida, G. Ercolano, G. Scognamiglio, G. Botti, G. Cirino, J.L. Wallace, A. Ianaro

1Dept of Pharmacy, University of Naples Federico II, Naples, Italy
2Unit of Pathology, Istituto Nazionale per lo Studio e la cura dei tumori 'Fondazione G. Pascale' IRCCS, Naples, Italy
3Dept of Physiology & Pharmacology, University of Calgary, Calgary, Alberta Canada

Increased cyclooxygenase-2 (COX-2) expression and enhanced prostaglandin E₂ (PGE₂) production are frequently attributed to the inflammation-associated cancers such as lung, colon, bladder, prostate and other cancer types. Hydrogen sulfide releasing non-steroidal anti-inflammatory drug (H₂S-NSAIDs) are an emerging novel class of compounds with significant anti-inflammatory properties (Wallace et al., 2010). They consist of a traditional NSAID to which an H₂S-releasing moiety is covalently attached. We have recently demonstrated that H₂S donors inhibit melanoma cell proliferation (Panza et al., 2014). In the current study, we evaluated the potential beneficial effects of ATB-346 [2-(6-methoxynapthalen-2-yl)-propionic acid 4-thiocarbamoyl-phenyl ester], a H₂S-releasing derivative of Naproxen, in a murine model of melanoma.

Aims & Methods: We utilized cell culture and a mouse melanoma model to evaluate: the effect of ATB-346 on: i) in vitro growth of human melanoma cells; ii) in vivo melanoma development in mice.

Results: Cell culture studies demonstrated that ATB-346 reduced the in vitro proliferation of human melanoma cells and this effect was associated to induction of apoptosis and inhibition of NF-κB activation. Moreover ATB-346 had novel Akt signaling inhibitory properties. Daily oral dosing of ATB-346 (43 μmol/kg) significantly reduced melanoma development in vivo in mice.

Conclusion: ATB-346, a novel H₂S-NSAID, inhibits human melanoma cells proliferation by inhibiting pro-survival pathways associated to NF-κB activation. Oral treatment with ATB-346 inhibits melanoma growth in vivo in mice. Our results suggest that the combination of inhibition of cyclooxygenase and delivery of H₂S operated by ATB-346 may offer a promising alternative to existing therapies for melanoma.

References