COACTION PUBLISHING

Aspirin and its related non-steroidal anti-inflammatory drugs

Aspirin or acetylsalicylic acid has been utilised by physicians for hundreds of years as an analgesic, anti-inflammatory and antipyretic (1). Derived from plant sources, such as the willow tree, it has the ability to induce apoptosis in cancer cells and stimulate angiogenesis (2–4). Earlier research has established that the therapeutic benefit of willow is related to the pro-drug, β-D-salicin, which is metabolised to salicylic acid (SA) in the gastrointestinal system and blood (Fig. 1) (1, 5). Pharmacologically, SA is capable of modulating inflammation via the inhibition of the transcription factor, NF-κB, and subsequently the expression of COX-2 (5). However, aspirin inhibits both COX-1 and -2 irreversibly, thereby inactivating prostanoid cascades for the production of prostaglandins, thromboxanes and prostacyclins, the essential fatty acid signalling molecules (6, 7). Thus, the non-specific mode of action of aspirin suggests the necessity for the development of more specific COX-2 inhibitors. Indeed, our recent research has clearly shown that a number of salicylate-related compounds exhibit modulation of inflammation and are more effective than aspirin (5, 8). For example, 4-hydroxybenzoate zinc was found to specifically inhibit COX-2 *via* the inactivation of the transcription factor NF-κB. Certainly, these were also more effective at inhibiting different cancer cell lines *in vitro* and in primary CLL cells when compared to aspirin (5, 8, 9). Despite a host of pharmacological benefits, aspirin is associated with potential side effects such as peptic ulcers, deafness and dizziness in toxicity, and it is relatively contraindicated in children (10). Therefore, further research into the potential of such aspirin-related compounds is imperative to produce safer and more targeted therapy.

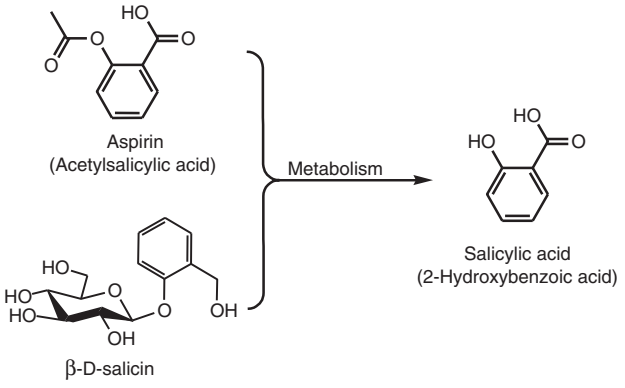

Fig. 1. The structures and metabolisms of salicylate compounds.

Eamon J. Mahdi
Department of Haematology
University Hospital of Wales, Cardiff, UK

References

1. Mahdi JG, Mahdi AJ, Bowen ID. The historical analysis of aspirin discovery, its relation to the willow tree and antiproliferative and anticancer potential. Cell Prolif. 2006; 39: 147–55.
2. Mione M, Zon LI. Cancer and inflammation: an aspirin a day keeps the cancer at bay. Curr Biol. 2012; 22: R522–5.
3. Hossain MA, Kim DH, Jang JY, Kang YJ, Yoon JH, Moon JO, et al. Aspirin induces apoptosis in vitro and inhibits tumor growth of human hepatocellular carcinoma cells in a nude mouse xenograft model. Int J Oncol. 2012; 40: 1298–304.
4. Watson AJM. An overview of apoptosis and the prevention of colorectal cancer. Crit Rev Oncol Hematol. 2006; 57: 107–21.
5. Mahdi JG, Al-Musayeib N, Mahdi E, Pepper C. Pharmacological importance of simple phenolic compounds on inflammation, cell proliferation and apoptosis with a special reference to β-D-salicin and hydroxybenzoic acid. Euro J Inflammation. 2013; 11: 327–36.
6. Bala M, Chin CN, Logan AT, Amin T, Marnett LJ, Boutaud O, et al. Acetylation of prostaglandin H2 synthases by aspirin is inhibited by redox cycling of the peroxidase. Biochem Pharma col. 2008; 75: 1472–81.
7. Vane JR, Botting RM. The mechanism of action of aspirin. Thromb Res. 2003; 110: 255–8.
8. Pepper CJ, Mahdi JG, Buggins AGS, Hewamana S, Walsby E, Mahdi EJ, et al. Two novel aspirin analogs show selective cytotoxicity in primary chronic lymphocytic leukemia cells mediated through the dual inhibition of Rel A and COX-2. Cell Prolif. 2011; 44: 380–90.
9. Mahdi JG, Alkarrawi MA, Mahdi AJ, Bowen ID, Humam D. Calcium salicylate-mediated apoptosis in human HT-1080 fibrosarcoma cells. Cell Prolif. 2006; 39: 249–60.
10. Stanton B. Fifty years ago in the journal of pediatrics editor's column: the story of aspirin. J Pediatr. 2007; 150: 246.

 Citation: Libyan J Med 2013, **8:** 21569 - http://dx.doi.org/10.3402/ljm.v8i0.21569