132P INHIBITION OF CYCLO-OXYGENASE-2 EXPRESSION BY RESVERATROL DERIVATIVES FROM PEANUTS

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A wide variety of plant phenolic substances possess anti-inflammatory and anti-carcinogenic activities, and for many of these substances inhibition of cyclo-oxygenase-2 (COX-2) appears to be an important mechanism of action (Surh *et al.,* 2001). The stilbene resveratrol (*trans*-3, 4', 5-trihydroxystilbene) is an inhibitor of the transcriptional activation of COX-2 (Subbaramaiah *et al.,* 1999). Peanuts have been shown to produce several stilbenes structurally related to resveratrol (Aguamah *et al.,* 1981). Hence it is of interest to evaluate these substances as inhibitors of COX-2 expression.

Resveratrol derivatives were induced in peanuts by fungal infection and the compounds were isolated and purified by thin layer chromatography. Structures of the compounds were confirmed by mass spectrometry. Effects on COX-2 protein expression were examined by western blot and COX-2 mRNA expression was measured using a Quantikine kit (R&D Systems, UK) in lipopolysaccharide (LPS) stimulated murine macrophages (cell line J774). Since the usefulness of resveratrol as an anti-inflammatory agent may be reduced due to its anti-proliferative activity against normal peripheral normal blood cells (Ferry-Dumazet *et al.,* 2002), we also examined the anti-proliferative effects of the resveratrol derivatives from peanuts.

Three compounds structurally related to resveratrol were isolated from peanuts and designated BS1/1, BS 1/2 and BS2. Resveratrol caused 43% cell death in LPS-stimulated J774 cells at doses of 50 μM and 80% cell death at a dose of 100 μM whereas BS2 caused <20% cytotoxicity at doses up to 100 μM. Non-cytotoxic concentrations of resveratrol (up to 30 μM) did not cause a statistically significant suppression of LPS-induced COX-2 protein expression in J774 cells, whereas COX-2 expression was reduced to 71.3 ± 9.9% of control values by 10 μM BS2 and to 58.6% ± 3.2 % by 30μM BS2 (means ± SE of 3 independent experiments). BS2 also caused greater suppression of COX-2 mRNA than resveratrol. Thus, whereas resveratrol suppressed COX-2 mRNA levels by 25% and 16% at 10μM and 30μM respectively, BS2 suppressed COX-2 mRNA levels by 50% and 58% at 10μM and 30μM respectively.

These data indicate that BS2 is a superior inhibitor of COX-2 expression in J774 macrophages than resveratrol and BS2 is less cytotoxic than resveratrol to these cells. Further studies will establish if BS2 may prove useful as an anti-inflammatory agent.

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