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Mechanisms involved in the anti-inflammatory effect of a standardized willow bark extract.

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Abstract
A standardized willow bark extract (STW 33-I) has been examined to clarify its possible mechanism of action as an anti-inflammatory agent. Various facets have been investigated in two inflammation models: the 6-day air pouch model in rats, representing the acute state and the adjuvant induced arthritis representing the chronic one. Parameters included leukocytic infiltration, levels of cytokines and prostanoids in blood, and effects on cyclo-oxygenase (COX)-1 and/or COX-2 enzymes as well as effects involving free radical production. The effect of the extract was compared at two dose levels with comparable anti-inflammatory doses of acetylsalicylic acid (CAS 50-78-2, ASA) as a non-selective COX inhibitor, and celecoxib (CAS 169590-42-5) as a selective COX-2 inhibitor. On a mg/kg basis, the extract was at least as effective as ASA in reducing inflammatory exudates and in inhibiting leukocytic infiltration as well as in preventing the rise in cytokines, and was more effective than ASA in suppressing leukotrienes, but equally effective in suppressing prostaglandins. On COX-2, STW 33-I was more effective than ASA. The present findings show that STW 33-I significantly raises GSH (reduced glutathione) levels, an effect which helps to limit lipid peroxidation. The extract was more potent than either ASA or celecoxib. Higher doses of the extract also reduced malondialdehyde levels and raised shows definite superiority to either ASA or celecoxib in protecting the body against oxidative stress. It is therefore evident that STW 33-I is at least as active as ASA on all the parameters of inflammatory mediators measured, when both are given on a similar mg/kg dose. Considering, however, that the extract contains only 24% salicin (molecular weight 286.2), while ASA has a molecular weight of 180.3, it follows that on a molar basis of salicin vs salicylate, the extract contains less than a sixth of the amount of salicin as the amount of salicylate in ASA. Thus it appears that STW 33-I with its lower “salicin” content than an equivalent dose of ASA, is at least as active as ASA on the measured parameters, a fact that leads one to speculate that other constituents of the extract contribute to its overall activity. The presence of polyphenols in STW 33-I probably plays a significant role in enhancing its free radical scavenging properties. The fact that STW 33-I was superior to ASA in this respect would suggest that the extract may have a better anti-inflammatory effect than ASA on a weight to weight basis, with possibly less side effects.