Influence of anti-inflammatory flavonoids on degranulation and arachidonic acid release in rat neutrophils

We assessed the effects of 24 flavonoid derivatives, reported as anti-inflammatory, on lysosomal enzyme secretion and arachidonic acid release in rat neutrophils. Amentoflavone, quercetagetin-7-O-glucoside, apigenin, fisetin, kaempferol, luteolin and quercetin were the most potent inhibitors of beta-glucuronidase and lysozyme release. The first compound was also able to inhibit basal release. These flavonoids besides chrysin and to a reduced extent, naringenin, significantly inhibited arachidonic acid release from membranes. A correlation between degranulation and arachidonic acid release was found for this series of compounds. Structure-activity relationships and implications for the anti-inflammatory effects of these flavonoids were discussed. Tordera M, Ferrandiz ML, Alcaraz MJ. Z Naturforsch [C] 1994 Mar;49(3-4):235-240.

Flavonoids, leucocyte migration and eicosanoids

Quercetin reduced the concentration of prostaglandin E2 (PGE2) and leukotriene B4 (LTB4) in the pleural exudate induced in rats by 1% carrageenan given intrapleurally. Leucocyte migration in the exudate was also reduced by the flavonoid. Inhibition of eicosanoids and leucocytes in the exudate was dose-related. Quercetin also reduced LTB4 synthesis in cells stimulated with ionophore A23187, either ex-vivo or in-vitro. A similar, though less active, mode of action was found with quercitrin, while apigenin and luteolin reduced leucocyte accumulation and PGE2 formation, but not LTB4-formation. Mascolo N, Pinto A, Capasso F. J Pharm Pharmacol 1988 Apr;40(4):293-295.

Effect of quercetin on chemiluminescence of human platelets induced by arachidonic acid

Arachidonic acid (AA)-induced platelet chemiluminescence (CL) was measured with a lumiphotometer. Quercetin remarkably inhibited the CL, the IC50 of quercetin was 3 mumol.L-1. When quercetin plus aspirin, which inhibits only cyclooxygenase, was added, the inhibitory rate of platelet-CL obviously increased (P < 0.01). On the other hand, the quercetin had a scavenging effect on superoxide anion radical using alkaline sodium dithionite solution generation. The IC50 was 20.9 mumol.L-1. In addition, superoxide dismutase of 0.1 mg.ml-1 inhibited the platelet-CL by 97.8%, while mannitol, a hydroxyl radical scavenger, only by 43.3% at a concentration of 80 mg.ml-1. These results suggest that the mechanism of the inhibiting AA-induced platelet-CL by quercetin was associated with scavenging the superoxide anion radical directly and with inhibiting the cyclooxygenase. Gu ZL, Xie ML, Qian ZN. Zhongguo Yao Li Xue Bao 1993 May;14(3):263-5.

Nitric oxide scavenging by curcuminoids

Because curcumin, a compound with anti-inflammatory and anticancer activity, inhibits induction of nitric oxide synthase in activated macrophages and has been shown to be a potent scavenger of free radicals we have investigated whether it can scavenge nitric oxide directly. Curcumin reduced the amount of nitrite formed by the reaction between oxygen and nitric oxide generated from sodium nitroprusside. Other related compounds, e.g. demethoxycurcumin, bisdemethoxycurcumin and diacetylcurcumin were as active as curcumin, indicating that the methoxy and the phenolic groups are not essential for the scavenging activity. The results indicate curcumin to be a scavenger of nitric oxide. Because this compound is implicated in inflammation and cancer, the therapeutic properties of curcumin against these conditions might be at least partly explained by its free-radical scavenging properties, including those toward nitric oxide. Sreejayan; Rao MN. J Pharm Pharmacol 1997 Jan;49(1):105-7.

Inhibition of neutrophil response by curcumin

Blood neutrophils, when exposed to appropriate stimuli, aggregate, degranulate and generate superoxide anion. Curcumin, a non-steroidal antiinflammatory agent, modulated these functions, depending upon the kind of stimulus used. It inhibited monkey neutrophil aggregation induced by chemotactic peptide fmlp and zymosan activated plasma (ZAP) but did not affect that induced by serum treated zymosan (STZ) and arachidonic acid (AA). Generation of O2- radical was inhibited by curcumin,
when cells were stimulated by AA, STZ and fmlp. Curcumin inhibited the release of myeloperoxidase, an azurophilic granule marker enzyme. Release of lysozyme was less susceptible to inhibition by curcumin. The results suggest that curcumin interferes with neutrophil responses to various physiological stimuli and a part of its antiinflammatory action is mediated via inhibition of neutrophil function. Inhibition of neutrophil function by curcumin appears to be mediated via calcium dependent mechanisms. Srivastava R. Agents Actions 1989 Nov;28(3-4):298-303.

Modification of certain inflammation-induced biochemical changes

Effect of Curcumin on some biochemical changes produced during subacute inflammation in rat has been studied and compared with ibuprofen. Curcumin was found to be more potent than ibuprofen as a stabilizer of lysosomal membrane and as an uncoupler of oxidative phosphorylation. At higher doses, curcumin was shown to act by stimulation of the adrenals resulting in the release of endogenous corticoids. Curcumin inhibited the synthesis of prostaglandins but was weaker than ibuprofen, in this respect. Srivastava R; Srimal RC. Indian J Med Res 1985 Feb;81:215-23.

Ginger (Zingiber officinale) in rheumatism and musculoskeletal disorder

One of the features of inflammation is increased oxygenation of arachidonic acid which is metabolized by two enzymic pathways—the cyclooxygenase (CO) and the 5-lipoxygenase (5-LO)—leading to the production of prostaglandins and leukotrienes respectively. Amongst the CO products, PGE2 and amongst the 5-LO products, LTB4 are considered important mediators of inflammation. More than 200 potential drugs ranging from non-steroidal anti-inflammatory drugs, corticosteroids, gold salts, disease modifying anti-rheumatic drugs, methotrexate, cyclosporine are being tested. None of the drugs has been found safe; all are known to produce from mild to serious side-effects. Ginger is described in Ayurvedian Tibb systems of medicine to be useful in inflammation and rheumatism. In all 56 patients (28 with rheumatoid arthritis, 18 with osteoarthritis and 10 with muscular discomfort) used powdered ginger against their afflictions. Amongst the arthritis patients more than three-quarters experienced, to varying degrees relief in pain and swelling. All the patients with muscular discomfort experienced relief in pain. None of the patients reported adverse effects during the period of ginger consumption which ranged from 3 months to 2.5 years. It is suggested that at least one of the mechanisms by which ginger shows its ameliorative effects could be related to inhibition of prostaglandin and leukotriene biosynthesis, i.e. it works as a dual inhibitor of eicosanoid biosynthesis. Srivastava KC, Mustafa T. Med Hypotheses 1992 Dec;39(4):342-8.

Effect of bromelain on kaolin-induced inflammation in rats

The effects of stem bromelain on the plasma kallikrein system, bradykinin levels and plasma exudation at the inflammatory site were examined in rats with a kaolin-induced inflammation of an air pouch. Bromelain (5, 7.5 mg/kg) caused a dose-dependent decrease of bradykinin levels at the inflammatory site and a parallel decrease of the prekallikrein levels in sera. Plasma exudation was also reduced dose dependently. Bradykinin-degrading activity in sera was elevated after treatment with bromelain, although it was unchanged in the pouch fluid. These data indicate that bromelain inhibits plasma exudation through inhibiting the generation of bradykinin at the inflammatory site via depletion of the plasma kallikrein system. Kumakura S, Yamashita M, Tsuruji S. Eur J Pharmacol 1988 Jun 10;150(3):295-301.

Isolation of a fibrinolysis enzyme activator from commercial bromelain

A fibrinolysis enzyme activator was isolated from commercial bromelain. This enzyme preparation is used medicinally. A by-product of bromelain production, the acetone still residue, was used as a starting material to develop an isolation scheme which began with reversed phase chromatography, was followed by ion exchange chromatography, and ended with ultrafiltration. It had polarity and ion exchange properties similar to those of a neutral amino acid. The active substance has no intrinsic fibrinolytic activity but appears to enhance the activity of one of the fibrinolytic enzymes. The presence of the fibrinolysis enzyme activator in commercial bromelain may explain some of the physiological and clinical effects observed following the oral administration of the enzyme preparation. Ako H, Cheung AH, Matsuura PK. Arch Int Pharmacodyn Ther 1981 Nov;254(1):157-167.

Possible involvement of eicosanoids in the pharmacological action of bromelain

Bromelain, a proteolytic enzyme extracted from pineapple plants, was investigated for its capacity to interfere with arachidonic acid metabolism, since prostaglandins and other eicosanoids are well-known to be involved in the pathogenesis of inflammatory diseases. Bromelain was tested for its ability to interfere with eicosanoids generation in vivo in two experimentally-induced inflammatory reactions in the rat. Also antiplatelet aggregation activity of bromelain was studied in ex vivo rat platelets. The
results seem to indicate an interference of bromelain with arachidonic acid cascade, which, however, deserves further investigation to be better assessed. Vellini M, Desideri D, Milanese A, Omini C, Daffonchio L, Hernandez A, Brunelli G. Arzneimittelforschung 1986;36(1):110-112.

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