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LETTERS TO THE EDITOR

The relation between clinical anti-inflammatory activity and the displacement of L-tryptophan and a dipeptide from human serum *in vitro*

It has been reported (McArthur, Dawkins & Smith, 1971) that salicylate, phenylbutazone, indomethacin, prednisolone, chloroquine and gold salts share a common action in displacing L-tryptophan, and several dipeptides, particularly L-phenylalanyl-L-phenylalanine, from their binding sites to bovine albumin and to human serum proteins *in vitro*. We have observed that this action is shared by two other potent anti-inflammatory substances, mefenamic and flufenamic acids, but not by other drugs that resemble the commonly used antirheumatic remedies in being administered over long periods of time.

We have found that phenobarbitone, penicillin V, ampicillin, cloxacillin, ascorbic acid or paracetamol, when studied in a range of concentrations at least twice those encountered in the circulation during therapy, did not displace either L-tryptophan or L-phenylalanyl-L-phenylalanine, from human serum when this was investigated by the techniques described by McArthur, Dawkins & Smith (1971). The failure of paracetamol to show this effect is of particular interest since the drug does not possess clinical anti-inflammatory activity (Fremont-Smith & Bayles, 1965; Boardman & Hart, 1967) but is frequently administered as an analgesic in rheumatoid arthritis.

It has been proposed (McArthur, Dawkins & others, 1971) that antirheumatic drugs act by displacing certain peptides from their binding sites to circulating proteins and that the free fractions of these peptides protect susceptible tissues against the effect of chronic inflammatory reactions. In patients with rheumatoid arthritis and and similar disorders the peptides are bound to an abnormal extent to the serum proteins and the drugs act by restoring the equilibrium to normal. The behaviour of L-tryptophan and L-phenylalanyl-L-phenylalanine mimics that of the hypothetical protective peptides. The present report provides additional evidence in favour of this hypothesis since it shows that a displacing action is common to antirheumatic drugs but is not given by other drugs that bind to human serum proteins and are administered in divided doses over similar periods of time.

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