added to the medium in order to inhibit neuronal uptake only. As our study has shown cocaine to be a direct agonist at α-adrenoceptors and also to potentiate responses to acetylcholine by a postjunctional mechanism in the rat anococcygeus the use of cocaine in such studies with this tissue would seem inadvisable.

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Leukotriene B_4 in synovial fluid

E. M. DAVIDSON, S. A. RAE, M. J. H. SMITH, *Department of Chemical Pathology, King's College Hospital Medical School, Denmark Hill, London SE5 8RX.*

Leukotriene B_4 (LTB_4) is generated enzymatically from arachidonic acid by human leucocytes in vitro (Smith 1981). Recent work suggests that LTB_4 is a putative mediator of inflammation in vivo since it both increases leucocyte infiltration and, in the presence of vasodilatory prostaglandins, causes increased vascular permeability (Smith 1982). A second criterion is whether it is present at sites of inflammatory reactions and here the only quantitative evidence is that of Klickstein et al (1980). The LTB_4 was separated from 2 to 3 ml samples of synovial fluid by solvent extraction, column chromatography and reverse phase high performance liquid chromatography (h.p.l.c.); recognized by a comparison of retention times with standard material and measured by ultraviolet absorption techniques. In synovial fluid from eighteen patients with rheumatoid arthritis the reported values (mean ± s.e.m.) were 141 ± 34 ng ml^{-1} (Klickstein et al 1980).

There are objections to relying on physicochemical methods only for the measurement of LTB_4. There are a number of isomers of the leukotriene which are not only difficult to separate completely from the authentic material but also are either much less active or devoid of the relevant biological activities. Also, more recent work (Hansson et al 1981) has shown that LTB_4 is metabolized by human leucocytes to more polar hydroxy and carboxy compounds which are far less potent as leucotactic agents.

We have therefore repeated the work measuring the LTB_4 in the final h.p.l.c. fraction both by ultraviolet absorption and a sensitive and specific bioassay method (Cunningham et al 1980). In synovial fluid specimens, ranging in volume from 10 to 24 ml, from 12 patients with rheumatoid arthritis we could find no LTB_4 using the ultraviolet absorption method. In our hands the lower limit of detection with this technique is 50 ng per whole specimen i.e. approximately 2·5 ng ml^{-1}. The more sensitive bioassay procedure yielded a mean value of 0·34 ± 0·14 ng ml^{-1} of LTB_4.

It seems likely that the reason only traces of LTB_4 are present in synovial fluid is that the leukotriene is rapidly metabolized by the inflammatory cells present in the exudate. In other experiments human peripheral PMNs, human synovial fluid cells or rat peritoneal PMNs metabolized radiolabelled LTB_4 to more polar compounds and caused a loss of biological activity from unlabelled LTB_4 within minutes.

If LTB_4 is generated by leucocytes which enter and accumulate in inflammatory exudates, such as synovial fluid in patients with rheumatoid arthritis, then it will not persist as such but will be removed by metabolism. In this respect it resembles other inflammatory mediators including histamine, bradykinin and the complement-derived cytotaxin, C5a.

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