

transferred alpha particle was treated as a single particle and no account was taken of its internal structure; this is called the cluster approximation. This analysis gave a ratio of spectroscopic amplitudes for the two reactions of  $S(0.727 \text{ MeV } 2^+)/S(\text{g.s.}) = 0.64 \pm 0.13$ . Only the ratio could be obtained as the cluster approximation introduces unknown uncertainties in the absolute value of the calculated cross section.

The nucleus  $^{212}\text{Po}$  also decays radioactively, and the analysis of the half-lives for alpha emission gives comparable spectroscopic information. Several different potentials were used to calculate the barrier penetration probabilities, and although the absolute values differed considerably they gave a consistent value of the ratio of spectroscopic amplitudes for the same two processes of  $0.61 \pm 0.24$ .

Although they are still subject to considerable uncertainties, these two values of the ratio of the spectroscopic amplitudes from alpha transfer and alpha decay are certainly consistent, and provide good overall confirmation of the two theories used to obtain them. In particular, the agreement supports the interpretation of the alpha-transfer reaction as a single one-step process that can be treated by the cluster approximation. □

## Aspirin's target in anti-inflammatory action

from R. J. Flower

THE multi-enzyme complex which synthesises prostaglandins (PGs) ("PG synthetase", "fatty acid cyclo-oxygenase") is bound firmly to the "microsomal" membranes of cells, a fact which has naturally proved very frustrating both to enzymologists and pharmacologists who would like to study pure preparations of this unique dioxygenase. A definite advance was made last year when three Japanese workers (Miyamoto, Yamamoto and Hayaishi, *Proc. natn. Acad. Sci. U.S.A.*, **71**, 3645; 1974) succeeded in solubilising the enzyme and resolving it into separate "oxygenase" (catalysing the transformation of endoperoxide intermediates) and "isomerase" (catalysing the transformation of endoperoxides to  $\text{PGE}_2$ ) components.

Now another step forward has been made by a group at the Washington University School of Medicine who have further characterised this enzyme and reported that the catalytic unit is a protein of molecular weight 85,000. To accomplish this, Roth, Stanford and Majerus (*Proc. natn. Acad. Sci.*

*U.S.A.*, **72**, 3073; 1975) used an ingenious adaptation of the finding that aspirin (acetylsalicylic acid) and its congeners inhibit PG synthetase (Vane, *Nature new Biol.*, **231**, 232; 1971; Smith and Willis, *ibid.*, 235; Ferreira *et al.*, *ibid.*, 237). Although the detailed mechanism of aspirin inhibition of the enzyme was unknown, the Washington University group used as a working hypothesis the known ability of the drug to acetylate proteins. After synthesising aspirin with a tritium label on the labile acetyl group, they incubated the drug with crude PG synthetase preparations derived from human platelets, and sheep and ox seminal vesicles. After incubation the enzyme was solubilised in sodium dodecyl sulphate and subjected to polyacrylamide gel electrophoresis. The bulk of the radioactivity in each of the tissue digests was found to migrate as a protein of molecular weight 85,000. No incorporation of radioactivity was found when the aspirin was labelled in the aromatic ring. Evidence that PG synthetase (and not other microsomal proteins) was specifically acetylated came from the good correlation between the low concentrations of aspirin required for acetylation and enzyme inhibition and the rapid time taken for both reactions. The authors' claim was further substantiated when it was found that protein acetylation was blocked by the fatty acid substrates of the enzyme (arachidonic and dihomogamma-linolenic acid) as well as by another potent PG synthetase inhibitor, indomethacin. Aspirin is thought to block the initial dioxygenase reaction and it would thus seem that the catalytic unit (or subunit) of the dioxygenase enzyme has a molecular weight of about 85,000, and that acetylation of the active site is the mechanism of aspirin inhibition—although as the authors are careful to point out, aspirin binding at a distant "allosteric" site could also prevent arachidonic acid binding at the true catalytic site.

How will this finding increase our understanding of PG synthetase? As well as contributing an important piece of information about the enzyme it suggests many other fascinating experiments: the acetylated protein could itself be digested and the labelled amino acid identified. This would be helpful in building up a picture of the enzyme's catalytic centre, and ultimately aiding the design of novel anti-inflammatory agents. Pharmacologists will undoubtedly want to know whether any other "aspirin-like" drugs act in an analogous fashion, and perhaps the specific labelling of the enzyme with aspirin will help solve the vexed question—in which membrane fraction is PG synthetase actually located?

Because of the great diversity of

structures amongst the aspirin-like drugs (see Flower, *Pharmac. Rev.*, **26**, 33; 1974) it would seem unlikely that they could all work by way of the mechanism which Roth and his colleagues propose. One obvious exception is salicylic acid itself which lacks acetylating capacity, and which *in vivo* (though not *in vitro*) is equally effective in inhibiting prostaglandin synthesis (Hamberg, *Biochem. biophys. Res. Commun.*, **49**, 720; 1972), although there are differences in its latency of action. Coming as it does, however, in the midst of so many new developments in the PG area, this finding by the Washington University group could prove to be a timely stimulus to further research on the enzyme complex itself.

## Christmas trees

from Peter D. Moore

As yuletide approaches, a botanist's mind inevitably turns to thoughts of the gymnosperms and their symbolic significance to man. From early pre-historic times certain members of this group, including that Christmas favourite, the spruce *Picea abies*, seem to have had their fortunes closely linked with the activity of man. For example, Markgraf (*Nature*, **228**, 249; 1970) has suggested, on the evidence of numerous radiocarbon dated pollen diagrams, that the spread of spruce in Switzerland occurred at different times in different areas, but was frequently accompanied by evidence of human disturbance of the forest, such as weed and cereal pollen. She felt that prior to disturbance the spruce was unable to invade the stable forests of *Abies alba*, *Pinus cembra* and the mixed deciduous forests.

Moe (*Bot. Notiser*, **123**, 61; 1970) has also shown that the spread of spruce in Fennoscandia was slow. It arrived in eastern Finland around 3,000 BC, but had still not penetrated far into Sweden by 500 BC. But Tallantire (*Nature*, **236**, 64; 1972; *Norweg. J. Bot.*, **19**, 1; 1972) does not regard man as the primary cause of its western migration in Fennoscandia. He believes that the distribution of spruce is essentially climatically determined, the critical factors being high summer and low winter temperatures. The spread of spruce, he claims, was a stepwise process, each advance corresponding to a period of suitable climate. He is prepared to admit that once established in an area its subsequent spread and population expansion in the locality could be assisted by human clearance of virgin forest. Thus, from micro-climatically and edaphically favourable nuclei, spruce could attain a wide-