carbenoxolone, namely enoxolone, and an analogue, cicloxolone were also included. To enable comparison with other workers we used both crystalline bovine (BSA) and human (HSA) serum albumin solutions (Jun, *et al.*, 1972; Mason & McQueen, 1974).

Initially we found a difference in binding potential between HSA and BSA. With BSA only one class of binding site was seen for the probe whereas two classes were seen with HSA. Moreover, carbenoxolone and phenylbutazone were both bound at the same class of site to BSA but at different classes of sites to HSA. For the remainder of the study HSA was used.

The binding characteristics of HSA of the drugs used formed three distinct groups;

Group 1 consisted of drugs with strong binding affinities to the class I site and included the three triterpenoids of which carbenoxolone was the most strongly bound.

Group 2 also included strongly bound drugs, but these were binding at the class II sites. Of these flufenamic acid was the most strongly bound, followed by phenylbutazone warfarin and tolbutamide, respectively.

Group 3 comprised the weakly bound drugs binding at both class I and II sites. Of these aspirin was the most strongly bound, followed by phenytoin, prednisolone, and imipramine, respectively.

Thus it is probable that interaction, due to displacement from binding sites, between drugs of groups 1 and 2 is unlikely. The weak binding affinities, to both classes of binding sites, of drugs in group 3 indicate that they may be susceptible to displacement by the drugs in both groups 1 and 2. Within each of the three groups of drugs, displacement may be expected of the drugs with the lowest binding affinities by those with a higher affinity within the same group.

Further studies are in progress designed to examine the specificity of carbenoxolone binding and to examine the indicated possible *in vivo* interactions.

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Tryptophan metabolism by the isolated perfused rat liver

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Increased rat liver tryptophan pyrrolase activity following hydrocortisone (5 mg/kg) injection decreases tryptophan concentrations in liver and brain and is accompanied by decreased brain 5-hydroxytryptamine synthesis (Green, Woods, Knott & Curzon, 1975). In this and other experiments investigating the effect of drugs on pyrrolase activity the enzyme has been measured *in vitro* following prior treatment of the animals *in vivo*. In an attempt to observe whether these *in vitro* observations have any relevance to the activity of the enzyme *in vivo*, we have investigated the effect of certain drugs on the activity of the enzyme in the isolated perfused rat liver. The concentration of kynurenine in the medium has been used as an index of enzyme activity. A small lobe of liver was also removed at the beginning and end of the perfusion and enzyme activity measured *in vitro*.

Rat livers were perfused by the method of Hems, Ross, Berry & Krebs (1966) with a semi-synthetic medium (Woods, Eggleston & Krebs, 1970); *in vitro* enzyme activity was measured as described by Curzon & Green (1969).

Perfusion of the basal medium without the addition of tryptophan resulted in a small amount of kynurenine appearing in the medium at the end of a 60 min perfusion (2.0 ± 0.1 μg kynurenine/g liver (wet weight)). The concentration of tryptophan in the basal medium was 0.84 ± 0.15 μg

tryptophan/ml and rose linearly during the perfusion to reach a concentration of 4.6 ± 0.2 μg/ml at 60 minutes.

At the end of a 60 min perfusion and when 0.1 mM tryptophan was perfused the mean concentration of kynurenine was 6.64 μg/g liver (wet weight) and when 1.0 mM tryptophan was in the medium the final mean concentration of kynurenine in the medium was 31.1 μg/g liver. Pretreatment of the rats with hydrocortisone (5 mg/kg) 3 h before the start of the perfusion resulted in a threefold increase of pyrrolase activity as measured *in vitro* and increased the concentration of kynurenine in the medium at the end of the 60 min perfusion to 14.45 ± 2.82 μg/g when 0.1 mM tryptophan was perfused and 145 ± 13.3 μg/g when 1.0 mM tryptophan was perfused.

When allopurinol (20 mg/kg) was injected with the hydrocortisone (5 mg/kg) and also added to the 0.1 mM tryptophan medium (4 mg allopurinol /100 ml medium) it totally inhibited the hydrocortisone-induced rise in kynurenine concentration in the medium. The rise in pyrrolase activity (measured *in vitro*) produced by hydrocortisone injection was totally inhibited by the simultaneous injection of allopurinol (20 mg/kg).

The disappearance of tryptophan from the medium did not always reflect the activity of pyrrolase measured either *in vitro* or by the appearance of kynurenine in the medium. This is in agreement with the observations of Kim & Miller (1969). Unlike these authors, however, we find that hydrocortisone pretreatment increases subsequent kynurenine production by the isolated perfused rat liver. Furthermore, we observed that changes in pyrrolase activity measured *in vitro* were of the same order as the changes in kynurenine concentration in the perfusion medium.

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Role of platelet aggregation in bronchoconstriction in guinea-pigs

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Non-steroidal anti-inflammatory drugs (NSAID) prevent bronchoconstriction due to bradykinin (B) (Collier & Shorley, 1960), ATP and ADP (Collier, James & Schneider, 1966), arachidonic acid (AA) (Berry, 1966) and slow reacting substances (Berry & Collier, 1964; Vargaftig, Miranda & Lacoume, 1969). Since some of these agents cause platelet aggregation which is inhibited by NSAID, we tested the hypothesis that bronchoconstriction by B, by AA and by ADP or ATP are mediated by platelet release reaction occurring when clumps are trapped in lung vessels. This possibility was investigated in pentobarbitone anaesthetized guinea-pigs prepared for recording of bronchial resistance to inflation (Konzett-Rössler method) and of carotid blood pressure. Acetylcholine (5-20 μg kg^{-1} i.v.) was injected 3-5 times, until constant responses were obtained, after which other drugs were given. Platelet counts were made on arterial blood, and aggregation was studied by standard techniques (Born & Cross, 1963; Vargaftig, Tranier & Chignard, 1974) on guinea-pig platelet rich plasma obtained from citrated blood. Anti-platelet plasma (APP) was prepared by injecting thrice washed broken guinea-pig platelets in complete Freunds adjuvant into both fore paws of a rabbit. Two further s.c. injections were made at weekly intervals, blood was collected in citrate on the 21st day. APP lysed guinea-pig platelets placed on the aggregometer, which was inhibited by Na_2EDTA (2.5 mM) but unaffected by indomethacin (0.5 mM). Lyophilized APP was reconstituted to its initial volume with 0.9% NaCl (w/v) and injected slowly (1 h) i.v. into the guinea-pig (1 ml kg^{-1}).

Circulating platelets decreased 62 ± 4.8%