for the longer experiments were reduced from 0·4 g to 0·1 g in an attempt to reduce the amount of calcium and phosphorus being withdrawn from the solution. The results of these experiments using solutions containing both calcium-45 and phosphorus-32 revealed that simultaneous deposition of calcium and phosphorus into aortic tissue increases for at least 123 h in the case of tissue II and at least 200 h for the other two specimens (Fig. 1), whereas the incorporation of either calcium or phosphorus alone showed little increase after 24 h. Because the uptake of either calcium or phosphorus alone shows no significant increase after 24 h in any of the specimens (Fig. 1), it can therefore be assumed that subsequent calcium and phosphorus uptake is chiefly, if not entirely, caused by calcification. Considerably more calcification took place in the experiments involving tissues I and III (Fig. 1). This was probably because of the time and weight changes previously described.

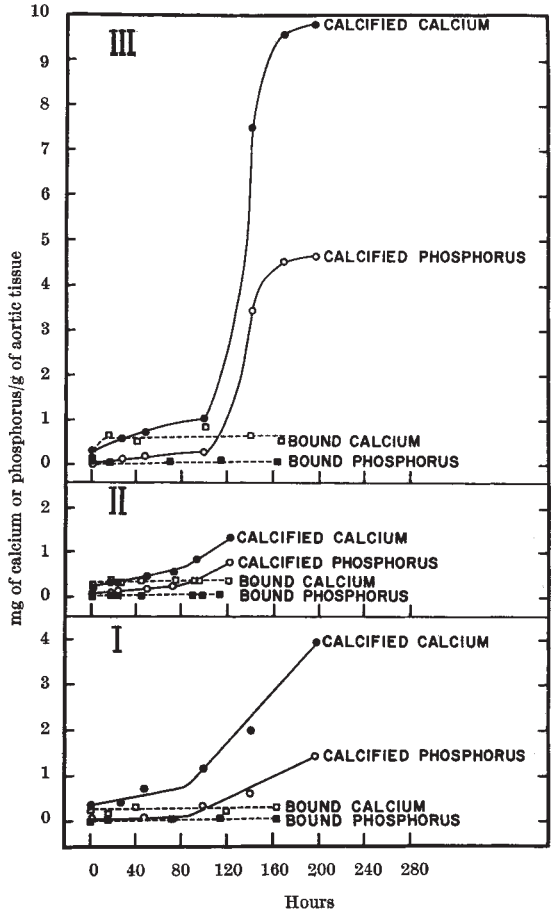

Fig. 1. The uptake of calcium (●) and phosphorus (○) during calcification is represented by the curves marked "calcified calcium" and "calcified phosphorus". The incorporation of calcium in the absence of phosphorus (□) and phosphorus in the absence of calcium (■) is represented by the curves marked "bound calcium" and "bound phosphorus". I, 26 yr old male; II, 37 yr old male; III, 56 yr old female.

A comparison of the rates of uptake of calcium-45 and phosphorus-32 during *in vitro* calcification of the three tissue samples as shown in Fig. 1 reveals some interesting similarities. The graphs for each tissue (Fig. 1) show a lag period followed by an inflexion point between 80 and 100 h and a subsequent increase in the slope of the curve. The patterns during the lag period are very similar and for tissues I and III are nearly superimposable up to the inflexion point. Apparently the weight difference between tissues I and II had no effect on the experiment until after the time of the inflexion point. The significance of the lag period described here is currently being investigated.

Aortic tissue samples from tissues I and III placed in calcifying solution for 200 h were subjected to X-ray diffraction procedures. The results showed a hydroxyapatite pattern, indicating that hydroxyapatite was formed during the calcification study. It is interesting that hydroxyapatite has also been found during calcification of aortic tissue *in vivo*[7] as well as in *in vitro* calcification studies with animal aortic tissues[4]. A Von Kossa stain done on the *in vitro* calcified aortic tissues was positive within the media as early as 72 h when cell nuclei were distinctly identifiable in haematoxylin and eosin.

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Alteration by Pretreatment with Iproniazid and an Inactive Mescaline Analogue of a Behaviour Change induced by Mescaline

THERE have been several conflicting reports on the interaction of mescaline with monoamine oxidase inhibitors. Friedhoff and Goldstein[1], who gave 100 mg/kg iproniazid to rats, 24 h and 3 h before mescaline, found that this pretreatment had no effect on the gross behavioural changes induced by mescaline at 10, 25 and 100 mg/kg. The iproniazid pretreatment itself had produced a slight behavioural excitation at the time of administration of mescaline, and urine estimations of labelled mescaline showed that levels of the unmetabolized amine were considerably increased. *In vitro* experiments suggest that monoamine oxidase does not affect the metabolism of mescaline. Diamine oxidase (histamine oxidase) and a specific mescaline oxidase (found in rabbit liver), however, are probably involved in the oxidation. Iproniazid is not a specific monoamine oxidase inhibitor and is capable of inhibiting both histamine and mescaline oxidase, which would explain the increase in unmetabolized mescaline in urine. Goldwurm and Gualandri (personal communica-

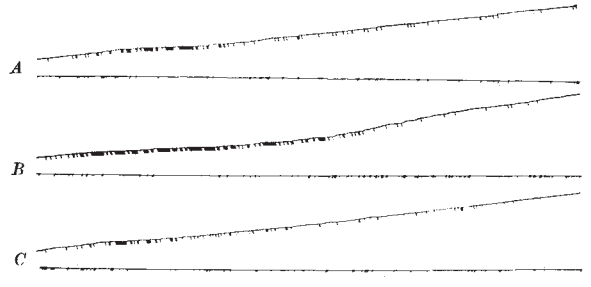

Fig. 1. Effects of iproniazid pretreatment on the mescaline response. *A* and *C*, 17·5 mg/kg mescaline; *B*, 17·5 mg/kg mescaline pretreated with 50 mg/kg iproniazid.

tion) found that pretreatment with iproniazid abolished the inhibitory action of mescaline on shuttle box avoidance in the rat. Steiner and Sulman[2] reported that iproniazid given before mescaline in the rabbit induced an anxiety reaction together with EEG changes.

We have examined the effect on rats of pretreatment with iproniazid. The subjects were three experimentally naive male hooded rats which were trained on a continuous discriminated avoidance schedule in a Skinner box until a stable level of performance was achieved. On this schedule an animal receives a shock of 0·5 sec duration every 10 sec unless it makes a bar press which postpones the shock for 30 sec. During the last 10 sec of this response-shock interval a discriminative stimulus light is turned on inside the experimental chamber. The stimulus light remains on until the animal makes a response which initiates a new cycle.

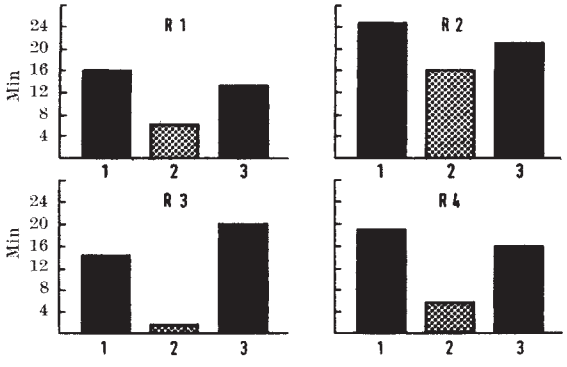

Fig. 2. Duration of inhibitory period for four experimental animals subjected to the three drug conditions. 1 and 3, 12·5 mg/kg mescaline; 2, 12·5 mg/kg mescaline pretreated with 25 mg/kg 2,4,5-trimethoxyphenylethylamine.

Throughout the experiment, each subject was tested at the same time every day for 2·75 h. The experimental session can be sub-divided into a 15 min "warm-up" period, a 30 min pre-injection or control period and a 2 h test period. Each subject served as its own control and was injected with a control physiological saline solution on the days before and after drug administration. With the exception of the days before the treatment started, all drugs were given after the pre-injection period and the subject was immediately placed in the Skinner box for the 2 h test period. A pilot study revealed that 100 mg/kg of iproniazid had some behavioural effects on the avoidance schedule so the pretreatment dosage was halved to 50 mg/kg. At this dose there was no behavioural effect at any time after injection. Initially, the response of each animal to 17·5 mg/kg mescaline was determined (Fig. 1*A*). Previous experiments had shown that this dosage would have a noticeable, but not extreme, effect on behaviour. Fourteen days later each animal received 50 mg/kg of iproniazid (intraperitoneally) 3 h before the administration of 17·5 mg/kg of mescaline. As a further control 17·5 mg/kg of mescaline was given again after 4 weeks. Fig. 1*B* shows the influence of iproniazid pretreatment on the action of this dose of mescaline. There is a marked increase in the effect of the drug. The entire procedure was repeated for each animal and the increase in the effect of mescaline was verified.

This finding does not support the theory that mescaline acts through a metabolite but suggests that the free amine level is the critical factor. An alternative hypothesis is that the increased levels of other monoamines, after iproniazid pretreatment, in some way facilitate the hallucinogenic activity of mescaline. A number of experiments are suggested by the latter hypothesis. If endogenous amine levels are involved, then pretreatment with amine depleters such as reserpine or tetrabenazine should decrease hallucinogenic activity and specific monoamine oxidase inhibitors (possibly N-octanol) should enhance hallucinogenic activity. The reversal of the mescaline effect by pretreatment with tetrabenazine would avoid any interpretation of the results as the summated effects of two independent processes. That is, because both mescaline and tetrabenazine block the conditioned avoidance response, then any reversal of the mescaline effect would be in the opposite direction to both manipulations. Furthermore, because pharmacological agents are available which selectively interfere with the synthesis of particular amines, then it might be possible to delineate further the precise action of mescaline.

A second pretreatment experiment was undertaken in order to throw some light on the specificity of the mescaline molecule. Four experimentally naive male hooded rats were kept on a restricted 23·5 h water deprivation schedule. All subjects were trained to press a lever in a Skinner box for access for 1 sec to water reinforcement. After preliminary training, reinforcements were only delivered when a response occurred at least 15 sec after the previous one (DRL 15). When the animals had reached a stable level of performance, each subject was initially treated with 12·5 mg/kg mescaline. The effect of the drug is to cause a period of complete suppression of lever pressing. It has already been shown that the duration of the inhibitory period is a good index of drug dose.

Fourteen days later these animals were given 25 mg/kg of 2,4,5-trimethoxyphenylethylamine (2,4,5-TMPE) followed after 15 min by 12·5 mg/kg of 3,4,5-trimethoxyphenylethylamine (mescaline). The pretreatment compound is inactive at this dosage[3]. After a further 14 days, 12·5 mg/kg of mescaline was again administered. The duration of the inhibitory period was measured for all three conditions (Fig. 2). It is clear that the effect of pretreatment was to decrease the mescaline response.

The antagonism between these two closely related compounds would suggest that 2,4,5-TMPE is capable of occupying the mescaline receptor site or blocking related transport mechanisms, though itself having no central effect. In this case a systematic study of the other fifteen inactive ring methoxylated phenylethylamines[3] in this situation may yield data as to properties of the receptor site involved.

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Weissenberg Effect as an End-point in Coagulation Studies

During a recent investigation of the viscosity changes which occur when thrombin is added continuously to fibrinogen, the substrate solution suddenly and rapidly climbed the shaft of a motor driven paddle at about the conventional coagulation point. This phenomenon is familiar to investigators of artificial high polymers as the Weissenberg effect[1–3], which is usually observed where the macromolecules or other structures form a network of temporary entanglements or permanent cross-linkages.