and it was mainly in the supernatant fraction. This was confirmed by a final experiment in which the 1000 *g* and supernatant fractions were incubated together with *S*-adenosyl-L-methionine (methyl ^{14}C) and norlaudanosoline followed by extraction of the total alkaloids from both fractions and subsequent autoradiography after development by t.l.c. using acetone–toluene–ethanol–ammonia (conc.) (10:10:3:½) (Antoun, 1974). Radioactive reticuline, codeine, thebaine and papaverine were found. Narcotine was not present indicating either that the enzymes involved in its formation were not active at the time of collection of latex or that its biosynthesis occurs outside the laticiferous vessels.

This preliminary work has shown that poppy latex was capable not only of carrying out the necessary methylation reactions of the alkaloids, but also capable of demethylating thebaine to codeine and possibly morphine.

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Preliminary characterization of the histamine releasing activity of cotton dust

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Aqueous extracts of cotton dust possess histamine releasing activity (HRA) which is believed to play an important role in the aetiology of the acute symptoms of the occupational disease, byssinosis (Nicholls, Nicholls & Bouhuys, 1967). In this preliminary study an attempt has been made to characterize the chemical nature of this pharmacological activity.

HRA was determined by an *in vitro* technique using pig lung (Nicholls, Evans & others, 1973). The extractability of HRA from cotton dust by various solvents decreased in the order; distilled water > aqueous ethanol (50%, v/v) > aqueous ethanol (75%, v/v) > methanol > acetone > di-ethyl ether. The ether extract possessed about one-fifth of the HRA of the water extract. About one-third of the HRA of aqueous extracts of the dust was dialysable through a cellulose (Visking) membrane. The HRA of aqueous extracts of dust was extensively absorbed onto a weak cationic exchange resin. In aqueous extracts of cotton dust the activity was stable to boiling at neutral and alkaline but not acidic pH values.

Thin layer chromatography on cellulose plates in butan-1-ol, acetic acid, water (4,1,5, v/v) separated the HRA into three areas of R_F 0·73(A), 0·54(B) and 0·17(C) respectively. Spot A was lime-green in colour and gave a positive reaction for phenols and tannins (ferric chloride-ferricyanide reagent; Smith, 1960). The absorption spectrum and chromatographic mobility of this spot were identical to those of the flavonoid, rutin which has previously been found in the cotton plant (Greensmith, 1969). Rutin released histamine from pig lung *in vitro*.

Spot B possessed a chromatographic mobility and staining reaction to ninhydrin (crimson) identical to that of trimethylamine which has been also found in the cotton plant (Greensmith, 1969). This amine was found to be a histamine releasing agent with lung tissue.

Spot C was a yellow-brown colour which gave a whitish fluorescence under light at 350 nm and stained with ninhydrin. The material isolated from this area of the t.l.c. plate was insoluble in ether but readily soluble in water. It was precipitated from aqueous solution by addition of acetone to 70% (v/v). Hydrolysis of this fraction with acid followed by paper and thin layer chromatography demonstrated the presence of several amino acids and sugars. Hydrolysis also destroyed the HRA of this material. It is suggested that Spot C, which is the main histamine releasing component of cotton dust, is a polysaccharide-protein complex. Full characterization of this material is in progress.

Thus it is evident that cotton dust contains several agents of diverse chemical composition which are capable of releasing histamine.

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The equivalence of oxytetracycline tablets B.P.

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The inequivalence of bioavailability of oxytetracycline hydrochloride from capsules has been known for several years (Brice & Hammer, 1969; Blair, Barnes & others 1971). The B.P. tablet contains the dihydrate and a recent study has shown that the dissolution at pH 2·0 varies between products obtained from different manufacturers and between batches from one source (Groves, 1973).

We have carried out bioavailability studies on formulations giving equivalent dissolution profiles at pH 2·0 and these have shown markedly different serum levels in volunteers.

A more critical examination of the conditions of the dissolution test suggests that the pH of the dissolution medium is an important parameter. The percentage of drug released from a tablet in a given time was found to be directly related to the pH—solubility profile which exhibits a minimum at pH 5 (Merck Index, 1968). Dissolution tests at this pH highlight differences in serum levels from different formulations (for example see Table 1).

	Peak serum level (μg ml^{-1})	Dissolution—T_{50} (min)	
		pH 2	pH 5
Formulation A	1·44	14·9	32·3
Formulation B	0·71	13·2	>100

Samples of oxytetracycline dihydrate B.P. from various sources varied in particle size between 7·8 and 170 μm. This variation was found to give rise to difference in bioavailability and dissolution of the formulated tablet. For example the percentage dissolved in 40 min at pH 5·1 was 55·8% using 170 μm material by comparison with 73·1% using 59 μm material.

The age of the tablets affected bioavailability and dissolution e.g. tablets from one source stored for 3 months at 20–25° showed a reduction in the percentage dissolved in 40 min at pH 5·1 from 68·9% to 40·3%. This is contrary to the findings of Groves, 1973.

The conditions of storage also affected dissolution and bioavailability the effect being more pronounced as the storage temperature rises. Samples of tablets from various commercial sources have been examined and found to exhibit differences in dissolution properties. Results as wide apart as 16–73% dissolved in 40 min at pH 5·1 were observed.

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