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Note

Stability of cocaine in biological fluids

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Cocaine is rapidly inactivated in man by the hydrolysis of one or both of the ester linkages. Even in water, at pH values greater than neutrality, the drug is readily de-esterified to benzoylecgonine. In blood or plasma, cocaine is hydrolyzed to ecgonine methyl ester by cholinesterase; the reaction rate is highly dependent on the drug concentration, and is inhibited by freezing, by the addition of fluoride, or by the presence of cholinesterase inhibitors[1]. The hydrolysis of cocaine to benzoylecgonine, on the other hand, is believed to occur non-enzymatically since neither serum nor liver esterases produce this compound from the parent drug[2].

Concentrations of intact cocaine have been observed to decline markedly over a period of one to two months in postmortem tissues[3] and whole blood[4]. This study was undertaken to determine the effect of time, temperature, drug concentration, and sodium fluoride on the stability of cocaine in blood and plasma, and the effect of time, pH and fluoride on its stability in urine.

EXPERIMENTAL

Specimen preparation

Outdated whole blood and plasma were obtained from a local blood bank, while urine was collected from volunteers. A pH 7.4 sodium acetate (0.05 *M*) buffer was prepared for use as a comparison fluid. Cocaine hydrochloride (1 mg/ml in methanol) was added to the above fluids in amounts sufficient to produce cocaine concentrations of 0.1 or 1.0 mg/l as the free base. Sodium fluoride was added to some aliquots of these solutions at a concentration of 0.5%. The test solutions were stored in the dark at either room temperature (25°C) or under refrigeration (4°C) throughout the period of the study.

Method of drug assay

Cocaine was analyzed using gas chromatography with nitrogen-specific detection following solvent extraction from the aqueous specimen[5].

RESULTS AND DISCUSSION

At a concentration of 0.1 mg/l, a level that is consistent with therapeutic administration of the drug to surgical patients[6], cocaine disappeared rapidly from re-

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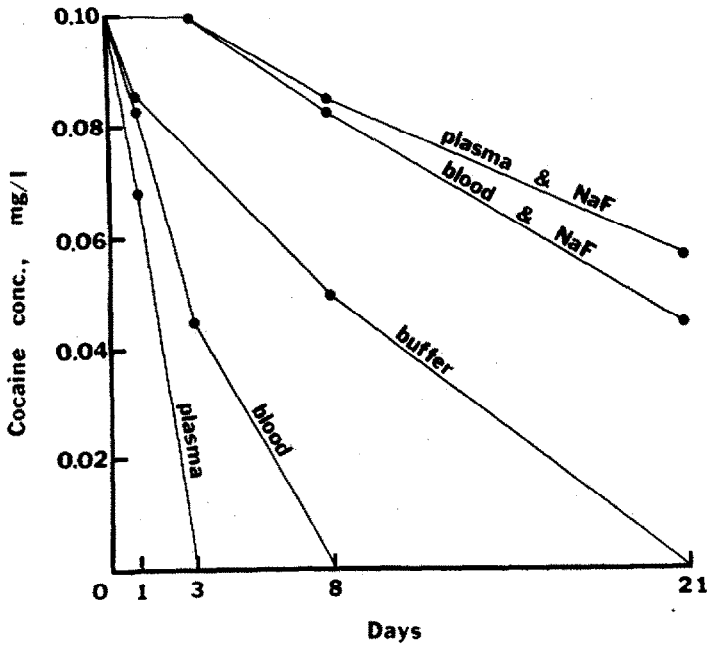

Fig. 1. Decline in cocaine concentrations of blood, plasma and pH 7.4 buffer, with and without 0.5% sodium fluoride, when maintained at 4°C for 21 days. Initial cocaine concentration of 0.1 mg/l.

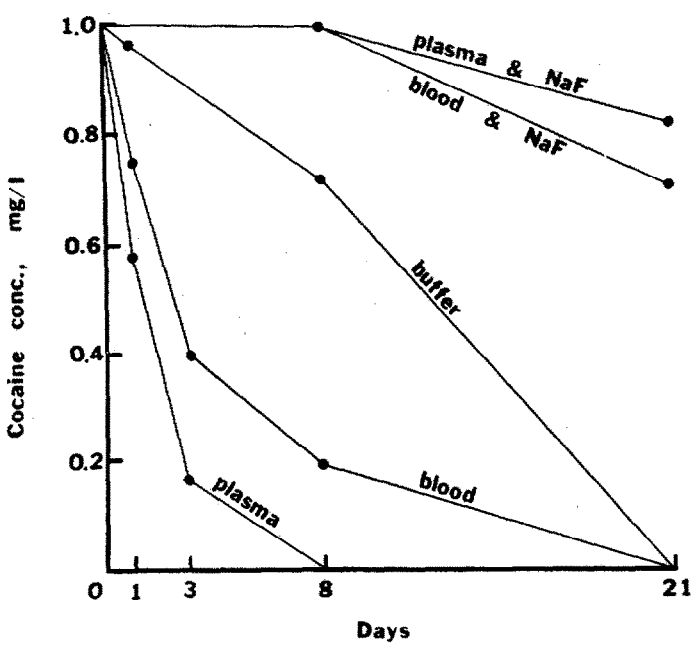

Fig. 2. Decline in cocaine concentrations of blood, plasma and pH 7.4 buffer, with and without 0.5% sodium fluoride, when maintained at 4°C for 21 days. Initial cocaine concentration of 1.0 mg/l.

frigerated, but non-fluoridated, blood and plasma (Fig. 1). It was no longer detectable in plasma on day 3 and in blood on day 8. It was still present in fluoridated blood and plasma on day 21, but at only 40–60% of the original value. The drug vanished from pH 7.4 buffer even more rapidly than from the fluoridated blood or plasma. This was explained when it was found that by day 21, while the pH of the buffer had remained constant, the pH of the biological specimens had fallen to 7.0, a condition which is less favorable to the spontaneous hydrolysis of cocaine.

At a concentration of 1.0 mg/l, much the same pattern was observed (Fig. 2), although cocaine was still detectable in non-fluoridated plasma and blood after 3 and 8 days, respectively, and up to 80% of the original concentration was still intact in the fluoridated specimens after 21 days. After a period of six weeks (this is not shown on the graph) the fluoridated specimens showed no detectable cocaine. This level of 1.0 mg/l is considered to be a minimal fatal concentration of cocaine in blood; levels of 0.9–21 mg/l have been observed in 18 fatal cases reported in the literature[6].

A further comparison was made on two fluoridated blood specimens containing 1 mg/l of cocaine, one refrigerated and the other maintained at room temperature. As suspected, the higher temperature caused a more rapid disappearance of the drug, with nearly 90% lost after 21 days (Fig. 3).

Finally, cocaine was added to urine at a concentration of 1 mg/l and the specimens maintained at 4°C at 2 different pH values, with or without 0.5% sodium fluoride. At pH 5, after 21 days, the urine cocaine concentration was essentially unchanged and the presence or absence of fluoride was an insignificant factor (Fig. 4). At pH 8, a significant diminution in cocaine concentration occurred, and the

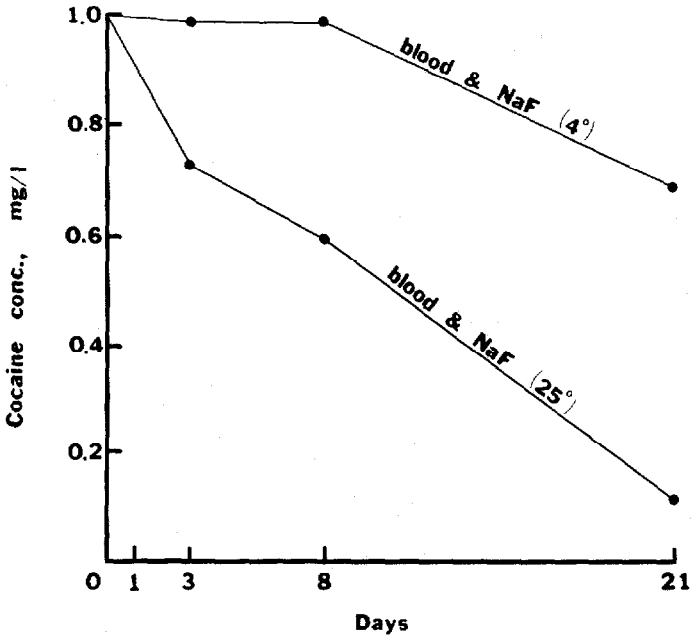

Fig. 3. Decline in cocaine concentrations of blood with 0.5% sodium fluoride maintained at either 4 or 25°C for 21 days. Initial cocaine concentration of 1.0 mg/l.

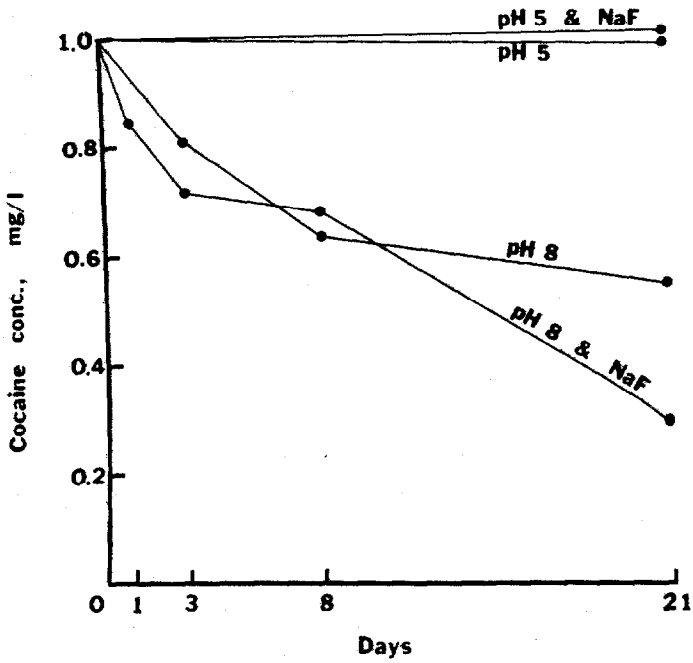

Fig. 4. Decline in cocaine concentrations of urine, with and without 0.5% sodium fluoride, adjusted to either pH 5 or 8, when maintained at 4°C for 21 days. Initial cocaine concentration of 1.0 mg/l.

fluoride actually appeared to have a negative influence on the stability of the drug, but it is doubtful that this observation would stand up to repetitive investigation.

In conclusion, it has been shown that with 0.5% sodium fluoride and refrigeration at 4°C blood specimens may be meaningfully assayed for intact cocaine after sampling for a period of time that is dependent on the initial drug concentration. In other biological fluids that do not contain esterases, pH is probably the most important factor affecting the stability of this drug.

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