

The occurrence of diltiazem in illicit cocaine

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Large-scale production of illicit cocaine

- *Erythroxylon coca* plant leaves contain 0.5–2.0% cocaine, plus other alkaloids. These alkaloids occur in different proportions in different ‘commercial’ varieties.
- Cocaine is extracted from the leaves and is refined to a purity of almost 100% as the hydrochloride.
- At the trafficking stage, a number of adulterants are added to increase profits, for example, phenacetin, caffeine, lignocaine, paracetamol and procaine. Adulterants may also be added once the drug has arrived in the UK.
- Further dilution is made within the UK. Cutting agents such as mannitol, lactose and glucose are commonly used.
- Crack cocaine (alkaloidal base) is formed from cocaine hydrochloride, usually in small batches in the UK (around 200 deals in one batch).

Forensic Alliance findings

Since July 2004, 14 separate cases of seized cocaine (both crack and hydrochloride) have been found to contain diltiazem. This has not been encountered previously.

The cocaine samples were seized from forces spread across southern England for both possession and supply charges (Table 1). A total of 26 items was found to contain both cocaine and diltiazem; 14 of these were crack cocaine, 4 cocaine hydrochloride, and 4 were not characterised.

Case type	Drugs detected	Cocaine quantity	Cocaine purity
1 Supply	Cocaine HCl	2.61 g	80%
	Cocaine HCl	192 mg	84%
	Cocaine HCl	264 mg	84%
	Cocaine HCl	3.16 g	81%
2 Possession	Cocaine (unspecified)	827 mg	35%
	Cocaine (unspecified)	3.48 g	33%
3 Possession	Cocaine (unspecified)	Trace	n/a
	Crack	103 mg	51%
5 Supply	Crack	658 mg	45%
	Crack	1.10 g	49%
	Crack	2.93 g	51%
	Crack	21.2 g	41%
6 Supply	Crack	657 mg	64%
	Crack	290 mg	66%
	Crack	288 mg	70%
	Crack	2.68 g	63%
7 Possession	Crack	256 mg	90%
	Crack	110 mg	68%
9 Supply	Crack	17.3 g	81%
	Crack	12.5 g	82%
11 Supply	Crack	1.31 g	32%
	Crack	15.2 g	78%
12 Supply	Crack	1.15 g	82%
	Cocaine (unspecified)	Trace	n/a
13 Supply	Heroin + Crack	891 mg	95%
14 Supply	Crack	279 mg	80%

Table 1: Cocaine seizures containing diltiazem

The diltiazem in these cocaine samples appeared to be present in a substantial quantity rather than trace amounts (Figures 1 and 2). In one case, the amount of diltiazem was determined to be 8–10%.

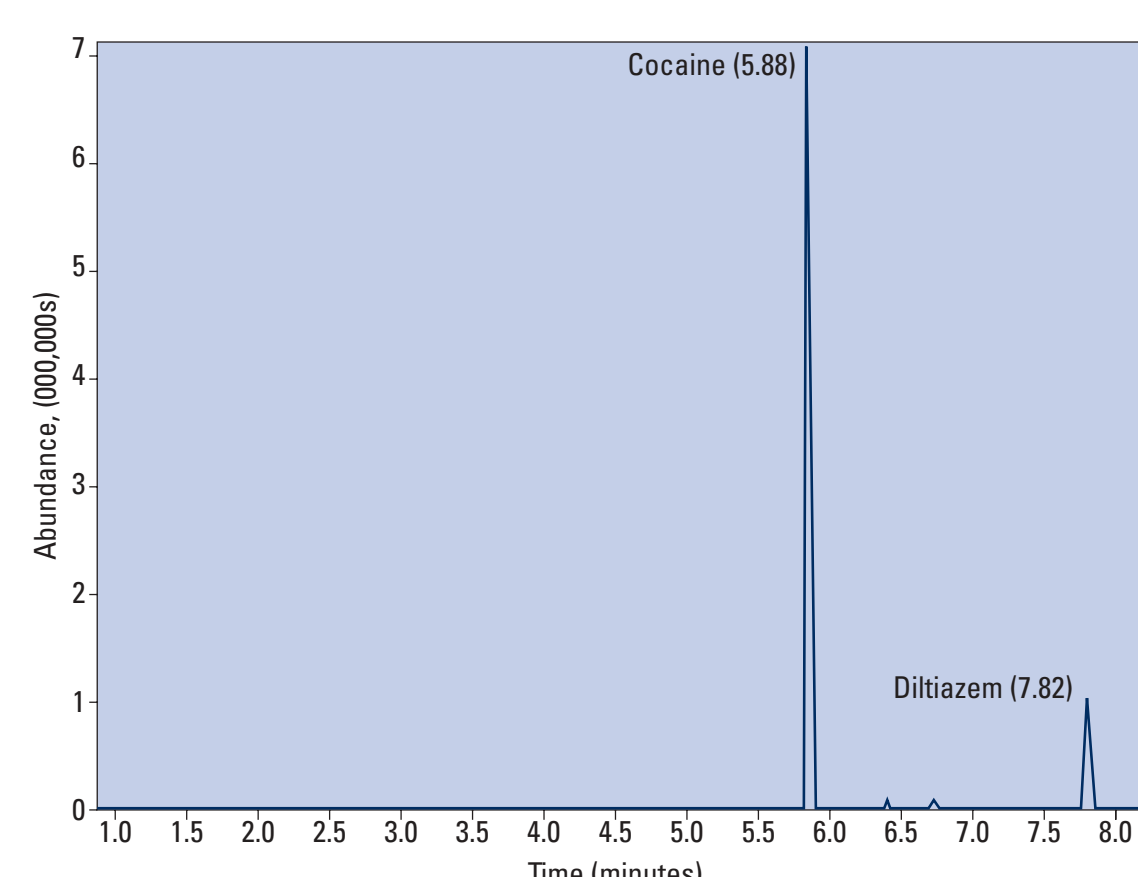


Figure 1: Cocaine and diltiazem detected by GC-MS routine qualitative screen

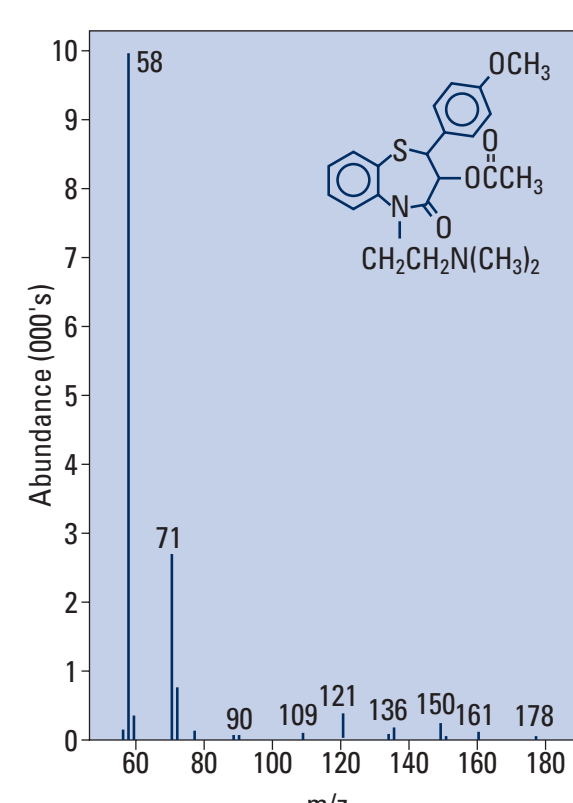


Figure 2: Mass spectrum and structure of diltiazem

Diltiazem

Diltiazem is a calcium-channel blocker available as a prescription-only medicine in the UK. It is used for the treatment of angina pectoris, hypertension and cardiac arrhythmia. It has a relatively short half-life (2.8–9.2 hours, average 4.5 hours). In comparison, the half-life of cocaine is 0.7–1.5 hours.

- Diltiazem takes effect on myocardial cells (heart muscle) and vascular smooth muscle cells.
- It interferes with the inward displacement of calcium ions through cell membranes, leading to reduced contractility (a negative inotropic effect).
- Peripheral and coronary vasodilation lead to increased blood flow through the heart and decreased blood pressure. This in turn decreases oxygen demand.
- Decrease in heart rate (chronotropic effect) is effected by the depression of the formation and the propagation of electrical impulses.

Diltiazem is contra-indicated with existing bradycardia, left ventricular failure, second- or third-degree atrioventricular block and sick sinus syndrome. Concurrent administration of beta blockers with diltiazem should be undertaken with caution.

Cocaine cardiotoxicity

- The primary cardiotoxic effect of cocaine appears to result from the excess of catecholamines. This causes an increase in calcium levels within the myocytes. Excess free calcium in cells can precipitate effects such as increased contraction of the myofilaments, contraction band necrosis, abnormal impulses, lesions and arrhythmia.
- As a local anaesthetic, cocaine blocks the fast sodium channel of the cell membranes. This causes a number of intraventricular conduction abnormalities, such as negative inotropic and chronotropic effects, which lead to, for example, bradycardia and decreased blood pressure. These local anaesthetic effects occur rarely and mostly in cases of massive cocaine administration (Karch, 1996).

Cocaine abuse

Acute exposure to cocaine causes coronary vasoconstriction, increased myocardial oxygen demand and coronary artery spasm. Chronic use of cocaine also increases platelet aggregability and may lead to *in situ* thrombus formation. Other cardiac changes such as contraction band necrosis are also associated with long-term abuse (Figure 3).

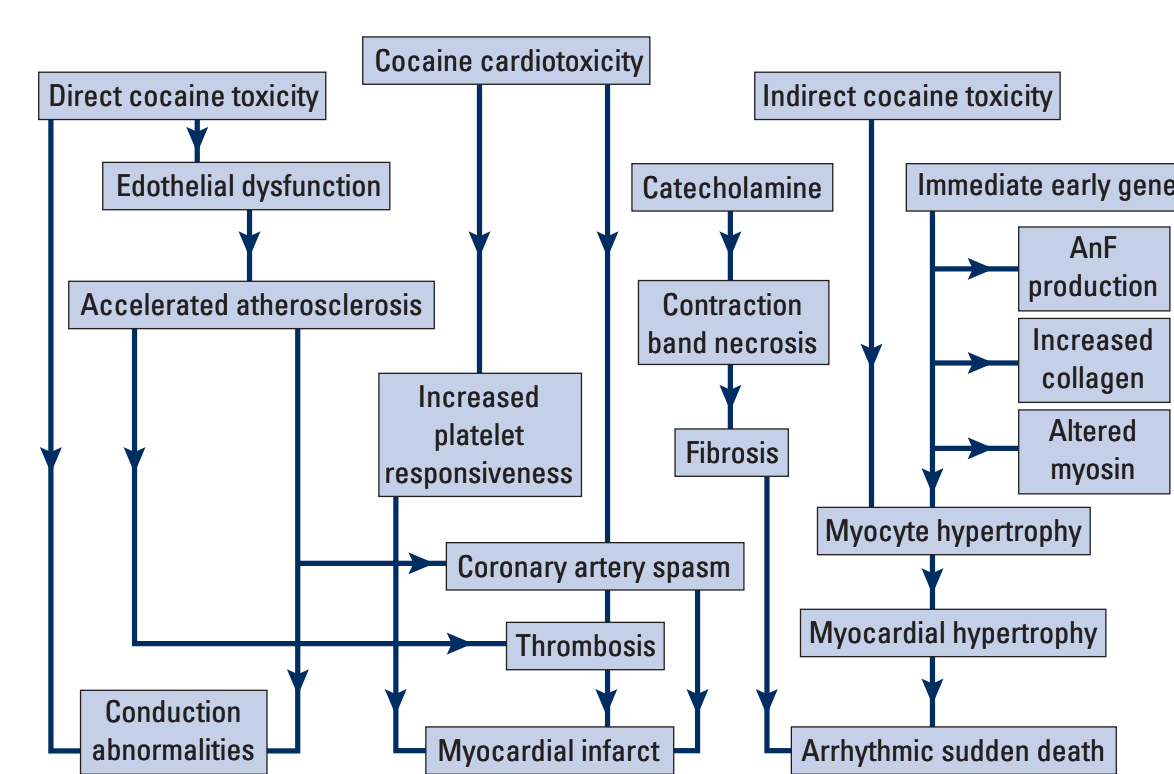


Figure 3: Mechanisms of cocaine cardiotoxicity (Karch, 1996)

The complications most commonly encountered following cocaine abuse are

- Hypertension
- Global myocardial ischaemia
- Myocardial infarction
- Myocarditis
- Aortic rupture
- Cardiac arrhythmia
- Regional myocardial ischaemia
- Cardiomyopathy
- Endocarditis
- Diffuse microaneurysms (Ellenhorn, 1997).

Potential interactions of cocaine and diltiazem

- Animal studies show that calcium channel blockers can prevent arrhythmia, blunt negative inotropic effects, decrease vascular resistance and protect against myocardial infarction (Billman, 1993).
- Diltiazem given to six healthy human subjects 120 minutes prior to cocaine administration did not alter their physiological response to cocaine (Rowbotham, 1987).
- Diltiazem may give a degree of cardiac protection. However, in those cases where hypotension and/or left ventricular failure occurs, it may, in fact, potentiate the overall cardiotoxic effect of cocaine.
- Additionally, any treatment with beta blockers may lead to an unexpected interaction, with resulting complications such as bradycardia.

Origin of adulteration?

- Illicit production of cocaine often utilises inexpensive ‘recycled’ solvents (owing to legal restrictions) that may be contaminated with pharmaceuticals such as diltiazem. However, this source seems unlikely, given the relatively high levels of diltiazem detected.
- Adulteration is presumably performed to provide the user with a degree of protection against the cardiotoxic effects of cocaine. Diltiazem is, however, expensive.
- Forensic Alliance is monitoring the occurrence of diltiazem in cocaine and, as yet, there is no available intelligence to trace the potential source of the adulteration. The toxicology department has not yet had any cases involving cocaine and diltiazem together.

Conclusions

Overall, the literature on the beneficial effects of diltiazem on cocaine-induced cardiotoxicity in humans is limited. Diltiazem is used in the treatment of cocaine-induced hypertension and, therefore, it may be useful to bear this drug in mind when analysing, treating and interpreting cocaine-related cases.

References

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