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CASE REPORT

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Forensic toxicological implication of acute fatal poisoning cases due to benfuracarb ingestion

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Abstract We describe here three cases involving acute fatalities due to benfuracarb ingestion and the forensic toxicological implications. Benfuracarb, a carbamate insecticide and its main metabolite carbofuran, were detected using thin layer chromatography (TLC) and gas chromatography/mass spectrophotometry (GC/MS) after extraction with ethyl acetate and then quantified using gas chromatography (GC) equipped with NPD. The blood levels of benfuracarb and carbofuran were in the range of 0.30~2.32 μg/ml and 1.45~1.47 μg/ml, respectively. Benfuracarb was not detected in urine, but carbofuran was detected in the range of 0.53~2.66 μg/ml.

Key words Poisoning · Benfuracarb · Carbofuran · Human · Blood · Urine

Introduction

Benfuracarb [2,3-dihydro-2,2-dimethyl-7-benzofuranyl-2-methyl-4-(1-methylethyl)-7-oxo-8-oxa-3-thia-2,4-diazadecanoate, Fig. 1] is a carbamate insecticide used to control insect pests in citrus, maize, sugar beet and vegetables. Like other carbamate insecticides, benfuracarb inhibits cholinesterase [1, 2] and is assigned to the toxicity class WHO Ib [2]. There have been reports about the metabolism of benfuracarb in rats and in plants [2–5]. In rats, benfuracarb is metabolized rapidly to carbofuran (Fig. 1), one of the main metabolites and almost completely excreted in the urine and faeces within 7 days [2]. Rare fatal cases due to pesticide have been recently reported [6–9]. Because benfuracarb is widely used and has a high toxicity, there is the possibility of fatal poisoning due to accidental ingestion or for suicidal or homicidal purposes. To the best of our knowledge, however, no fatal case involving humans has been published in the literature. We describe here three fatal cases due to ingestion of benfuracarb which occurred in Korea, detecting benfuracarb and its metabolite carbofuran in blood and urine and the forensic toxicological implications.

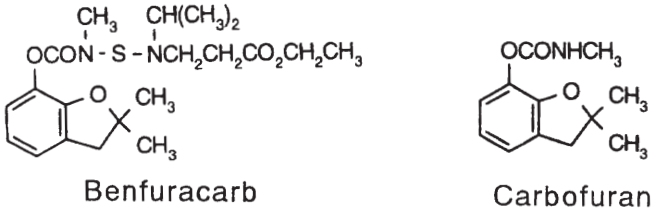

Fig. 1 Chemical structures of benfuracarb and its metabolite carbofuran

Case histories

Case 1

A 25-year-old man was found dead in his house with no evidence of violence. A brown glass bottle labeled Oncol EC was found near the body.

Case 2

A 38-year-old unemployed man was found unconscious with blue lips on a sofa in his house. He died while being transported to the hospital.

Case 3

A 44-year-old housewife was found lying dead in a room at home.

The autopsy findings of the three subjects indicated no external evidence of violence, but miosis, pulmonary edema and congestion of all organs. In the stomach, there were foul-odored gastric con-

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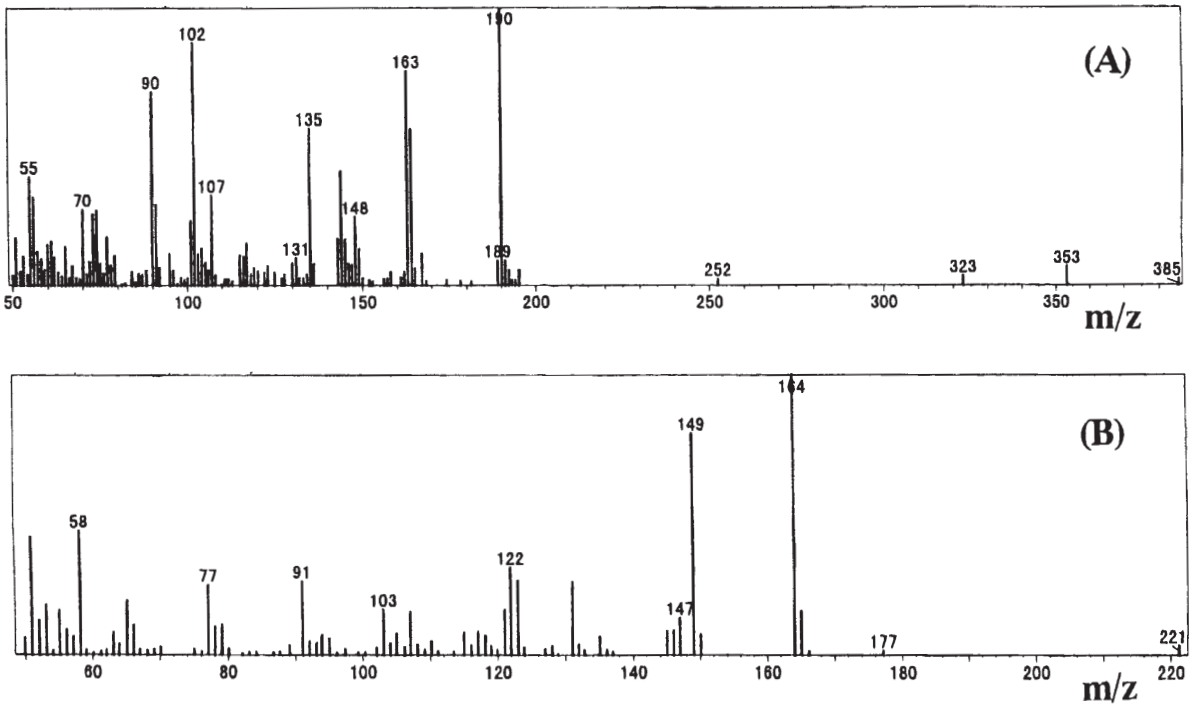

Fig. 2 EI mass spectra of benfuracarb (A) and carbofuran (B) extracted from blood. Characteristic ions at 190, 163, 135 and 102 m/z for benfuracarb and at 64, 149, 122 and 58 m/z for carbofuran were detected

tents, suggesting pesticide ingestion. Histological examination revealed unremarkable changes except for congestion in the three victims, and mild fatty changes and portal infiltrations of mononuclear cells in the liver of case 2. At autopsy, we collected the stomach contents, blood and urine for toxicological analysis. Police investigations and autopsy findings indicated that each of the victims had ingested benfuracarb insecticide in an attempt to commit suicide.

Materials and methods

We used the gastric contents for the qualification of benfuracarb and carbofuran by TLC [10] and GC/MS analysis and the blood and urine for quantitation by GC-NPD.

After extraction of about 1~5 ml of a sample by ethyl acetate, the organic extract layer was evaporated to dryness. The residue was redissolved in methanol with and without carbaryl as an internal standard (IS, 20 μg/ml) and then used for analysis.

The operation conditions of GC/MS were as follows; Equipment: Finnigan GCQ, capillary column: DB-5 MS, (15 m × 0.25 mm i.d. × 0.25 μm film thickness), temperature: oven: programmed from 120° C (1 min hold) to 260° C at 20° C/min (10 min hold), injector: 250° C, carrier gas: He, ionization: electron impact (EI) by 70 eV. The main conditions for GC analysis including column, temperature and carrier gas were the same as those for GC/MS. The detector was NPD. The column temperature was increased at 10° C/min.

Results and discussion

In the analysis of gastric contents by TLC and GC/MS, we detected two spots of benfuracarb and carbofuran with Rf values of 0.39 and 0.22 and also detected EI mass spectra of those as shown in Fig. 2. We conclude that in these cases only benfuracarb was ingested because a large amount of benfuracarb compared with carbofuran was detected in the gastric contents and the production of a slight amount of carbofuran from benfuracarb under acidic conditions has been reported [2].

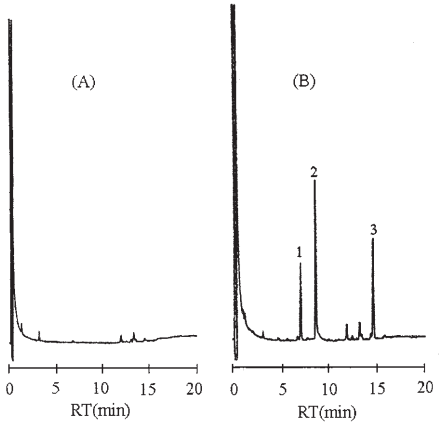

Fig. 3 Gas chromatograms of blank blood (A) and sample blood of case 3 (B). Retention times of carbofuran (1), carbaryl (2) and benfuracarb (3) were 7.02, 8.57 and 14.60 min, respectively

Figure 3 shows the typical GC-NPD chromatograms of blank blood and sample blood in case 3. No interference peaks for quantitation of benfuracarb and carbofuran were observed in the chromatograms. Table 1 shows benfuracarb and carbofuran concentrations in blood and urine of three poisoning cases. In case 1, carbofuran was not analysed because at that moment we had no information about benfuracarb poisoning and metabolism of benfu-

Table 1 Concentrations of benfuracarb and carbofuran in the three poisoning cases

Carbamate	Case 1		Case 2		Case 3	
	Blood	Urine	Blood	Urine	Blood	Urine
Benfuracarb (μg/ml)	2.32	ND	0.31	ND	0.30	ND
Carbofuran (μg/ml)	NA	NA	1.47	2.66	1.45	0.53

ND: not detected; NA: not analyzed

racarb. Among the three cases, the blood benfuracarb level in case 1 is about 7 times higher than in the other two cases. Differences of these levels are thought to be related to the dose of benfuracarb and survival time after ingestion to death. In cases 2 and 3, the blood concentrations of benfuracarb, from which carbofuran can be metabolized, were about one-fifth of the carbofuran concentrations, but carbofuran only was detected in urine. These results indicate that benfuracarb is rapidly metabolized to carbofuran in the human body as described in rat experiments [2]. For analytical toxicology various kinds of biological samples must be collected in order to identify benfuracarb poisoning because carbofuran only could be detected in the urine in spite of poisoning due to benfuracarb.

For the toxicological evaluation of benfuracarb poisoning, benfuracarb and carbofuran must be quantified simultaneously in biological materials because the toxicity of carbofuran (oral LD_{50} value in rats; 8 mg/kg) is more than 17 times higher than that of benfuracarb (oral LD_{50} value in rats; 138 mg/kg) [2]. In previous carbofuran poisoning cases, the fatal blood levels were 8.0 μg/ml [6] and 29.3 μg/ml [7]. Based on these published data, the carbofuran levels in our benfuracarb poisoning cases cannot be considered fatal. Therefore, we estimate that death in our cases was induced by the combined toxicity of benfuracarb itself and its metabolite carbofuran.

We infer here that fatal blood level ranges of benfuracarb and carbofuran due to ingestion of benfuracarb are 0.30~2.32 μg/ml and 1.45~1.47 μg/ml, respectively, and that benfuracarb might not be detected in urine, although its metabolite, carbofuran, can be present in the range of 0.53~2.66 μg/ml. This is the first report of benfuracarb fatalaties in humans and therefore these data should be very useful for further studies.

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