

*Kasuistik · Casuistry*

## **Chlorobutanol Poisoning. Report of a Fatal Case**

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Ein Fall von tödlicher Chlorobutanol-Vergiftung

*Summary:* A fatal chlorobutanol intoxication is reported and a gas chromatographic method for the determination of this drug in human fluids and tissues is described. Analytical findings for blood, urine, stomach contents, bile, liver, kidney, spleen, and brain are reported.

*Zusammenfassung:* Ein Fall von tödlicher Vergiftung mit Chlorobutanol und eine gaschromatographische Methode zur Bestimmung dieser Verbindung in Leichermaterial wurde beschrieben. Es wurden die analytischen Ergebnisse von Blut, Harn, Mageninhalt, Leber, Niere, Milz und Gehirn referiert.

*Key words:* Chlorobutanol, fatal intoxication - Poisoning, chlorobutanol

Chlorobutanol is used as a preservative, local anesthetic, hypnotic, and topical analgesic in toothache drops. Its hypnotic action reportedly resembles that of chloral hydrate with a somewhat greater potency (GOODMAN and GILMAN, 1965). A literature search revealed no previous report of a method of chlorobutanol determination in human biological materials and consequently no interpretation of concentrations in body fluids. This report presents a sensitive method for the determination of chlorobutanol in biological materials and gives the concentrations of this drug found in body fluids and tissues following a fatal overdose.

### METHOD

To 2.00 ml of blood, urine and bile were added 2.0 ml of water and 10.0 ml of the extraction solvent (hexane, isoamyl alcohol 100 : 1.7 by volume). Tissue samples were prepared by homogenizing 2.00 g in the presence of 2.0 ml of water followed by the addition of 10.0 ml of the extraction solvent. The tubes containing the mixtures were capped, rotated at approximately 8 rpm for 20 min and centrifuged at 1500 rpm for several min. Aliquots of 1.00, 2.00 or 3.00 microliters of the upper (hexane) layers were injected into the gas chromatograph.

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The reference solutions used for quantitating the samples in question were prepared by adding 2.0 ml aliquots of aqueous chlorobutanol at several concentrations to blank blood, urine, bile and tissue (liver). The quantitation of each sample was made by comparing its chromatographic peak area to those standards prepared in similar media.

The gas chromatograph used was Hewlett-Packard Model 5713 equipped with a constant current  $^{63}\text{Ni}$  detector. The column used was glass, 1 m X 4 mm I.D., packed with 5% OV-7 on 80-100 mesh Anakrom ABS. The oven and injector were maintained at  $90^{\circ}\text{C}$ ; the detector was maintained at  $300^{\circ}\text{C}$ . The flow rate of carrier gas (5% methane in argon) was approximately 50 ml per min.

Chromatographic peak areas were measured by means of a Perkin-Elmer PEP Data Reduction System.

#### CASE REPORT

The deceased, a 45 year old woman being treated for chronic schizophrenia, was found in her apartment lying on the bathroom floor. She had had previous hospitalizations for consuming shoe polish, hair spray and other substances. No suicide note was found but near her body a nearly empty, one ounce bottle of Dentalone, Parke-Davis, Detroit, Michigan, was found. The label indicated that the contents contained 175 grains per ounce of chlorobutanol. Other ingredients listed, without quantity, on the label were oil cloves, methyl salicylate, oil cassia and cinnamic aldehyde.

Table 1. *Chlorobutanol response versus concentration*

| Concentration<br>(mg/100ml) | Peak Area<br>(arbitrary units) |
|-----------------------------|--------------------------------|
| 2.00                        | 8.854                          |
| 4.00                        | 16.543                         |
| 6.00                        | 25.637                         |
| 12.00                       | 49.068                         |
| 18.00                       | 75.123                         |

Table 2. *Chlorobutanol concentrations in body fluids and tissues*

| Media                         | Concentration<br>(mg/100ml) |
|-------------------------------|-----------------------------|
| whole blood                   | 6.4                         |
| plasma                        | 6.5                         |
| urine                         | 3.1                         |
| stomach contents <sup>a</sup> | $3.2 \times 10^3$           |
| brain                         | 16.1 <sup>b</sup>           |
| liver                         | 14.1 <sup>b</sup>           |
| bile                          | 12.3 <sup>b</sup>           |
| spleen                        | 12.0 <sup>b</sup>           |
| kidney                        | 8.7 <sup>b</sup>            |

<sup>a</sup>Total amount present was 3.2 g. <sup>b</sup>Concentration in mg per 100 g

Autopsy revealed unremarkable pathological tissue findings. Only agonal changes were noted. The stomach contents had an aroma similar to that from the Dentalone bottle.

#### RESULTS AND DISCUSSION

The injection of various amounts of chlorobutanol into the gas chromatograph yielded a linear response of peak area versus concentration within a range of 2 to 18 mg/100 ml. Further concentrations were not investigated. Listed in Table 1 are the data from a series of aqueous standards analyzed as described under Method injecting 1.00 microliter of the extraction solvent.

The standard deviation of the method was determined to be 0.232 area units by repetitive (8 X 2.00 microliters) injections of an extract from a reference containing 2.0 mg chlorobutanol per dl of blood. The coefficient of variation was 1.80%. The minimum detectable concentration was approximately 0.01 mg of chlorobutanol per 100 ml of sample which was equivalent to 80 picograms on column.

The recovery of chlorobutanol from the various media was determined chromatographically to be 92% from urine or water, 91% from bile, 90% from blood, and 82% from homogenized tissue (liver).

Listed in Table 2 are the results of fluid and tissue distributions of chlorobutanol found in the fatal case. Only one peak, corresponding to chlorobutanol, was observed in each sample. Consequently if metabolite or metabolites were present, one would conclude that they were either inseparable from the parent drug on the gas chromatographic column or that they were not susceptible to electron capture detection.

Other toxicological analyses revealed that the stomach contents contained 310 mg of methyl salicylate. The blood and urine were found to contain no ethyl alcohol, methyl alcohol, acetone, aldehydes or barbiturates. No organic bases were detected in the urine or stomach contents.

#### REFERENCES

GOODMAN, L.S., GILMAN, A.: The Pharmacological Basis of Therapeutics, 3th. pg. 133 New York: The Macmillan Company 1965

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