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Report of a Human Fatality Due to Caffeine

Caffeine (1-, 3-, 7-trimethylxanthine) is probably the most widely used and socially acceptable drug in the world today. The United States alone uses more than three billion pounds of coffee annually. A cup of brewed coffee beverage will contain from 100 to 150 mg of the alkaloid per 8 oz portion, while tea contains 30 to 50 mg per 8 oz portion and cola drinks contain about 1 mg per oz. In addition to the consumption of caffeine in beverage form, many prescription, as well as over-the-counter drugs contain varying amounts of caffeine. An example of the former is Cafergot® (Sandoz Pharmaceuticals) while No-Doz® (J. B. Williams Co.) and analgesics such as Empirin® (Burroughs-Wellcome & Co.) or diuretic preparations such as Aqua-Ban® (The Thompson Medical Co.) exemplify the latter. Caffeine is not generally considered to be a drug of misuse although it has mild cortical stimulatory properties. Excessive consumption of the compound is generally prevented by another of its pharmacological properties, that of potent gastric irritation. The individual bent on misuse usually vomits before a lethal amount of the drug can be consumed. In rate instances, however, it is possible to ingest enough caffeine to cause death. Such an instance occurred in Benton County, Indiana in 1964, when an individual contemplating suicide ingested a minimum of 6.5 g and possibly as much as 9–12 g of caffeine alkaloid.

It is believed that the case reported here is the only documented case of lethal caffeine poisoning in the United States at this time.

Postmortem Anatomic Examination

The subject was a 27 year old, divorced white female who was last seen alive shortly before midnight on 31 Jan. 1964. She was found dead in bed about 7 h later at her residence, along with a suicide note. A large bottle, unmarked and unlabelled and containing numerous orange lozenge-shaped tablets mixed with occasional green tablets, was found with the body.

Autopsy, after arterial embalming, revealed fingers severely clenched into the palms of the hands, bilateral severe pulmonary edema, pulmonary atelectasis, mild passive congestion and mild lymphocytic infiltration of periportal spaces of a slightly enlarged liver, and a dilated gastrointestinal tract. The gall bladder had been surgically removed within the past year and ancient fibrous adhesions involved the gall bladder bed area. Pulmonary edema and atelectasis were the only significant gross and microscopic anatomic findings.

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When careful postmortem examination did not reveal an apparent anatomical cause of death, appropriate specimens were referred to the Indiana State Toxicology Laboratory for further studies. The specimens included blood (obtained prior to arterial embalming) brain, liver, kidney, and stomach contents. In addition to the biological materials, 3 plastic vials of drugs were sent and found to contain, respectively, Darvon-65® (Eli Lilly and Co.) Elavil® (Merck, Sharpe and Dohme), and Iodoniacin® (Cole Pharmaceuticals). Included in the specimens sent for toxicological examination was a large brown glass pharmacy jar containing numerous tablets, as described previously.

Postmortem Toxicological Examination

All tissue specimens were found to be in good condition upon arrival at the Toxicology Laboratory, and the blood was found to be free of aldehydes and methyl alcohol.

An analysis of blood and other tissues for common poisons revealed a blood ethanol concentration of 0.037 per cent (weight/volume) and excluded significant concentrations of glycols and carbon monoxide. Tissues were examined for the presence of heavy metals, barbiturates, morphine derivatives, strychnine, synthetic narcotics, phenothiazines, and amphetamines and none were found to be present. Tests for miscellaneous poisons such as cyanides, chlorals, phenols, and reducing substances were also conducted and none of these were found to be present.

Caffeine and ethanol were the only exogenous compounds found to be present in significant concentrations. Quantitative analytical results are shown in Table 1. To obtain these results, tissues and stomach contents were extracted with chloroform under alkaline conditions and the chloroform was back extracted into 0.5 *N* sulfuric acid which was subjected to UV spectrophotometry. The UV absorption curve was characteristic of caffeine under these conditions with an absorption maximum at 272 nm. Confirmation of these results was made by thin-layer chromatography.

TABLE 1—*Tissue concentrations of caffeine following ingestion of an unknown lethal quantity of the drug.*

Tissue	Concentration, mg/100g
Brain	7.47
Liver	32.90
Kidney	12.96
Stomach and contents	150.66

The large brown pharmacy jar, submitted along with the biological specimens, contained 175 orange oval-shaped and 4 green tablets, which were found to contain caffeine as the active ingredient when analyzed in a manner similar to that employed for tissue analysis. The prescription vials were found to be correctly labeled when the contents were analyzed, and a check of the contents against the original prescription revealed that only insignificant numbers, if any, were missing. None of the prescription drugs were found in the tissue samples.

After careful review of the postmortem anatomic and toxicologic findings in the case, it was concluded, that in the absence of other immediate causes, death was most likely due to an overdose with caffeine and should be recorded as due to caffeine intoxication. It has been shown by Axelrod and Reichenthal [*1*] that caffeine is readily absorbed from the gastrointestinal tract and distributes evenly in the body water. On this basis, taking the

least concentration in biological tissue (brain, 7.47 mg/100 g tissue), it may be estimated that the deceased person had consumed a minimum of 6.5 g of caffeine. This estimation is in agreement with an estimated lethal dose of 5.0–10.0 grams described in the literature [*2*].

It is impossible to state whether the ethanol concentration reflects an absorption or disappearance phase, so the contribution of this compound to the death cannot be stated. However, it is probable that neither caffeine nor ethanol significantly affected the action of the other. There is no evidence that these compounds are mutually antagonistic, as popularly believed. Indeed, studies by Forney and Hughes [*3*] in the human, and animal studies by Hughes and Forney [*4*] and Alstott [*5*] do not support the concept of antagonism of ethanol-induced depression by caffeine. In the human, as in animal species, both caffeine and ethanol affect the respiratory system, although by different mechanisms [*6,7*]. In the case described here, there was evidence of a previously impaired respiratory system, and either or both drugs could have contributed to the death.

Summary

Caffeine and ethanol are widely used compounds, each being of relatively low toxicity. Lethalities due to ethanol are not uncommon but deaths resulting from caffeine ingestion are very rare. The results of toxicological and pathological investigation of a human death believed to be due to caffeine poisoning have been presented.

References

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