International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 1719-1722 www.ijprajournal.com ISSN: 2456-4494

# Oral severe hemorrhage caused by acetone. First case report

George Brătulescu
*University of Craiova, Faculty of Science, Calea Bucureşti 107i, Craiova, Romania*

Date of Submission: 01-06-2024 Date of Acceptance: 10-06-2024

**ABSTRACT**
This paper describes the first case of severe hemorrhage caused by accidentally aspirated acetone in the oral cavity. The event took place many years ago in 1994, when the author of the article was working on the first cotutelle doctoral thesis in the history of Romania and France at École Nationale Supérieure de Chimie de Toulouse (France). Bleeding was stopped by the author by precipitation of blood proteins with anhydrous ethanol. A biochemical mechanism was depicted.
**Keywords:** Hemorrhage, Acetone, Mouth cavity, Blood, Anhydrous ethanol, Biochemical mechanism.

## I. INTRODUCTION

Acetone is one of the most important organic solvents produced by the chemical industry. The compound is a volatile, polar, aprotic solvent, completely miscible with water, having a dipole moment μ=2.88 D and a dielectric constant ε=21 (at 20°C), which makes it very useful in dissolving organic and inorganic compounds [1].

The most used process for obtaining acetone is the autoxidation of isopropylbenzene (cumene) followed by acidolysis with sulfuric acid (Scheme 1). The same process also produces phenol [2].

Besides being used as a solvent, acetone is also an intermediate in organic syntheses. Thus, it is used in the manufacture of varnishes, paints, pharmaceutical products and pesticides. People who work in these sectors of activity are exposed to the effects of acetone [3].

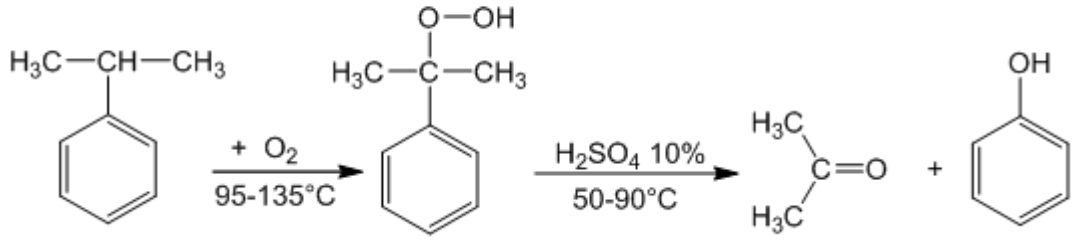
Acetone has the octanol-water partition coefficient log $P_{o/w}$=-0.24 (Table 1). This partition coefficient measures the relationship between the lipophilic character of acetone and its hydrophilic character. The negative value of its logarithm proves that the organic substance is more soluble in water than in fats [4].

The acetone is easily absorbed through the skin, ingestion and inhalation, after which it diffuses throughout the body. Being lipophilic, acetone diffuses into the tissues. In the human body, acetone is metabolized by the liver cell when it is in lower concentrations and *via* the extrahepatic route, through excretion, at higher concentrations. Through metabolism, acetone passes into methylglyoxal. At higher doses, it is metabolized to propanediol. The half-life of acetone elimination from the blood is 3-4 hours for people exposed to doses of 100-500 ppm for 2-4 hours [5].

Significant amounts of acetone are produced in the body of people with diabetes, fasting or very tired. Acetone is synthesized in the liver, and in small amounts in the kidneys and lungs. Further, the ketone bodies pass into the blood and are transported by the blood to all tissues. Some ketone bodies like acetoacetate and beta-hydroxybutyrate give metabolic acidolysis because they form organic acids [6].

The median lethal dose LD50 of acetone has a high value in the case of the tested animals (Table 1). This means that the substance is practically non-toxic. Intoxication caused by acetone is rarely reported in the scientific literature. The reported cases show people poisoned by acetone ingestion [7]. However, a case of death of a student who was poisoned with acetone is documented in the literature. It is not known how the acetone got into the student's body. Microscopic analysis of the liver tissue (Figure 1) showed its degradation by acetone: microvesicular changes, macrovesicular changes, confluent necrosis, and portal inflammation [8].

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 1719-1722 www.ijprajournal.com ISSN: 2456-4494




**Scheme 1.** Acetone synthesis from cumene [2].

**Table 1.** Some physico-chemical properties of acetone [4].

| No | Drug name | Structure |
|---|---|---|
| 1 | Chemical formula | $H_3C$-CO-$CH_3$ |
| 2 | Physical state | Clear liquid |
| 3 | Water solubility | Miscible |
| 4 | Boiling point | 56.5°V |
| 5 | Melting point | -94°C |
| 6 | Median lethal dose $DL_{50}$ | 5800 mg/kg (rate, oral)<br>5340 mg/kg (rabbit, oral)<br>3,687 mg/kg (guinea pigs, oral)<br>3000 mg/kg (mouse, oral) |
| 7 | Log $P_{o/w}$ | -0.24 |
| 8 | Dipole moment | 2.88 |
| 9 | Dielectric constant | 21 (20°C) |
| 10 | Odor | Fruity, Mint-like, Ethereal |
| 11 | Taste | Pungent, Sweetish |
| 13 | Hazard Classification | Flammable liquid |

**Table 2.** The effect of some water-ethanol mixtures on oral hemorrhage.

| No | Ethanol-water solution | Hemorrhage |
|---|---|---|
| 1 | Water | Yes |
| 2 | 25% Ethanol | Yes |
| 3 | 50% Ethanol | Yes |
| 4 | 75% Ethanol | Yes |
| 5 | 96% Ethanol | No |
| 6 | Anhydrous ethanol | No |

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 1719-1722 www.ijprajournal.com ISSN: 2456-4494

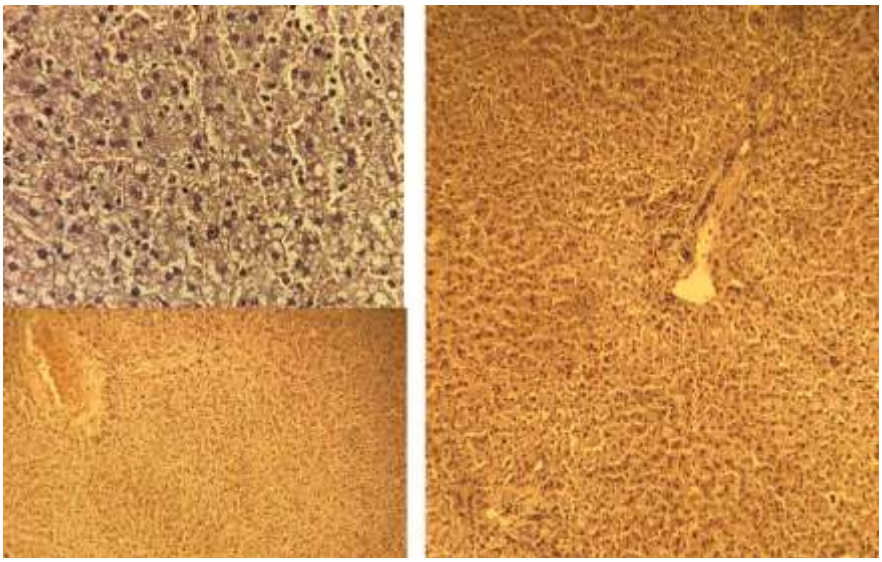


**Figure 1.** Liver tissue degraded by acetone and stained with hematoxylin and eosin [8].

## II. RESULTS AND DISCUSSION

The event that occurred and caused injury is described below. In 1994, I carried out scientific research for the first PhD cotutelle thesis from history of Romania and France, but also of the European Union, which would later lead me to obtain two doctorate degrees in different specialties: organic chemistry and agroresource science. The scientific research is carried out at the laboratory of École Nationale Supérieure de Chimie de Toulouse, France. I was trying to find the green conditions for the Williamson reaction. The organic and inorganic reactants had to be brought into contact as best as possible in the reaction medium to allow the reaction to proceed more quickly. For this, the solid medium, possibly pasty, had to be as uniform as possible. I bring the reactants into contact by dissolving them in an acetone solution or another organic solvent. Further, acetone was removed from the reaction medium by evaporation at atmospheric pressure. The resulting heterogeneous medium is then subjected to chemical transformation either by conventional, thermal means, or by non-conventional means with the help of electromagnetic microwaves.

In a hurry, I stopped using rubber bulb type safety pipette fillers to suck up the necessary volume of acetone with a glass pipette from the original solvent bottle. I aspirated the acetone into the glass pipette by mouth pipetting. Unfortunately for me, a quantity of acetone, about 20 mL, ended up in my oral cavity.

Immediately after the acetone entered the mouth, an intense hemorrhage started in the oral cavity, which instantly filled with blood. I did not panic and observed in the mirror of the laboratory that was near my workplace, what happened and the resulting injuries. The massive bleeding was emerged from two areas of the oral cavity. The first area where the blood flowed, were the blood vessels of the gums of all the teeth. The second area was the tongue, more precisely the blood vessels located on the dorsal surface of the tongue, the other regions of the tongue not being affected. The largest amount of blood flowed from the tongue in the form of a jet that gushed from the dorsal surface of the tongue. The jet increased in intensity with each contraction of the heart, being perfectly correlated with the cardiac cycle. There was no one in the laboratory near me to help me.

I thought that I had to plug the pores of the blood vessels in the oral cavity that the acetone has damaged, and through which the blood was gushing out. To stop the bleeding, I tried several solutions of non-toxic solvents, water-ethanol mixtures, which I had available in the laboratory (Table 2). First, I washed my mouth with water. However, the bleeding did not stop, after each wash it became more intense. Finally, I washed the oral cavity with anhydrous ethyl alcohol that had just been ordered by the faculty and had arrived in the research laboratory a few days ago. The pain caused in the mouth by the anhydrous ethanol was very intense, but it managed to stop the bleeding.

I noticed, after washing with anhydrous ethanol that had stopped the oral bleeding, that the

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 1719-1722 www.ijprajournal.com ISSN: 2456-4494

gums had receded so far from all the teeth that their roots could be seen. The image was one of the horror movies, a vampire's mouth looked well than mine. I also mention that the mixture of blood and anhydrous ethanol produced the most beautiful black color. It was around 10:30 in the morning, when I decided to leave the laboratory, taking care not to open my mouth, to the questions of the other colleagues and the French PhD supervisor, amazed that I was leaving so early. I came back to the university after five days, which was necessary for the gums to return to their original shape. Colleagues and staff were worried about my disappearance. Some were sent by the French doctoral supervisor to look for me at home, but I didn't answer them, I was waiting to heal myself first. Healing occurred without any medication. However, they were happy to my return and eager to know on which trip I had gone and with which French girl!?

Biochemical mechanism of action of anhydrous ethanol. Anhydrous ethyl alcohol was able to precipitate proteins (denatured states) from the blood plasma, then the protein precipitates were deposited on the surface of the pores of the damaged blood vessels, plugging them and stopping the blood flow. Precipitation of blood plasma proteins by ethanol may involve the following reactions: a) breaking of hydrogen bonds between groups of protein molecules and water molecules in the blood; b) the protein molecule adds ethyl alcohol; c) the hydrophobic interior of the protein molecule disorganizes and d) the formation of molecular aggregates of dehydrated proteins, disorganized by means of intermolecular hydrophobic bonds or by protein-electrolyte interactions [9].

## III. CONCLUSIONS

An intense hemorrhage of blood was caused by the accidental aspiration of acetone in the mouth during an organic chemistry experiment. The victim's gums and tongue were damaged. The bleeding was stopped with anhydrous ethyl alcohol. Complete healing took five days. A biochemical mechanism has been proposed.

## REFERENCES

[1]. Brătulescu, G., "Organic chemistry. Unconventional methods (in Romanian)," Ed. Sitech, Craiova, 2008, p.14.
[2]. Brătulescu, G., "Organic chemistry. Functions (in Romanian)," Ed. Alma, Craiova, 2023, p. 166.
[3]. Nelson, D.L.; and Webb, B.P., Acetone. In: Grayson M. ed. Kirk-Othmer Encyclopedia of Chemical Technology, 1978, vol. 1, 3rd ed. New York, NY: John Wiley and Sons, 179-191.
[4]. .Budavari, S; O'Neil, M.J.; Smith, A; and Heckelman, P.E., The Merck Index. Whitehouse Station, NJ: Merck & Co., Inc., 1996, p. 12.
[5]. ***Department of Health and Human Services (DHHS), Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Acetone; ATSDR: Atlanta, GA, 1994, p. 79.
[6]. Luttrell, W.E.; and LaGrow, A.L., J. Chem. Health Saf. 2014, 21, 3, 29–31.
[7]. Kumarvel, V.; and Da Fonseca, J. Eur. J. Anaesthesiol., 2007, 24, 805 – 806.
[8]. Mohammadzadeh, H.; Mohammadi, H.; Tavakoli, M.A.; and Sadeghi, S., PBR, 2021, 7, 217-220.
[9]. Morr, C.V.; and Lin, S.H.C., JDS, 1970, 53, 1162-1170.