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Cyclododecane: how dangerous is it?

Martin Adlem

This paper summarises a short presentation delivered at the conference 'Volatile Binding Media in Heritage Conservation'. The author, a health and safety advisor, was asked to comment on the safety of cyclododecane (CDD) to human health, given recent debate about this issue. This paper discusses the possible routes of exposure to CDD for conservators, and looks at these in the light of known safety data. The author concludes that CDD is not hazardous to use.

1 Introduction

There has been much discussion about whether cyclododecane (CDD) is safe to use or not. The material safety data sheets say it is safe and yet some organisations (anecdotally) have banned its use. I was asked to give a short presentation regarding this question, the text of which is reproduced below.

First we need to understand what makes a substance dangerous or not. There are four factors that need to be considered:

- Effect on the body and/or the environment
- Route of entry
- Physical form of the chemical
- Dose

Obviously, the actual effect of the substance is a primary factor. Some substances react with the skin, eyes or mucus membranes to burn or irritate them. Others interfere with a bodily process: for example, lead replaces calcium in the bones and this reduces the long bones' ability to produce red corpuscles, causing an affected person to develop anaemia. This example shows another potential problem: the so-called cumulative poison. Some substances can build up within an organ, and therefore a non-toxic dose taken regularly will build up to a harmful level. Other substances damage particular organs – for example, alcohol (like many solvents) affects the nervous system immediately, but damages the liver over time. The liver is the body's chemical factory and often takes damage from the reactions that occur within it; it is designed to do this and humans typically regrow 80 g of liver each day. However, regular dosage of excessive amounts will overcome this process and cause cirrhosis. Finally, some substances react on a molecular level and actually affect the DNA, causing genetic damage that can lead to mutation, cancer or reproductive difficulties.

How can we find out the effects? Anyone selling a substance must put appropriate hazard warnings on the label and must supply a Material Safety Data Sheet (MSDS, sometimes referred to as an SDS). This document may also contain more detailed toxicological data and will give advice on how to handle the material (although this tends to be generic information and is usually targeted at larger industrial processes).

Another piece of information usually found on an MSDS is how the material attacks the body – the so-called 'route of entry'. There are three basic routes that substances can take to enter or attack the body:

- Skin and eye contact
- Ingestion
- Inhalation

If we can combine this information with the form that the material takes, or that it becomes in the process of use, we can consider the appropriate controls and precautions to take. If the material is absorbed through the skin then gloves and aprons are appropriate, but if it may splash or spray then we would also want a screen or face shield. A material that sublimes (that is, a solid that becomes a vapour without going through a liquid phase) will produce an inhalation risk. A dust in the atmosphere is an obvious inhalation risk, but it will settle and so may produce a risk to skin as well.

The factor seems to be least well known is the concept of dose. Paracelsus (1493–1541) said 'Poison is in everything, and no thing is without poison. The dosage makes it either a poison or a remedy.'[1] If a person ate only carrots, they would soon turn orange and die of carotene poisoning. There is even a toxic dose for water (about 6 litres taken in one dose). Obviously the smaller the dose that causes harm the greater the concern about the material.

2 Cyclododecane safety data

Having considered what makes a substance dangerous, let us now consider what is known about CDD. The information used in this section can be found summarised in the PubChem Open Chemistry Database (2018).

Toxicity results for CDD are given as "LD_{50}, subcutaneous mouse >10,000 mg/kg; LD_{50}, oral rat >10,000 mg/kg". What does this mean? LD_{50} means the lethal dose for 50% of a population of animals that have been dosed with the material in the way described, within a given time period. The dose is quoted as milligrams of poison to kilograms of animal. This allows for the variation in size and allows one to calculate the dose for say a 70 kg man, or at least a 70 kg rat. Therefore assuming our mythical 70 kg rat/mouse/man we are looking at a toxic dose of greater than 700 g, possibly a lot more, that is about a third of a bag of sugar, to be taken as one dose. We are not looking at a harmful chemical here. Tests have also shown no sign of irritancy or corrosion to skin.

The Ames test indicates whether a chemical has the potential to change the DNA and cause mutation. The negative result for CDD shows that it is not a mutagen, and it is therefore incredibly unlikely to have any carcinogenic properties or to affect the reproductive process.

There are a couple of reports that CDD has shown ecotoxic potential, causing damage to fish and algae; however, there are also reports of negative results in similar tests. The positive tests have not been validated and there is no general concern that CDD is toxic to the aquatic environment.

The biggest concern that has been raised is that CDD would appear to be a bioaccumulator – that is, it will build up within living organisms, and that it will be absorbed faster than it is excreted (see, for example Rowe and Rozeik (2008)). This concern is not surprising, as CDD is an unreactive, lipophilic substance. It has no reactive groups and no chemical bonds that are under strain or energetic, therefore the body's metabolic process will not target it for breakdown. It will be attracted to and absorbed in the fat deposits around the body so will tend not to be quickly excreted through the normal channels. It is likely therefore to build up over time, given prolonged exposure. Is this a concern? An example of bioaccumulation is the ecological disaster in Japan, in which mercury was released at low levels as industrial effluent, then accumulated within the food chain as various algae, plants and animals each absorbed it from the water and from the food they ate. Thus, the animal at the top of the food chain (humans) consumed harmful doses of mercury – not enough to kill the people eating the fish down river, but enough to cause frightful genetic mutations and deformity in their foetuses and children. Could the same bioaccumulative effects be seen with CDD? My question would be: what will be the effect of bioaccumulation of CDD? Since it is not harmful of itself until we get to massive dosage, I do not see how will there be a problem with the relatively small amounts used.

There is some anecdotal evidence of conservators feeling unwell (nausea from the smell) and developing headaches after prolonged exposure. CDD does not have a pleasant smell, so nausea from regular exposure is not surprising. Smell and taste are very closely related, so a gag reaction to bad smells is well known. The headaches that some have reported also do not surprise me: the liver will require water to metabolise CDD (as with many solvents and organic materials), which will cause dehydration and its related symptoms (better known as a hangover). Of course, these are my hypotheses and no research has been done to prove them.

In summary, there is no evidence that CDD is harmful – indeed there is much evidence that it is not. As a chemist, I am not surprised by this conclusion: as CDD contains no active groups, it is not reactive. Indeed, it would appear to be broken down in the environment only in the upper levels of the atmosphere where there are concentrations of free radicals to attack it.

1 From Paracelsus' *Third Defence* (1538), as quoted in https://en.wikipedia.org/wiki/The_dose_makes_the_poison (accessed 21 November 2018).

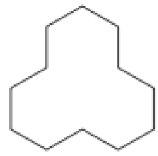
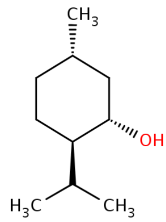
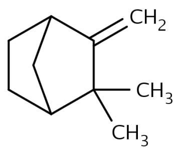
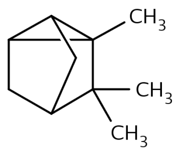
Substance	Hazard warnings	Structure
Cyclododecane $C_{12}H_{24}$	No hazard warnings	
Menthol $C_{10}H_{20}O$	H315 Causes skin irritation H318 Causes serious eye damage H335 May cause respiratory irritation	
Camphene $C_{10}H_{16}$	H228 Flammable solid H319 Causes serious eye irritation H410 Very toxic to aquatic life with long-lasting effects	
Tricyclene $C_{10}H_{16}$	No hazard warnings	

Table 1 Hazard warnings for the volatile binding media most commonly used in conservation

3 Other VBMs

Finally, I would like to carry out a brief comparison with some of the alternative chemicals used by conservators to do similar activities (Table 1).

Menthol and camphene both have distinct health hazards and, looking at the chemical structure, one can see that there are active chemical groups that probably account for them. CDD and tricyclene have no active groups and do not have health hazards recorded on their MSDSs (although I could not find an MSDS for tricyclene). The major difference, chemically, is that tricyclene's molecular structure will hold the molecule in a rigid form whereas CDD will be 'floppy'. The lack of a data sheet and this more rigid form would lead me to choose CDD, but otherwise there seems little difference between them from a health and safety point of view.

In conclusion, to answer the question of how dangerous is CDD: I would say not very! As a health and safety professional, I must stress that no activity can be made risk free, as there is always a risk and the object of health and safety is to try to control that risk to an acceptable level. Sometimes the process of risk assessment – when carried out by people without some level of training and, dare I say it, common sense – leads to conservators worrying unnecessarily about minor hazards (whilst sometimes ignoring the more serious ones). If you have a safety concern that you feel you do not understand, then ask someone who does.

Biographies

Martin Adlem studied chemistry at Southampton University and went on to work for BDH Ltd manufacturing fine chemicals. In 1989, he moved into the Health & Safety department as an internal advisor for the company, initially training and acting as an Occupational Hygienist, and then expanding into more general Health & Safety. He went freelance in 1999 and has worked for 'anyone who will pay' ever since. Clients have included schools, the Institute of Conservation, museums, an orchestra, a port, chemical suppliers, builders' merchants, printers, estate agents, retail companies and a variety of small construction companies.

Email: keptin@globalnet.co.uk

References

PubChem Open Chemistry Database (2018), 'Cyclododecane: compound summary for cid 9268', http://pubchem.ncbi.nlm.nih.gov/compound/cyclododecane (accessed 1 November 2018).

Rowe, S. and Rozeik, C. (2008), 'The uses of cyclododecane in conservation', *Reviews in Conservation* **9**, pp. 17–31.