



How toxic is it?

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How 'toxic' a chemical is depends to a great extent on the definition of the word. This article discusses the relative danger from toxicity of some typical chemicals and tries to put the dangers in perspective.

Everybody agrees that cyanides are dangerously toxic and treats them with respect. By one commonly used measure of toxicity vanadates are nearly as toxic as cyanides, yet they are not regarded with the same awe. Barium compounds are widely known to be toxic and again treated as such; sodium nitrite has similar toxicity ratings yet is treated in much the same way as we would sodium nitrate. What does all this mean? Are we too concerned about cyanides and barium salts or are we running a great risk in our laboratories by underestimating nitrites and vanadates?

First let us widen the comparison of (relatively) common chemicals and see how they rank according to their toxicity measured in various ways, by 'LD₅₀', HSC Control limits and EEC labelling classification. The list is chosen to cover a range of toxicities. If it seems idiosyncratic, that is due to the need to include substances for which the data available is complete.

Ranked in order of LD₅₀ for rate my list is as follows [1]:

(Most toxic)

potassium cyanide (about 10 mg kg⁻¹)
vanadium(V) oxide
mercury(II) chloride
silver nitrate(V)
sodium nitrate(III) (nitrite)
barium chloride (about 100 mg kg⁻¹)
potassium chromate(VII)
lead(II) nitrate(V)
copper(II) sulphate(VI) (about 1000 mg kg⁻¹)

(Least toxic)

One might think that the levels of dust allowed in air would follow the same order but here is the list ranked according to Recommended or Control Limits set by the HSC[2];

(Least allowed)

silver nitrate(V) (0.01 mg m³)
mercury(II) chloride

lead(II) nitrate(V)
barium chloride (0.05 mg m³)
vanadium(V) oxide
copper(II) sulphate(VI)
(Most allowed)
potassium cyanide (0.5 mg m³)

Sodium nitrite does not have a Recommended Limit set. It should be emphasized that levels well below those given should be sought whenever reasonably practicable.

Yet another classification is implied by the labelling regulations.

Using these our list becomes something like:

Toxic

mercury(II) chloride
potassium cyanide
sodium nitrite

Harmful (a lesser degree of toxicity)

barium chloride
lead(II) nitrate(V)
vanadium(V) oxide

Corrosive

silver nitrate

Irritant (effectively a lesser degree of corrosiveness)

potassium chromate(VII)

(Copper(II) sulphate requires none of these warning signs; within groups the order is alphabetic only.)

The preceding argument has used some sophisticated concepts without explanation. LD₅₀ is, loosely, the dose required to kill half of a population of test animals expressed in tenths of the amount given per unit body weight. LD₅₀s can be measured using several different methods of administering the chemical; the figures I have used here relate to oral administration. Quite apart from the ethical considerations, LD₅₀ is now regarded as having limited validity in assessing toxicity but for many chemicals it is all that is known. Indeed, in attempting to compare toxicities of chemicals as varied as the list I have chosen, LD₅₀ for rates is usually the only parameter known for the whole set.

A far more relevant measure is the LD_{LO} for humans. This is the lowest known fatal dose, again expressed in terms of amount taken per unit body weight. Not surprisingly, however, this figure is not recorded for the vast majority of chemicals. If we look at the cases from our list of chemicals where human LD_{LO} is known the following figures emerge. (I have given the estimated fatal dose for a 75-kg man.) Of course these figures are open for revision downwards! Consideration of the likely fatal doses of solutions of these chemicals reveals that a 0.01 mol dm⁻¹ solution even of cyanide does not necessarily present too serious a risk.

Interestingly a lowest known toxic (not fatal) dose of 14 mg kg⁻¹ (equivalent to about 1 g for a 75 kg man) is reported for sodium nitrite, suggesting that, despite its low lethal dose for rats, it may not be as bad as barium chloride for man.

Substance	Fatal Dose		
	Solid	Solution	
		1 mol dm ⁻¹	0.01 mol dm ⁻¹
Potassium cyanide	200 mg	3 cm ³	300 cm ³
Barium chloride	900 mg	4 cm ³	400 cm ³

A major problem with lethal dose measurements such as LD₅₀ is that they take no account of long-term or sub-lethal effects. Lead salts really are of relatively low toxicity if death is the only criterion but, as is well known, they are cumulative poisons causing a variety of disabling symptoms. On the other hand, the ingestion of sub-lethal doses of cyanide is probably long-term effect. (The cyanide ion features in some body chemistry at very low concentration in any case.)

The surprisingly high limit for cyanides in the air is explained by such considerations. These limits are set with the intention of preventing ill-effect even to workers who spend a lifetime working with the chemical and could be exposed to such levels eight hours per day for five days a week. Chemicals that can accumulate in the body by this route or that can cause serious lung or respiratory tract disease through persistent irritation have low limits set. Cyanides, on the other hand, so long as the dose is well below the lethal level, should not carry such long-term risks. At the level of 5 mg m³ set for cyanides it would be difficult to absorb as much as 5 mg in one hour (even assuming all that in the air breathed was absorbed). This is well below the fatal dose of about 200 mg. In any case, on a time scale such as this the body would safely metabolize the cyanide as it was absorbed [3].

Why then are we so careful with cyanides and less so with nitrites and vanadates? I think the answer is partly emotional; cyanide is well-known as a murder weapon and death is known to be swift if a fatal dose is taken, with little time for medical intervention. Other factors may include the powdery nature of potassium cyanide and its low density. It is easy to disperse some in the air if it is handled carelessly and (if a fume-cupboard is not used) the well-known almond taste can become worryingly apparent on the lips etc.

It is difficult to place the toxicity of vanadium compounds in context as information on poisoning by their ingestion in man is scanty and contradictory. It is known that, like cyanides, vanadium salts are acute only poisons — if you survive there will be no long-term effects. It is interesting in view of this that tests have shown that, although most is eliminated rapidly, about ten per cent of ingested vanadium remains in the body, presumably deposited in a harmless form in bone etc. It is known that the highest tolerated dose and toxic dose do not differ greatly and 100 mg per day of one vanadium salt has caused no ill effect to volunteers (!) over some time. Animal tests suggest that the various compounds vary greatly in their toxicity. Ammonium vanadate killed fifty per cent of rats at 18 mg kg⁻¹: sodium vanadate, on the other hand, only killed the most susceptible rats in a test at 200 mg kg⁻¹ [4].

Another element with surprisingly varied toxic effects in different compounds is mercury. A very full and interesting discussion is given in Hazards in the Chemical Laboratory from the RSC [5]. Some organic mercury compounds are severely neurotoxic; others have been used in the past as diuretics without too severe side effects. Even the

mercury alkyls vary widely in their toxicity depending upon the particular alkyl group(s) involved with the methyl mercury ion causing severe brain damage. On the other hand, the inorganic compounds cause a range of disabling symptoms but are not appreciably toxic to the brain. Mercury(I) chloride is 60 times less toxic than mercury(II) chloride, partly due to its lower solubility.

Nitrate and nitrites illustrate well that there can be no absolute demarcation between toxic and non-toxic substances. It has been shown above that sodium nitrite is poisonous enough to warrant special care in its handling in the laboratory yet low levels are used in curing bacon. Sodium nitrate is also used in some meat curing techniques and is generally regarded as relatively safe yet concern is growing about the toxic effects (especially in babies) of relatively low levels of nitrate in water supplies. (There is, of course, also some concern about nitrites in bacon because they may take part in carcinogen-forming reactions in the stomach.) Perhaps we over-react to poisoning risks. Even moderately careful laboratory techniques will prevent poisoning by vanadates, nitrites and barium salts. (Always assuming, of course, that mouth- pipetting is quite outlawed!) The same cannot be said of the inhalation risks presented by chlorine and tetrachloromethane outside of an efficient fume cupboard.

There is a need to relate the hazards associated with a chemical with the ease of control of that hazard. Solutions are generally easily controlled assuming they are labelled carefully to alert others to any danger. Dusts and vapours, on the other hand, can easily become uncontrolled so light, powdery, solid chemicals such as phenylhydrazine need special care to avoid the hazards they present. (The hazard may be other than toxicity, calcium oxide has caused severe eye damage due to its corrosive nature and light, easily- blown powder form.) Similarly, volatile hazardous chemicals such as phenylamine or iodine need extra care and the use of a fume cupboard in their handling is important. Many chemicals that have toxic vapour also can poison by skin absorption and it should be remembered that a fume cupboard will not necessarily protect against this danger.

In conclusion I would like to suggest that the EEC-inspired labelling system now used on all laboratory chemicals is a good guide to the care required in handling them. In deciding on the classification (TOXIC, IRRITANT, etc) the experts involved have taken the above considerations, and others, into account. All chemicals labelled toxic should be handled with great care. It should go without saying that good laboratory technique in handling all substances is the safest course.

This article was published in SSR, No. 252, March 1989, but was reviewed in July 2015 and is still considered to offer a generally valid analysis. However, readers need to be aware that whilst the broad principles discussed here are still relevant, there have been significant changes in the legislation about labelling chemicals and in a few cases the hazards presented by some chemicals (eg tetrachloromethane) have been re-assessed and their suitability for use in schools and elsewhere re-considered. Note also that some of the figures quoted for LD50 and dust control limits (now, Workplace Exposure Limits) have been revised (some upwards, some downwards) and should not be relied as current.

The author no longer works for CLEAPSE (which is now CLEAPSS).