CURRENT SCIENCE

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NEWS

The Bhopal tragedy: Mechanism of the transport of MIC to various organs

The Bhopal disaster, in which about 3500 inhabitants of that city died and hundreds of thousands were seriously ill after breathing the toxic gas that engulfed the city, is perhaps the worst industrial accident the world has ever known. It occurred on 2 December 1984 when 30 to 40 tonnes of methyl isocyanate (MIC) leaked (from the Union Carbide Chemical Factory). Many people who breathed the MIC died of asphyxiation as the lungs got filled with fluid due to pulmonary oedema.

MIC damages the lungs, attaching itself to the sulphur atoms of the proteins in tissues and membranes. The lungs of people who survived became permanently scarred. But what appeared mysterious was the diversity of unexplained symptoms in organs other than the lungs. The organs and tissues damaged ranged from the eyes, heart, bones, muscles, gastrointestinal tract. Thousands of survivors had their immune systems impaired, or had reproductive problems. Spontaneous abortions too were common, and children born since the disaster suffered from a range of complex ailments.

Some possibilities of what might have happened have been described by Baillie and Slatter (*Chemical Research in Toxicology*, 1991, **4**, 157; *Accounts of Chemical Research*, 1991, **24**, No. 9). They feel that glutathione which is abundant in the fluid which lines the lung possibly plays an important role in transporting the toxic material to all parts of the body.

The first clue that MIC got distributed rapidly and extensively throughout the body came from the experiment of B. K. Bhattacharya and his colleagues at the Defence Research Establishment, Gwalior, India, almost immediately after the disaster, when they exposed rats to air-borne MIC labelled with radioactive carbon. The radioactive breakdown products of MIC appeared in the urine, bile and tissue proteins of the animals. The means by which the toxin spread was not identified.

Glutathione is vital for the survival of all animals. That glutathione may be the mode of transportation was suspected by many workers. It conjugates with toxic chemicals in our blood and tissues and carries them out of the body through the excretory organs. Baillie and Slatter in a series of experiments showed that the glutathione–toxin conjugate sometimes breaks down much before the complex gets excreted. Hence a toxic agent is liberated far from where it was originally formed. The actual reason why the glutathione–MIC conjugate breaks down easily has not been identified, except that the breaking up of the conjugate readily takes place under alkaline conditions, which is known to occur in living tissues. Glutathione therefore acts as a vehicle to transport the toxic agent all over the body. Baillie and Slatter also found glutathione linking MIC and cysteine; living cells were seriously harmed when their toxic cargo of MIC was unloaded into proteins and membranes of the cells.

Even if the mechanism suggested is valid it is probably of no assistance to the survivors of the Bhopal tragedy because the damage they have suffered may be irreparable. It does, however, raise hopes for developing antidotes to compounds like MIC.

S. Ramaseshan

RESEARCH NEWS

Liquid crystals for visual differentiation of enantiomers

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Crown ethers are cyclic compounds in which oxygen atoms link ethylene units. Generally these can complex with metal salts and ammonium salts. The positive ions of these salts get bound in the cavities of the crown ethers. Chiral (optically active) crown ethers which exhibit enantioselectivity in complexation with chiral alkylammonium salts are known[1]. A chromogenic crown ether[2] can be obtained by attaching the crown ether to a dye When different

metal ions are complexed with such crown dyes, the wavelength of maximum absorption in the UV/VIS spectra shifts by different extents[3]. Thus complexation of different metal ions in the molecule can be made visual by a colour change.

A chiral chromogenic crown ether complexing with two enantiomers of an alkylammonium salt would result in diastereomeric products. The wavelengths of maximum absorption of these diastereomers could be different. If this difference is large enough, a visual distinction through colour would be possible between the diastereomers and hence the enantiomers. This idea of making a visual distinction between enantiomers and relating the differences to their absolute configurations has been pursued for some years[4]. The best results obtained using chiral crown dyes yielded shifts of 11 nm in the absorption maxima between complexes with enantiomeric chiral amines[5]. However this difference could not afford a visual distinction.

The desired differentiation was achieved by using the optical properties of cholesteric liquid crystals[6]. In the cholesteric phase, the molecules lie parallel to a common axis which itself twists in an orthogonal direction (Figure 1). The cholesteric phase strongly reflects in a band of wavelengths whose value depends on the pitch of the helix. For an appropriate steroidal crown ether, complexation with metal ions in a cholesteric matrix affected the pitch and hence the wavelength of maximum reflection[7]. The pitch of the helix was also found to be affected by the size of the counter-anions.

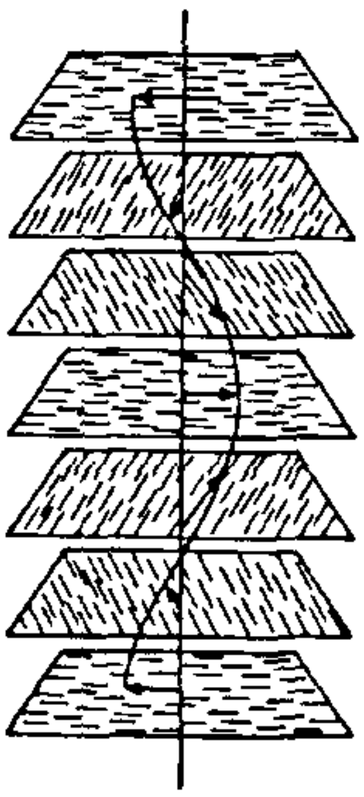


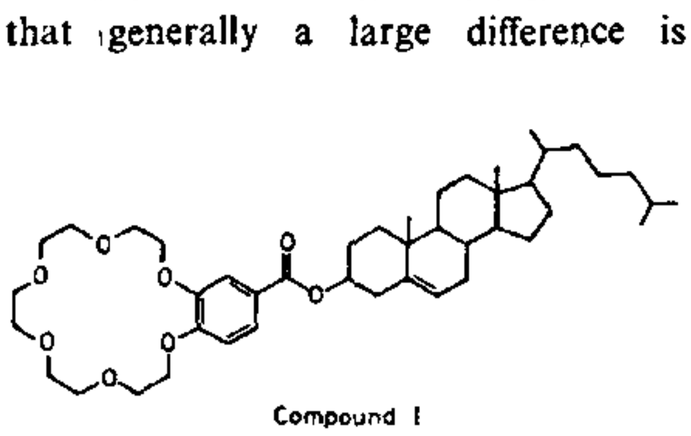
Figure 1.

The same system was then tested for differentiating enantiomers[6]. Thus the steroidal crown ether I (see Figure 2) was complexed with D and L enantiomers of some ammonium salts. A mixture of cholesteryl nonanoate (II) and cholesteryl chloride (III), which exhibits the cholesteric phase at room temperature, was used as a matrix. The shifts in the wavelengths of maximum reflection for the diastereomers were measured spectrophotometrically. The results obtained are shown in the table. In the case of the ammonium salt of phenylalanine methyl ester the difference is 64 nm and thus observable by the naked eye. For *N*,*N*,*N*-trimethyl-1-phenylethylammonium iodide, which does not complex with the crown ether, no shift in the reflection wavelength is observed. Hence an interaction between the ammonium ion with the crown ether is necessary. Also, when a methyl group replaces the steroidal moiety of compound I no shift in the wavelength is observed. This indicates the importance of linking the steroidal moiety to the crown ether. From the table it is seen that generally a large difference is obtained for ammonium ions having bulky substituents. Also, though the shift in the wavelength of reflection moves in the same direction in a few cases, the wavelength of reflection is always longer for the D isomer.

Table. Shift (nm) of λ_R induced by added amine hydrochlorides $(R^*NH_3^+ Cl^-)^*$

$R^*NH_3^+ Cl^-$	D Isomer	L Isomer
1-Phenylethylamine hydrochloride	+81±3	+25±3
Phenylglycine methyl ester hydrochloride	+39±7	−26±3
Alanine methyl ester hydrochloride	−11±1	−16±4
Phenylalanine methyl ester hydrochloride	+45±7	−19±4
Valine methyl ester hydrochloride	+35±2	−1±1
Tryptophan methyl ester hydrochloride	+31±1	−6±7
N,*N*,*N*-Trimethyl-1-phenylethylammonium iodide	−1±4	−5±5

*1:II:III = 9:12:8. $[R^*NH_3^+ Cl^-]/[I] = 0.8$. The λ_R values are the average of four repeated runs. The λ_R in the absence of $R^*NH_3^+ Cl^-$ is 455 nm.



Compound I

Figure 2.

It may be noted that the conventional chromophoric dye is not required as the liquid-crystalline system itself simulates a chromophore. Reports of this system being used to differentiate enantiomers of alkali metal salts of mandelic acid have also appeared[8]. In conclusion it can be said that a suitable cholesteric liquid-crystal matrix enables differentiation of enantiomers by the colour of their crown-ether complexes.

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