applied excellence

Advanced techniques in routine use at The Radiochemical Centre.

Described below are just two examples of the many up-to-date techniques, which have been pioneered or applied for routine use at The Radiochemical Centre. These developments are part of our constant endeavour to maintain our position at the forefront of the specialised field of tracer methodology, so that we can continue our supply of radiochemicals of the highest quality and technical specifications.

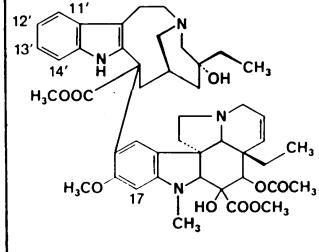
Distribution of labelling in tritium compounds

Modern techniques for the production of tritiated compounds are more sophisticated than those used in the early days of tritium labelling, and produce compounds labelled in specific positions rather than generally labelled. Nevertheless, it is necessary for many tracer applications of tritium compounds to know the *precise* position and configuration of the tritium labels. Traditional chemical methods of doing this are tedious and time consuming and subject to considerable error, and so the routine supply of such information has until recently not been possible.

The Radiochemical Centre, in collaboration with the University of Surrey, has developed over the past eight years the technique of tritium nuclear magnetic resonance (tnmr) spectroscopy for this purpose. This method is much quicker and more accurate than the traditional chemical or biochemical methods for determining distribution of tritium labelling.

It is now used routinely to establish the distribution of tritium labelling produced by the usual methods of tritiation employed at The Radiochemical Centre. We supply accurate details as to the position and configuration of the tritium labels for an increasing number of our labelled compounds.

A number of examples are given below:



[G-³H]VINBLASTINE
Code TRK.507
17 ..... 44% 11' 8%
12,13' ..... 46% 14' 2%

[1β, 2β(n)-³H]TESTOSTERONE
Code TRK.162
1α ..... 5.9% 2α 8.2%
1β ..... 46.0% 2β 39.9%

[6-³H]BENZO[a]PYRENE
Code TRK.501
6 ..... >95% 1 ..... <5%

D-[2-³H]GLUCOSE
Code TRK.361
2(α) ..... 40% 2(β) 60%

L-[3,4(n)-³H]VALINE
Code TRA/K.533
2 ..... 8% 4 ..... 64%
3 ..... 28%

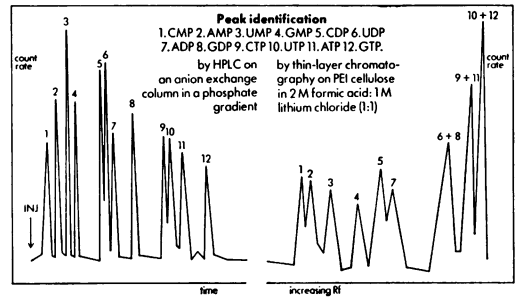
High performance liquid chromatography (HPLC)

This relatively new development of column chromatography is carried out using high efficiency microparticulate column packings of closely defined size.

Chromatography is carried out under pressure to ensure good flow rates and reduce diffusion of separated compounds. Dead volumes are kept to an absolute minimum. The result is that many separations can be carried out more quickly and with better resolution than with previously used chromatographic methods such as thin-layer chromatography or conventional column chromatography.

Work aimed at developing the applications of this method to radiolabelled compound separations is still in progress, but The Radiochemical Centre is already using the technique in many of its production processes, and in analytical applications. The result is purer compounds for the customer and greater efficiency of working.

The example illustrated below illustrates the clear superiority of HPLC when used as an analytical tool. The mixture used comprised the tritium labelled mono-, di- and triphosphates of adenosine, cytidine, guanosine and uridine, and all are clearly separated in the HPLC system.



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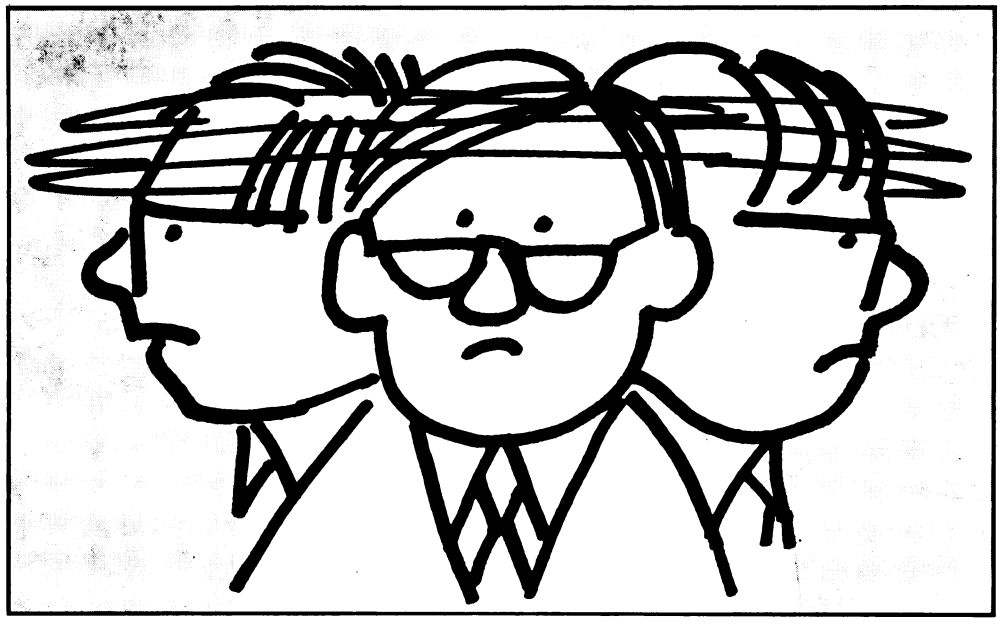
1465/11/77

The latest of our publications is as follows:
AL-RAWI, J.M.A., BLOXSIDE, J.P., ELVIDGE, J.A., JONES, J.R., CHAMBERS, V.E.M., CHAMBERS, V.M.A. and EVANS, E.A., Steroids vol. 28 (3), p.p. 359-375, 1976.



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0880

2,3-Dimercapto-1-propanesulfonic acid, sodium salt

Heavy-metal chelating agent: $HSCH_2CHCH_2SO_3Na$ (SH)

Increasing awareness of the chemical pollution of our environment results in greater efforts to study and eliminate the sources of the pollutants, as well as to eliminate their effects. Heavy-metal poisoning is an effect of such environmental or industrial pollution. Moreover, heavy-metal poisoning is encountered in the clinical use of heavy metals as chemotherapeutic agents. Thus, the efficacy of **2,3-dimercapto-1-propanesulfonic acid, sodium salt (DMPS, Dimaval®)** in the treatment of poisoning by inorganic[1] and organic[2] mercury, arsenic,[3] antimony,[4] gold[5] and cadmium[6] has been studied.

The influence of several chelating agents* (administered intraperitoneally in rats) on the excretion of inorganic mercury (as $^{203}HgCl$) and its distribution in the organs was studied.[1] 2,3-Dimercapto-1-propanol (British Anti-Lewisite, BAL) and D-penicillamine were effective, but the water-soluble **DMPS** significantly increased the urinary excretion of Hg, while lowering its concentration in the organs.[2]

In the case of methylmercury (as $CH_3{}^{203}HgCl$) intoxication in rats, **DMPS** proved to be clearly superior to chelating agents of known effectiveness, such as DL-*N*-acetylhomocysteine thiolactone and D-penicillamine, in enhancing cumulative excretion of Hg.[2]

Hauser and Weger have reported that **DMPS** was very effective in the treatment of arsenic poisoning in mice.[3] Results showed a therapeutic index of 70 for **DMPS**, compared with 3 for BAL.[3]

DMPS was compared with D-penicillamine in reducing toxicity associated with tartar emetic (antimony potassium tartrate) in the treatment of experimental schistosomiasis.[4] **DMPS** effectively reduced the acute toxicity of tartar emetic by one-half, and thus, was clearly superior to D-penicillamine in reducing tissue antimony levels.[4] As an adjuvant to tartar emetic as an antischistosomal agent, **DMPS** was also superior to D-penicillamine.[4]

DMPS was effective in reducing the concentration of gold in rats injected with Auro-Detoxin®, and significantly improved urinary excretion of gold, as compared with D-penicillamine.[5] Concentration of gold in the skin and kidneys was markedly reduced.[5] **DMPS** also promises to be an effective replacement for BAL in chrysotherapy because it is much less toxic[5] and is given orally rather than by i.m. injection as is necessary for BAL.

It was found that in mixed-ligand therapy in acute cadmium poisoning in rats, ethylenediaminetetraacetic acid-**DMPS** combination resulted in 100% survival.[6]

The water solubility of **DMPS**, its low toxicity and its effectiveness as a heavy-metal chelating agent combine to make it a potentially useful agent for heavy-metal detoxification.

References:

1) B. Gabard, *Arch. Toxicol.*, 35, 15 (1976).
2) B. Gabard, *Acta Pharmacol. Toxicol.*, 39, 250 (1976).
3) W. Hauser and N. Weger, *7th International Congress of Pharmacology*, Paris, July 16-21, 1978, p. 764, abstract no. 2382.
4) M.T. Khayyal, F.H. Kemper, H.P. Bertram, and M. Renhof, *ibid.*, p. 55, abstract no. 132.
5) B. Gabard, submitted for publication.
6) J. Schubert and S.K. Derr, *Nature*, 275, 311 (1978).

19,452-2	**2,3-Dimercapto-1-propanesulfonic acid, sodium salt** (DMPS, Dimaval®)	**1g $12.00**
A1,660-2	DL-*N*-Acetylhomocysteine thiolactone*	**25g $6.00; 100g $16.50**
A1,900-8	*N*-Acetyl-DL-penicillamine*	**5g $15.00; 25g $49.50**
12,292-0	2-Aminoethanethiol hydrochloride* (cysteamine)	**25g $12.50; 100g $35.00**
18,665-1	18-Crown-6*	**5g $5.50; 25g $24.00**
D12,880-5	2,3-Dimercapto-1-propanol* (BAL)	**10g $14.00**
16,498-4	8-Hydroxyquinoline*, 99+%	**25g $3.50; 100g $8.25**
H5,875-7	8-Hydroxyquinoline-5-sulfonic acid dihydrate*	**100g $7.40; 500g $33.00**
P40-3	D-Penicillamine*	**1g $5.60; 5g $20.60; 25g $88.00; 100g $302.50**
13,209-8	Triethylenetetramine*	**500g $6.00; 3kg $23.50**
16,196-9	Triethylenetetramine tetrahydrochloride* (crystallized)	**25g $16.80; 100g $48.00**

*These were among 15 chemicals tested.

Note! Our products are sold for research only and not for drug use.

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