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 endeavor to maintain our position at the forefront of the specialized 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 (nmr) 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.

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.

Labelled compounds
you can trust

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4'-Methylphenazone

Internal standard for phenazone

**Chemical Structure**

![Chemical Structure](image)

**Phenazone**

**4'-Methylphenazone**

The well known antipyretic and analgesic drug phenazone (antipyrine) is well absorbed and extensively metabolized in the body with only minimal amounts being excreted unchanged in the urine. For these reasons, as well as for its negligible protein binding, the phenazone half-life has been used to investigate individual variation, disease, drug interactions, and environmental factors on hepatic microsomal drug metabolism in man.

One disadvantage of using phenazone in drug metabolism studies is that it has several metabolites. These include 4-hydroxyphenazone (mainly as the glucuronide), a primary metabolite which parallels the time course of disappearance of phenazone from plasma, 1-phenyl-3-hydroxyethyl-2-methyl-3-pyrazolin-5-one, 3-carboxy-2-methyl-1-phenyl-3-pyrazolin-5-one, and 3-methyl-1-phenyl-5-pyrazolone (norphenazone).

Present analytical techniques employed for the determination of phenazone and its metabolites are not reproducible for half-life determinations.

A sensitive and specific gas-liquid chromatographic method for phenazone has been developed, employing 2,3-dimethyl-1-(4-methylphenyl)-3-pyrazolin-5-one (4'-methylphenazone) as the internal standard. This method proved to be more sensitive than older techniques and could be applied to samples containing only 0.5 μg/ml. This technique rendered good reproducibility of plasma half-lives.

The method was modified and applied to the determination of phenazone levels in blood and plasma. Similar phenazone half-lives from plasma, blood and saliva were found using the internal standard method. Thus, phenazone now seems to be a suitable tool for pharmacokinetic studies.

**References**


21,405-1 2,3-Dimethyl-1(4-methylphenyl)-3-pyrazolin-5-one (4'-methylphenazone) 1000 μg $22.00

Aldrich offers many other drug reference standards, for instance:

- 19,452-1 10,11-Dihydrocarbamazine ......... 1000 μg $7.25
- 16,350-3 α-α-Dimethyl-β-ethylamincinnimide
- 250 μg $19.40; 1 g $51.10
- 19,496-4 2-Ethyl-2-(p-tolyl)malonamide ......... 250 μg $6.65
- 1 g $19.35
- 16,145-4 5-(4-Methylphenyl)-5-phenylhydantoin
- 1 g $7.80; 5 g $20.15
- 19,494-8 4-Methylpridimide ......... 250 μg $11.20; 1 g $29.65
- 19,495-6 α-Methyl-α-propylaminimid ..... 250 μg $9.70
- 1 g $30.25
- 20,841-8 N-Propionylprocanamide hydrochloride
- 2 g $13.20; 10 g $44.00

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