Radioisotopes

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The synchrocyclotron at IKO came into operation in 1949. The nuclear particles accelerated in a cyclotron can be made to collide with atomic nuclei of a suitably selected material in a target placed in the cyclotron. Radioactive isotopes are then formed as a result of the collision.

By 1946 two Philips scientists, A. H. W. Aten (who was later to become the director of the Institute's radiochemical department) and F. A. Heyn, had already published two articles in Philips Technical Review on the use of a cyclotron in research: 'The use of isotopes as tracers' [1] and 'The technique of investigations with radioactive and stable isotopes' [2]. In 1948 Aten left Eindhoven for the Institute, and he was soon able to put his ideas into practice there. In 1951 he was followed by a team of seven, led by J. Halberstadt, from what was then Philips-Roxane. The group was given control over their own budget for laboratory space and chemicals; it was modest even for the time: about 10,000 guilders or $2600 at 1951 rates.

The chemical department of the Institute, who were doing fundamental scientific research, and Philips-Roxane, who were making isotopes for medical and industrial use, had a great many interests in common. These included finding the best nuclear reaction for making a particular isotope, designing suitable targets for the irradiation of particular materials, the purification of the irradiated material by means of fast separation techniques and the preparation of isotopes without a 'carrier' (added nonradioactive material with the same chemical properties as the radioactive material). This led to intensive cooperative use of the cyclotron, and this continued even after Philips-Roxane, who in the meantime had become Philips-Duphar, had purchased other premises in Amsterdam in 1959. In the period between 1950 and 1970 the cyclotron was run for more than 8500 hours, often at night, to provide irradiation for the production of radioisotopes for Philips-Duphar.

Another form of cooperation was the help given by Institute analysts in tasks such as cutting irradiated lead targets for the manufacture of bismuth-206 (20 guilders danger money was paid for this) and in processing isotopes such as iodine-131, caesium-137, iridium-192 and gold-198 that had been made in a nuclear reactor elsewhere. In 1958, for example, about 500 curies (1 curie = 3.7 \times 10^{10} \text{ Bq}), in the form of all kinds of isotopes, was despatched from the Institute by car, train, bicycle and aeroplane. A general survey of the activities of Philips-Roxane is given in the thesis by H. H. P. Moeken [3]. He describes the results of 45 nuclear reactions of deuterons with various materials as a function of the irradiation energy. Cost/benefit analyses are also given.

In 1954 the Netherlands Organization for the Advancement of Pure Research asked Philips-Roxane and the Institute to organize a joint course on radioisotopes. The course was to give people working with radioisotopes (doctors, hospital dispensers, students, salesmen) thorough and detailed information about radioisotopes and methods of using them. By 1980 about fifty two-week courses had been held; in recent years instruction courses have been given for examinations leading to the qualification 'Manager of a low-radiation-level radiological laboratory'. This cooperative scheme came to an end recently when the Philips-Duphar isotope activities were taken over by Byk-Mallinckrodt: the courses are now run entirely by the Institute.

Examples

A list will now be given of some of the more important isotopes that have been manufactured for medical and biological applications; some of them are still being manufactured today.

Sodium-24 (half-life $T_{1/2} = 15$ hours)

Sodium-24 can be made from natural sodium in a nuclear reactor. When this isotope was required in the Netherlands, the irradiation was carried out in Kjeller, Norway and the isotopes were transferred from the Netherlands by air.

In about 1952 sodium-24 was required for osmosis research in Denmark, but without a 'carrier', i.e. pure radioactive sodium. When natural sodium is irradiated in a nuclear reactor the radioactive sodium

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This article arose partly out of discussions with W. B. Huising (formerly with Philips-Roxane and Philips-Duphar, now with Byk-Mallinckrodt) and J. Visser (IKO).
formed cannot be separated by chemical methods from the residual natural sodium — the major part of the end-product. The radioactive sodium was therefore made in Amsterdam by irradiating aluminium-27 with deuterons in the cyclotron, to form sodium-24 with the emission of a helium and a hydrogen nucleus. The radioactive sodium was separated from the remaining aluminium in a Dowex column (this took a great deal of time: at a flow rate of one drop per second the sodium was obtained from the column after five and a half hours, i.e. after 20000 drops). The isotope was then flown to Denmark; this meant that preparations of this isotope were travelling back and forth in aircraft flying between the Netherlands and Scandinavia.

Chlorine-34 \( (T_{1/2} = 32 \text{ minutes}) \), chlorine-38 \( (T_{1/2} = 37 \text{ minutes}) \)

The isotopes were prepared by irradiation of sodium chloride, distillation of the chlorine into a sodium-iodide solution and boiling off the iodine. The solution had to be sterile, with the same osmotic pressure as human blood. The solution was used in the teaching hospital of the University of Amsterdam for research work on blood circulation.

Gallium-67 \( (T_{1/2} = 3.2 \text{ days}) \)

This isotope, made from zinc, was used for investigating bone tissue. Interest in the isotope gradually decreased, but has revived recently, this time for locating tumours other than in bones. The methods used earlier are again being used in its preparation.

Iodine-131 \( (T_{1/2} = 8 \text{ days}) \)

In about 1950 di-iodide fluorescein, tagged with iodine-131, was used as a detector and localizer in the investigation of tumours, with a dog as the experimental animal \[^4\]. This investigation also involved the Physiological Laboratory of the University of Amsterdam.

Gold-198 \( (T_{1/2} = 2.7 \text{ days}) \)

Hundreds of curies of gold-198, prepared in a nuclear reactor, have been processed at the Institute into colloidal gold solutions stabilized with glucose and gelatin. The solution was used for locating liver and spleen abnormalities and for treating ascites in the abdominal cavity (as a result of malignant tumours), where the colloid adheres to the abdominal wall.

Bismuth-206 \( (T_{1/2} = 6.2 \text{ days}) \)

Formerly bismuth-206 was an isotope very much in demand, particularly for the therapy of chronic lymphatic leukaemia: in dissolved form ("liquid radium") it could be distributed through the lymphatic glands. When the cyclotron was built at Philips-Duphar, it was expected that almost half of the production time would be devoted to this isotope. Within two years, however, all interest had vanished.

Thallium-201 \( (T_{1/2} = 3 \text{ days}) \)

This isotope is much in use at the present time, particularly for heart studies. It is prepared by irradiating thallium with protons in a cyclotron and by separating the lead-201 formed \( (T_{1/2} = 9.4 \text{ hours}) \). The lead-201 decays into thallium-201 and this is then isolated again.

Today, Byk-Mallinckrodt's modern factory in Petten remains as an indirect inheritance — via Philips-Roxane and Philips-Duphar — of the cooperation between Philips and IKO in radioisotope work, an activity that started in about 1950 through the interest and efforts of a tiny group of people.