Serial No.	Chemical structure	Inhibitory concentration* (gm./100 ml.)	Chemotherapeutic activity	Intravenous toxicity		Hæmolytic ratio ('Triton *A*20'=1)
				LD_{50} in mgm.† (single injection)	Liver damage (course of injections of 15–25 mgm.)	
*D*2	I; n = 0, 1, 2, 3, etc.	1·0	+	>75·0	0	0·02
*D*2*a*	I; n = 2, 3, 4, etc.	1·0	+	>62·5	0	0·02
*D*3	*p*-Octylphenol polyoxyethylene ether	0·01	Too toxic for test	3·0		1,600
*D*4	I; n = 0	1·0	0	12·5		500
*D*9*a*	I; n = 1	>1·0	0	12·5	± (7·5 mgm.)	1·0
*D*10	I; n = 2, 4, 6, etc.	>1·0	+	>50·0	0	0·25
*D*10*a*	I; n = 2 (substantially)	>1·0	+	>50·0	0	0·25
*D*10*b*	I; n = 4, 6, etc. (and unexpelled I; n = 2)	>0·5	+	>25·0	0	0·25
*D*11	I; n = 2 (substantially)	>1·0	+	>25·0	±	
*D*12	I; n = 3 (substantially)		+	>50·0	±	
'Triton *A*20'		0·7	+	>25·0	±	1·0

* No growth at two weeks in synthetic medium containing 2·5 mgm. albumin and 0·0008 mgm. (moist weight) tubercle bacilli per ml.
† Mice weighed 18–20 gm. each.

'Triton *A*20' had a low hæmolytic activity *in vitro*, this finding being in agreement with other workers[11]. Tests with our products in comparison with this agent showed that *D*3 was 1,600, and *D*4 500, times as hæmolytic, while *D*9*a* had the same activity. The other products showed somewhat lower hæmolytic activities than 'Triton *A*20', particularly *D*2 and *D*2*a*, which gave values of one-fiftieth or less. Mouse serum was never seen to be pigmented even after the largest doses of 'Triton *A*20', or of any of the products that showed equal or lower hæmolytic activity *in vitro*. Capillary permeability tests with intravenous pontamine blue revealed a contrast between *D*4, which markedly increased leakage of the dye through the vessels into the tissues, and 'Triton *A*20', *D*2 and *D*2*a*, which showed no such effect.

Discussion

Within the limits of the present study, the products tend to be less toxic, and more active against tuberculous infection, as molecular size increases. Antituberculous activity in compounds of formula I may perhaps be limited to a definite range of values of n: it is worth noting that an increase of one unit in n raises the molecular weight by about 1,000.

Marked bacteriostatic activity *in vitro* was found only with the simplest compound (*D*3), which was too toxic to be tested chemotherapeutically. All our other products, both active and inactive *in vivo*, showed an approximately equal bacteriostatic power of a low order. It remains doubtful, therefore, whether direct bacteriostatic action is responsible for the antituberculous effect in mice, in spite of the high concentrations attainable in their blood. The relevance of the remarkable hyperlipæmia, and loss of lipids from the adrenal glands, to chemotherapeutic effectiveness is also doubtful, since 'Triton *A*20' was definitely antituberculous at doses too small to produce these phenomena, while they were not apparent even after the higher, and effective, doses of *D*12.

The detoxifying action of the higher polymers on the toxic lower members of the series, as well as their persistence in the blood, suggests the possibility of using these compounds in association with other, even toxic, drugs having high tuberculostatic activity *in vitro*.

Experiments are in progress with a method of reverse phase partition chromatography with the object of isolating the pure compounds containing four and more phenolic nuclei in the molecule. The substituents in the phenolic nuclei will also be varied. On the biological side, the reactions of the tissue white cells to these surface-active substances, and any possible antituberculous effect in animal species other than mice, will be investigated.

Some of this work is forming the subject of a patent application.

We are indebted to Dr. A. J. P. Martin for his advice in connexion with the partition chromatography.

Summary

The development of experimental tuberculosis in mice is markedly inhibited by injection of certain non-ionic, water-soluble, surface-active preparations of low toxicity, having the general formula I ($n > 1$), obtained by reaction of ethylene oxide with condensation products of formaldehyde with *p-tert*-octylphenol. Some of the more important results relating to these products are summarized in the accompanying table.

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RADIOCHEMICAL TECHNIQUES IN ANALYSIS

IN conventional radioactive tracer methodology a labelled substance is added to a system so that its physical or chemical fate in the system can be followed by its radioactivity. In this way radiochemical techniques have been more used as a research tool than as an aid to routine chemical analysis. There are several ways, however, in which radiochemical techniques may be effectively used in analytical chemistry, some of which were exemplified at the recent meeting organized by the Physical Methods Group of the Society of Public Analysts and Other Analytical Chemists. The meeting, under the chairmanship of B. S. Cooper, was held in the rooms of the Institute of Physics in London on

May 22. This 'radiochemistry meeting', which was the second to be held under that title, was well attended and very successful, and promises to become a useful annual event.

Four papers were presented at the meeting. The first, by F. P. W. Winteringham, A. Harrison and R. G. Bridges (Pest Infestation Laboratory), was read by the first author and described the application of radiochemical techniques to quantitative paper-chromatographic analysis. Radiochemical techniques have been so applied in three ways: (1) the mixture for analysis already contained labelled components as in tracer experiments, or it was exposed to a labelled reagent before chromatographic separation so that one or more of the components were converted into radio-active derivatives; (2) the finished paper chromato-gram was exposed to a labelled reagent which com-bined selectively with one or more of the separated components, the excess of reagent then being removed, leaving a radioactive isotope either associated or combined with the components; (3) the finished paper chromatogram was irradiated in the Harwell Pile so that any components containing an element of suit-able activation cross-section was made conspicuously radioactive. In all cases the labelled chromatograms were scanned radiometrically so that the labelled components could be located or estimated. A simple device was described in which uni-dimensional paper chromatograms or strips cut from a two-dimensional chromatogram were fed automatically at a controlled rate through a slot so that consecutive sections of the paper were exposed for a given time interval to a screened end-window Geiger–Müller tube under conditions of uniform geometry. By using a suitable integrating circuit connected to a pen-recording milliammeter or self-balancing potentiometer, the mean rate of count was plotted against the distance along the strip, giving the required radio-chromato-gram. The effects of β-particle self-absorption by the paper, and its variation, have been calculated to be small and unlikely to impair quantitative work even with soft β-emitters like carbon-14 or sulphur-35. Several radiochromatograms, obtained by the methods discussed, were presented.

The second paper, by E. Lester Smith and D. Allison (Glaxo Laboratories), dealt with the paper chromatographic analysis of penicillin mixtures labelled with radioactive sulphur-35. Dr. Lester Smith described how crystalline penicillins containing up to 600 microcuries of sulphur-35 per mgm. were prepared biosynthetically in a medium containing sodium sulphate labelled with sulphur-35. A point of interest was that the mould *P. chrysogenum*, Q176, tolerated up to one curie of sulphur-35 per litre of medium. The penicillin mixture was resolved on a buffered paper chromatogram by the method of Goodall and Levi. The separated components were located or estimated by three methods and the results compared. In the first method (Goodall and Levi) the developed chromatogram was placed against an agar plate inoculated with *B. subtilis* so that on incubation the separated penicillins were located and estimated by the zones of bacterial inhibition. In the second method the strips were placed against X-ray film in the dark so that the components labelled with sulphur-35 could be located autoradio-graphically. Finally, the paper chromatogram was cut up into equal sections which were mounted below a thin end-window Geiger–Müller tube and the β-activity of the sulphur-35 assayed radiometrically. The results by all three methods agreed well, and the experiments demonstrated clearly the value of a radioactive tracer technique in checking existing chemical and biological methods of assay. An inter-esting outcome of these experiments was that a significant fraction of the penicillins appeared to be destroyed after application to the paper strip, this being suggested by a zone of radioactivity at the origin not associated with antibiotic activity.

A. A. Smales read the third paper, contributed by himself and B. D. Pate (Harwell), and described a method for the ultra-micro determination of arsenic by neutron activation. Pile irradiation of a sample containing arsenic gives rise to radioactive arsenic-76 by means of the reaction $^{75}As(n,\gamma)^{76}As$. Arsenic-76 decays by β-emission of maximum energy 3·0 MeV. with a half-life of 27 hr. Radiation due to this isotope in a chemically separated fraction is characterized by its energy and decay period. The sensitivity and accuracy of the method were tested by a carrier technique in which a known excess of inactive arsenic was added to the irradiated sample and a known proportion isolated by conventional analytical techniques, the activity of arsenic-76 in the separated fraction then representing a known proportion of the arsenic originally present in the sample. Close agree-ment was obtained between chemical and activation analysis at high concentrations, and the results obtained by the activation method alone were con-sistent on samples diluted well beyond the limits of chemical detection. The data provide an excellent example of the sensitivity and accuracy of the methods of activation analysis. The determination of as little as 10^{-4} μgm. of arsenic in biological samples appears to be quite practicable. Their great sen-sitivity, notwithstanding the methods, are not without pitfalls for the unwary. This was illustrated in the application of the method to the assay of germanium dioxide for arsenic. On neutron activa-tion, germanium itself gives rise to more than one radioactive isotope of arsenic—for example, by the sequence, $^{74}Ge(n,\gamma)^{75}Ge \xrightarrow{\beta} {}^{75}As(n,\gamma)^{76}As$, so that 'spurious' arsenic appears as a result of the irradiation. Arsenic-77, which also arises from germanium, may be distinguished radiometrically. Mr. Smales sug-gested that a similar difficulty might arise during the irradiation of samples rich in bromine or selenium, for example, by the reaction $^{79}Br(n,\alpha)^{76}As$.

The last paper was presented by R. D. Keynes (Cambridge), who described the application of the methods of activation analysis to the determination of sodium and potassium in biological samples. Samples for analysis were irradiated in the Harwell Pile together with samples of spectroscopically pure sodium carbonate and potassium bicarbonate which were used as reference standards. It was found that, during the irradiation of desiccated nerve fibres isolated from cuttle-fish, sodium-24, potassium-42, phosphorus-32 and sulphur-35 were the principal radionuclides formed, the last no doubt partly arising from the reaction $^{35}Cl(n,p)^{35}S$. Sodium-24 and potassium-42 arise by neutron activation of the natural isotopes, so that the corresponding radio-activities are a direct measure of the sodium and potassium originally present. By a simple screening technique the sodium-24 and potassium-42 were distinguished by their energetic γ- and β-emission respectively, and chemical carrier separation was unnecessary. A small correction had to be made for the phosphorus-32, which could be determined after the short-lived sodium and potassium isotopes had

decayed to insignificance. A modification in estimating the potassium only was to add a known excess of potassium carbonate carrier to the irradiated sample and, precipitating a known fraction of the total potassium as the dipicrylaminate, this salt was then radiometrically assayed separately. These methods have been used successfully on a routine basis for the determination of weights of the order of 0·5 μgm. of sodium and 5 μgm. of potassium in biological samples. The results indicate that as little as 0·05 μgm. of sodium can be estimated to within a few per cent, so that the potentialities of the method in chemical analysis are obvious.

It would not be appropriate to record here more than a few points raised in the ensuing discussion. R. C. Chirnside asked if the decomposition of the penicillins noted during the paper chromatography of the labelled material minimizes the value of the Goodall and Levi method; Dr. Lester Smith replied that, unless the relative decomposition of the individual penicillins was unequal, the value of the original method would not be affected because it was used to show the proportional composition of the penicillin mixture rather than the individual weights. J. Haslam asked if the method of radioactivation analysis can be applied to the determination of iodine in sea water, to which Mr. Smales replied that the relatively short half-life of the iodine-128 produced by neutron activation of natural iodine makes the determination very difficult, since any separation and counting would have to be completed within a matter of two or three hours of removing the sample from the pile; however, Mr. Smales mentioned that the determination of a range of trace elements in water by radioactivation analysis is, in fact, being investigated. A. C. Mason wondered if the methods could be used for the determination of boron in plant material—a difficult problem in chemical analysis—and Mr. Smales replied that boron unfortunately gives rise to no suitable isotope on neutron irradiation. Other items discussed ranged from the particular advantages to be expected as a result of combining radioactive tracer techniques with paper chromatography to the use of radioactivation analysis for the detection of arsenic in poisoned victims.

F. P. W. WINTERINGHAM

UNIVERSITY OF GLASGOW

FIFTH CENTENARY CELEBRATIONS

ON the evening of June 29, the last of a series of 'At Homes' in the Bute Hall at the University brought the celebrations of the fifth centenary of the University of Glasgow to a close. They began almost a fortnight before with the arrival on June 17 and 18 of nearly two hundred delegates representing universities and other learned bodies in all parts of the world, and of many other distinguished scholars invited to receive honorary degrees.

On the afternoon of Monday, June 18, the guests were welcomed informally at faculty receptions in the College Rooms and Queen Margaret Union, and renewed or established friendships which were strengthened by the academic and social functions of the ensuing days. That evening many guests attended the first McEwen Memorial Concert in the Hunter Hall.

On Tuesday, June 19, a very full programme began with the presentation of addresses in the Bute Hall, when delegates, representatives and graduands from at home and abroad were welcomed by the Chancellor, Lord Boyd-Orr. Before a full assemblage of the Senatus, academic staff and honorary doctors of the University, the guests bringing messages of greeting were called in turn and handed their greetings to the Chancellor. More than two hundred such messages were presented, all graciously worded and many of them beautifully illustrated. They have been on display to the public, together with many other addresses received by post, in the Upper Library throughout the period of the celebrations, and have attracted many visitors.

One of the most colourful and impressive ceremonies took place on the Tuesday afternoon when, in robed processions, delegates, graduands and the Chancellor, Court and Senate of the University went in bright sunshine from the Royal Infirmary to the Commemoration Service in Glasgow Cathedral, the first home of the University congregations five hundred years ago. The whole of the Cathedral quire was filled with the academic gathering, while wives and friends occupied the nave, an assemblage in all of some 1,200. The sermon was preached by the Minister of Glasgow, and others officiating were the Principal, the Professor of Divinity, the Clerk of the Senate, the Moderator of the General Assembly of the Church of Scotland and the University Chaplain. The music was played by the Professor of Music.

On Tuesday evening some eight hundred guests were entertained to dinner in two gatherings, one at the Central Hotel presided over by the Chancellor, and the other at the adjacent Grosvenor Restaurant where the chairman was the Rector. It was a happy circumstance that the Prime Minister, who was to receive the next day the honorary degree of Doctor of Laws, and Mrs. Attlee arrived in time to be present. Among the speakers were the Lord Justice General, the President of the University of California, the Lord Bishop of Durham, Sir Oliver Franks, the Principal of McGill University, Prof. F. L. Ganshof, of the University of Ghent, Prof. J. M. Holst, of the University of Oslo, and Prof. M. Le Breton, of the University of Paris.

The mornings of June 20 and 21 were reserved for the two major academic functions, the honorary graduation ceremony and the commemoration oration by Lord Macmillan of Aberfeldy respectively. For these functions some 2,700 persons assembled on each occasion in St. Andrew's Hall, almost half of them in academic robes. The colourful splendour on each occasion was perhaps unprecedented in the history of the University or of the city.

At the graduation ceremony twelve honorary degrees of Doctor of Divinity and fifty-four of Doctor of Laws were conferred. Among those receiving the degree of LL.D. were the following: Prof. E. D. Adrian, professor of physiology in the University of Cambridge; Prof. A. C. Aitken, professor of mathematics in the University of Edinburgh; The Right Hon. C. R. Attlee, Prime Minister; Sir John Beazley, professor of archæology in the University of Oxford; Prof. Niels Bohr, professor of theoretical physics in the University of Copenhagen; Sir John Cockcroft, director of the Atomic Energy Research Establishment, Harwell; Sir John Craig, steelmaker in Glasgow; Dr. H. W. Dodds, president of Princeton University; Dr. R. Dohrn, director of the Zoological Station at Naples; Dr. P. J. Du Toit, president of the South African Council for Scientific and Industrial Research; Prof. T. G. Halle, professor of palæobotany in the University of Stock-