

United Kingdom and other Commonwealth countries, and 147 doctors were appointed in 1952, while there is a steadily increasing number of medical officers of local origin, particularly in the Far East, West Africa, the West Indies, Cyprus and Mauritius. Whereas on January 31, 1953, 638 Colonial students were reading medicine in the United Kingdom and Eire, young men qualifying locally still seemed to prefer private practice to entering government service. An increase in the number of specialist posts has been noticeable, and especially in the fields of radiology, anaesthetics, pathology and psychiatry it has been difficult to fill such posts by recruitment from the United Kingdom. In this section of the report emphasis is once again laid on the dependence of any solid expansion of the health services on the adequate training of sufficient numbers of auxiliary technical, clinical and nursing staff.

The scale of assistance sought by the Colonial territories under the Expanded Programme of United Nations Technical Assistance increased, and among the requests noted are those from the following countries: Tanganyika, three geologists for a mineral exploration team; the Federation of Malaya, an expert in the rehabilitation of the blind, for the training of radio-technicians and for an aero-magnetic survey; Jamaica, a palaeontologist; British Guiana, a hydro-electric expert; British Honduras, a rice expert; Kenya, a pineapple canning expert; and the Gold Coast, an expert in mass-education rural training centres. Considerable use is being made by the Colonial territories of the fellowship facilities offered by the United Nations and the Specialized Agencies, and eighty-one such fellowships and scholarships are now held.

The expenditure of £14 million on development and welfare schemes and on research schemes was approximately the same as during 1951-52; but although research schemes are specifically excepted from the statutory time limit, the available funds are already almost fully committed, and it is pointed out that the position will soon be reached when no new long-term projects can be undertaken, in the absence of further funds. The progress in research is reported fully in the subsequent report "Colonial Research, 1952-53", and it will suffice here to note that the West African Governments are considering proposals for the establishment of a West African Agricultural Research Advisory Committee with a permanent secretariat, that the Clove Research Unit in Zanzibar has established the causes of slow-decline, die-back and sudden-death in clove trees, and the Zanzibar Government is planning experiments to control the two fungi which are responsible for these diseases. The recruitment of field staff for geodetic and topographical surveys in the Colonial territories did not keep pace with resignations or transfers, but prospects of recruitment of field surveyors and other technical staff are now much better, and the total staff is expected to be increased by more than fifty during 1953-54. The overseas scientific staff of the Colonial Geological Surveys increased from 180 to 190 during 1952, and the universities continued to show their interest in the geology and natural resources of the Colonial territories.

Besides the expenditure from Colonial Development and Welfare Funds (which included replenishment of the central allocation for broadcasting by £250,000 to complete the programme of capital equipment, and of that for Students' Welfare by

£284,000 to permit continuance of existing services to March 31, 1956), approximately £25,250,000 was expended on the Colonial territories from the Vote for Colonial and Middle Eastern Services in 1952-53, part of this being grants for the repair of damage and for rehabilitation or reconstruction in the West Indies caused by earthquake, hurricane, flood or fire. Although the large financial contribution which the United Kingdom is making to Colonial development and welfare is fully displayed in this survey, it is equally pointed out how such developments depend upon closer co-operation and understanding between the United Kingdom Government and those of the Colonial territories, between the several departments concerned (for example, eradication of the tsetse-fly has required the co-operation of every field department of the Colonial governments), between local and overseas staff and between government and the people served. The educational developments recorded in this report are clearly contributing both to the supply of leaders able to fulfil their new and growing responsibilities with the goodwill and judgment that the present leaders, on the Gold Coast and elsewhere, are manifestly striving to show, and also to the training of a community able and willing to co-operate. The existence of a like goodwill on the part of the United Kingdom is also recorded, which joined to imagination could well make partnership a reality and no more a pious sentiment.

URIDYL TRANSFERASES AND THE FORMATION OF URIDINE TRIPHOSPHATE*

Enzymic Production of Uridine Triphosphate : Uridine Diphosphoglucose Pyrophosphorolysis

IN the present communication we wish to describe a hitherto unrecognized pathway by which uridine triphosphate can be formed. We have previously reported¹ that dialysed yeast maceration juice contains an enzyme which in the presence of uridine diphosphoglucose² brings about an incorporation of inorganic pyrophosphate labelled with phosphorus-32 into a uridine nucleotide with simultaneous splitting-off of glucose-1-phosphate. This enzyme, which we called uridine diphosphoglucose pyrophosphorylase³ (in analogy with other pyrophosphorylases), does not in any detectable way attack other known uridine diphosphoglycosyl compounds. However, it has been shown recently⁴ that a suspension of rat liver nuclei pyrophosphorylates uridine diphosphate-N-acetylglucosamine as well as uridine diphosphoglucose.

The specific uridine diphosphoglucose pyrophosphorylase is present in *Zwischenferment* preparations^{5,6}, particularly in the fraction precipitated by between 60 and 70 per cent saturated ammonium sulphate. If phosphoglucomutase and triphosphopyridine nucleotide are added, the liberation of glucose-1-phosphate from uridine diphosphoglucose can be followed⁵ at 340 mμ. For each mole of pyrophosphate incorporated into the nucleotide, one mole of α-glucose-1-phosphate is liberated. A demonstration

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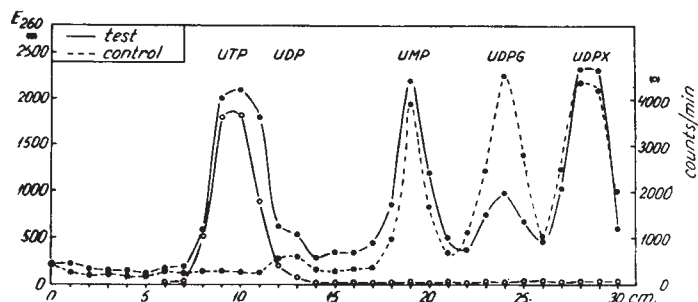


Fig. 1. Paper chromatogram of norite eluate from uridine diphosphoglucose pyrophosphorylase digest

Abscissa: distance from starting line in cm.; ordinate: extinction $\times 10^3$ at 260 m μ .

Reaction mixture: 0.2 μ mol. uridine diphosphoglucose; 2 μ mol. inorganic pyrophosphate (8×10^4 counts/min.); 50 μ l. *Zwischenferment* (3 mgm./ml.); 5 ml. *M/10 tris-hydroxymethyl amino methane hydrochloride*, pH 8.0; *M/100* magnesium chloride. Control mixture: same without pyrophosphate.

After 45 min. incubation the digests were acidified, adsorbed on norite and eluted with 50 per cent ethanol. Chromatographed 44 hr. in neutral solvent (ref. 9). Chromatogram scanned in the Beckman spectrophotometer at 260 m μ and in the Geiger counter

and purification of the new nucleotide, which was suspected to be uridine triphosphate, can be carried out on a microscale as described in Fig. 1. The nucleotide can also be isolated from a 'Dowex Cl' column by elution with 0.2 *M* sodium chloride in 0.01 *M* hydrochloric acid; other uridine compounds, including uridine diphosphate, can be eluted with 0.1 *M* sodium chloride in 0.01 *M* hydrochloric acid. The molar ratio of uracil, estimated at 260 m μ , to radioactive pyrophosphate was found to be 1.18 (calculated for uridine triphosphate, 1.00); total phosphorus/uracil was 2.7 (calculated for uridine triphosphate, 3.0).

Uridine triphosphate is active in two reactions in which the diphosphate was completely inactive. The first reaction is the phosphorylation of glucose⁷ via adenosine diphosphate, which is described in a separate communication⁸. This reaction, in which uridine triphosphate and adenosine diphosphate react to form adenosine triphosphate, which then phosphorylates glucose, has been used to assay

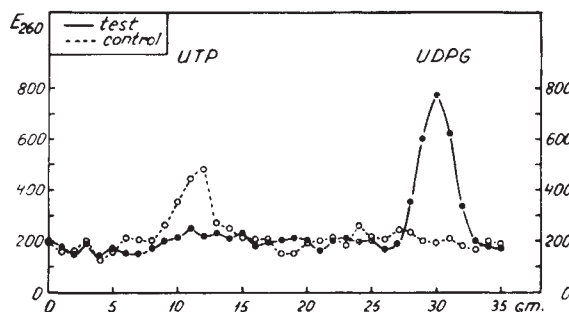


Fig. 2. Paper chromatogram of norite eluate from uridine triphosphate pyrophosphorylase digest

Abscissa: distance from starting line in cm.; ordinate: extinction $\times 10^3$ at 260 m μ .

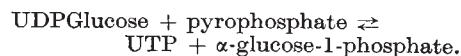
Reaction mixture: 0.2 μ mol. uridine triphosphate; 10 μ mol. α -glucose-1-phosphate; 100 μ l. inorganic pyrophosphatase; 50 μ l. *Zwischenferment* (3 mgm./ml.); 1 ml. *M/10 tris-hydroxymethyl aminomethane hydrochloride*, pH 8.0; *M/100* magnesium chloride. Control mixture: same without α -glucose-1-phosphate

After 50 min. incubation, the digests were acidified, adsorbed on norite and eluted with 50 per cent ethanol. Chromatographed 44 hr. in neutral solvent (ref. 9). Chromatogram scanned in the Beckman spectrophotometer at 260 m μ .

In the norite filtrates, inorganic phosphate was precipitated as magnesium-ammonia salt, washed with dilute ammonia and dissolved in 150 μ l. 0.2 *M* sulphuric acid. Counting the samples in the Geiger counter gave the following results, expressed as counts per min.: control, 186; test, 3,680

uridine triphosphate. It has then been possible to determine that an hour's exposure to 0.01 *M* mineral acid at 100°C. brings about a 50 per cent hydrolysis of uridine triphosphate.

In the second reaction, uridine triphosphate as well as uridine diphosphoglucose act as uridyl donors, that is, the so-called uridine diphosphoglucose pyrophosphorylase could also be called a uridyl transferase and the action could be formulated as follows:



The reaction from left to right has been described briefly¹. The reverse reaction, that is, formation of uridine diphosphoglucose from uridine triphosphate and α -glucose-1-phosphate, has been followed, using uridine triphosphate labelled with phosphorus-32 (uridine-P-³²P) and converting the inorganic pyrophosphate generated to orthophosphate by means of a specific pyrophosphatase for inorganic pyrophosphate. The results of a typical experiment are illustrated in Fig. 2.

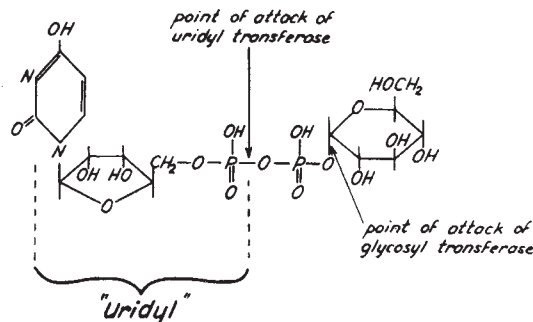


Fig. 3. Uridine diphosphoglucose

In accordance with observations made on the pyrophosphorolysis of uridine diphosphoglucose, the reaction can therefore be expressed according to the reaction written above. The enzyme catalysing this process in both directions could consequently be classified as a uridyl transferase with inorganic pyrophosphate or α -glucose-1-phosphate as uridyl acceptor. The location of fission by the transfer reaction can be illustrated by the formula shown in Fig. 3. The following communication illustrates that there exists at least one more acceptor for this type of reaction: α -galactose-1-phosphate.

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¹ Kalckar, H. M., and Cutolo, E., II^e Congr. de Biochimie, 260 (1952).

² Caputto, R., et al., *J. Biol. Chem.*, **184**, 333 (1950).

³ Kornberg, A., *J. Biol. Chem.*, **182**, 779 (1952).

⁴ Smith, E. E. B., Munch-Petersen, A., and Mills, G. T. (see p. 1038).

⁵ Warburg, O., and Christian, W., *Biochem. Z.*, **254**, 438 (1932).

⁶ LePage, G. A., and Mueller, G. C., *J. Biol. Chem.*, **180**, 975 (1949).

⁷ Kornberg, A., in McElroy and Glass, "Symposium on Phosphorus Metabolism", 1 (1951).

⁸ Berg, P., and Joklik, W., *Nature* [172, 1008 (1953)].

⁹ Paladini, A. C., and Leloir, L. F., *Biochem. J.*, **51**, 426 (1952).