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C-11-CO PRODUCTION BY METAL MAGNESIUM REDUCTION OF C-11-CO_2 .

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C-11-CO was used as a medical tracer in the studies of pulmonary function or blood volume measurement in the early days of positron studies. It was also used for the production of C-11-phosgene which is a useful precursor of C-11-labeled organic compounds such as ures, barbiturates or pimozide. Recently, C-11-butanol, an effective agent for CBF measurement, was prepared from C-11-CO.

C-11-CO is usually produced by the reduction of C-11-CO_2 with zinc metal, but reduction is sometimes troublesome because reaction temperature is close to the melting point of zinc. Though reduction can be also conducted with charcoal at 900°C (Ido et al.), specific activity is significantly lowered by the reaction of carbon with trace amount of oxygen. We reinvestigated the reduction of C-11-CO_2 and found metal magnesium is effective for the reaction. C-11-CO was produced in high yield at around 500°C. Temperature control was easy because melting point of magnesium is much higher than that of zinc. A column 7 mm internal diameter and 10 mm long was sufficient for the reduction at a flow rate of 100 ml/min.

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A RADIOPHARMACEUTICAL AS AMINO ACID METABOLISM MARKER (3). BASIC STUDIES FOR THE EVALUATION OF C-11-NATURAL AMINO ACIDS.

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Studies on amino acid (AA) metabolism as for the design of functional imaging radiopharmaceutical (RP) attracted our attention. Of interest was the study on C-11-natural AA behavior in various AA compartments. Due to their complex involvement, behavior of Met, a cyclotron available AA, and those of importance in major AA compartment, such as Leu (active membrane transport), Glu (free AA pool), Ser (protein) were selected for the present study. Also Phe, an aromatic AA representative was included. In-vitro rat tissue slices accumulation and in-vivo mice biodistribution studies were carried out with C-14 labeled AAs, taking the pancreas of high AA metabolic rate as model. In pancreas slices, Leu, Met and Phe (non-polar AA) showed high and energy-dependent accumulation, while Ser and Glu showed low value. In in-vivo studies, although non-polar AAs showed high pancreas uptake, great differences in metabolic behavior was detected. Of interest was the close relation of degree of pancreas uptake with active membrane transport. Thus, among non-polar AAs, potentiality of Met as an active AA transport marker, Phe as a protein synthesis marker, offered good basis for future design of RPs.

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SYNTHESIS OF (C-11)-1-PYRUVATE AND ITS CLINICAL APPLICATION.

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(C-11)-1-pyruvate was prepared enzymatically by an exchange reaction of (C-11)-carbon dioxide and the carboxyl group of pyruvic acid using pyruvate-ferredoxin oxidoreductase of Clostridium butyricum. The enzyme and substrate were set up as a kit system. The labeled pyruvate was purified by sublimation in a special cold-finger-type glassware. The radiochemical yield of pure injectable (C-11)-1-pyruvate was almost 100 %, at 30 min after E.O.B. of cyclotron run.

Pyruvate, natural constituent of blood plasma, is penetrable easily across cell membranes and blood-brain barrier. Once it is incorporated in the cell, it is metabolized, in most cases, into either acetyl-CoA plus carbon dioxide (in normal tissues) or lactate (in tumors, inflammatory tissues, anoxic-ischemic tissues and mitochondria-defective tissues). The label of (C-11)-1-pyruvate is transferred to carbon dioxide or lactate, of which the former stays short and the latter long in the tissue, and consequently represents the metabolic character of the tissue.

After confirmation of the safety and positive visualization of animal tumors, clinical studies were performed in more than 40 cases. The brain tumor, cerebral abscess, fresh cerebral infarction, cerebral anoxia-ischemia and mitochondrial encephalomyopathy always exhibited positive retention (accumulation) of radioactivity in the affected area of the brain in the PETT image when observed more than 10 min after i.v. injection of 20-40 mCi of (C-11)-1-pyruvate. Cerebral edema did not pick up the radioactivity. Some of psychiatric diseases (Pick's disease and schizophrenia) showed positive retention of radioactivity in the frontal and right temporal lobes of the brain in a preliminary study.

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RADIOSYNTHESIS OF O-15 LABELED BUTANOL FOR HUMAN USE.

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[^{15}O] water is a widely used tracer for measuring cerebral blood flow (CBF). But the method leads to an underestimation of CBF in areas of high CBF. It has been shown that [^{15}O] butanol from tributyl-borane (TBB) which was reported by Kabalka et al. Oxygen-15 was prepared by deuteron bombardment of 0.5 % oxygen in nitrogen.

The target gas was directed onto 1 ml of TBB which had been prepared on the column (SEP-PAK C_{18}). The oxygen (0.2 mmol) was trapped by nearly quantitative reaction with the TBB. After trapping of activity the resulting complex was hydrolysis with 0.5 ml of 20 % H_2O_2 aqueous solution which oxidized the resided TBB to butanol at the same time. Subsequently, 6 ml of water was passed over the trapping column and next one (SEP-PAK C_{18}) which was for purification of butanol. The first 1.3 ml of eluent was wasted and next 5 ml was collected as [^{15}O] butanol solution. Thus we synthesized [^{15}O] butanol in a radiochemical yield of 43 % with synthetic time of 2.5 minutes after end of bombardment and radiochemical purity of the final product was more than 93 % in HPLC. This synthetic method will be suitable for human use.