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Eckert & Ziegler ^{11}C Modular-Lab Chemistry Solution

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Answers for life.

Introduction

The Eckert and Ziegler (E&Z) ^{11}C Modular-Lab Chemistry Solution comprises Methyl Iodide/Methyl Triflate (MeI/MeOTf) system, Methylation system and HPLC system for the synthesis and purification of ^{11}C-labeled radiopharmaceuticals. Consumable products include PharmTracer cassettes for use with the Methylation system.

The table below shows a list of ^{11}C-labeled intermediates and compounds that can be synthesized using the Modular-Lab Chemistry Solution. The systems that are required for the synthesis of each compound are indicated.

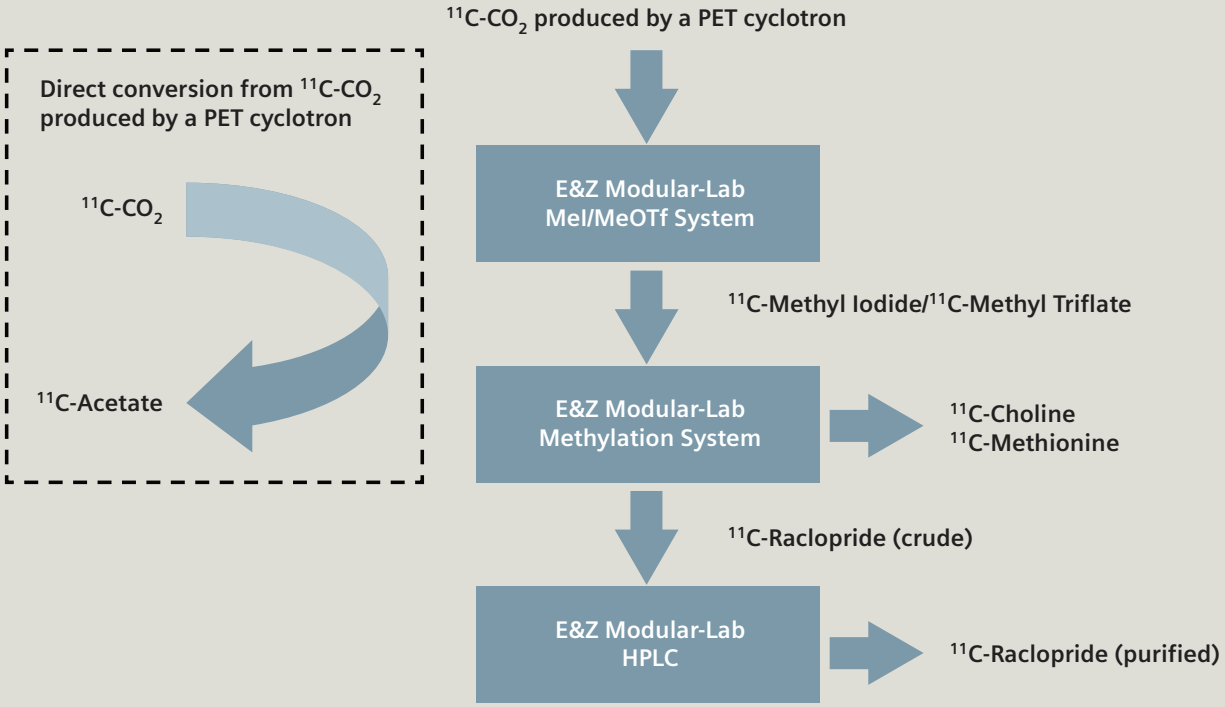
The entire E&Z ^{11}C Modular-Lab Chemistry Solution can either be installed in a single hot cell or in two mini-cells with the Modular-Lab MeI/MeOTf in one mini-cell and the Modular-Lab Methylation system and High Performance Liquid Chromatography (HPLC) system in a second mini-cell.

Biomarker*	MeI/MeOTf system	Methylation cassette system	HPLC system
^{11}C-Methyl Iodide	✓		
^{11}C-Methyl Triflate	✓		
^{11}C-Methionine	✓	✓	
^{11}C-Choline	✓	✓	
^{11}C-Acetate	✓	✓	
^{11}C-Raclopride	✓	✓	✓

** These agents are not approved by the US Food and Drug Administration for routine clinical use. Check with other regulatory authorities for marketing status outside the US.*

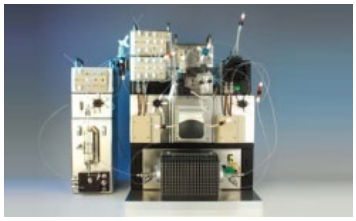
Background

The PET radioisotope ^{11}C is characterized by its relatively short half life (~20 minutes), which provides the advantage of being used for the synthesis of many short-lived imaging biomarkers, but also has a long enough half-life to support the synthesis of radiopharmaceuticals that require multiple steps. The process flow for the synthesis of various ^{11}C-labeled intermediates and compounds are depicted graphically in the schematic. The first step in the process involves the production of ^{11}C-CO_2 in a PET cyclotron using ^{14}N-N_2 gas as the starting material and the ^{14}N (p, α) ^{11}C reaction.



In the next step, ^{11}C-Methyl Iodide or ^{11}C-Methyl Triflate is synthesized from ^{11}C-CO_2 produced by the cyclotron using the E&Z Modular-Lab MeI/MeOTf system. ^{11}C-Methyl Iodide and ^{11}C-Methyl Triflate are the most important and frequently used secondary ^{11}C-labeling precursor used for the synthesis of a variety of compounds. Their versatility allows the synthesis of a broad variety of biologically relevant PET radiopharmaceuticals including ^{11}C-Methionine, ^{11}C-Choline and ^{11}C-Raclopride using the E&Z Modular-Lab Methylation system in the third step of the process. The crude ^{11}C-Raclopride produced is purified further in the final step of the process using the E&Z Modular-Lab HPLC system.

The E&Z Modular-Lab Methylation system can also be used for the synthesis of ^{11}C-Acetate directly from ^{11}C-CO_2 (^{11}C-CO_2 is trapped by MeI/MeOTf system) produced by a PET cyclotron.



E&Z Modular-Lab MeI/MeOTf System

Product Description

^{11}C-Methyl Iodide and ^{11}C-Methyl Triflate can be easily produced with the fully automated Modular-Lab synthesis device. The synthesis occurs via a gas-phase* approach that results in the production of labeled compounds with high radiochemical yield and specific activity.

The ^{11}C-CO_2 produced by the cyclotron is reversibly adsorbed to molecular sieves. After controlled release via heating, the adsorbed ^{11}C-CO_2 is converted into ^{11}C-Methane by hydrogenation of ^{11}C-CO_2 in a palladium oven. The resulting ^{11}C-Methane is then adsorbed and processed to ^{11}C-Methyl Bromide, which can be converted to ^{11}C-Methyl Iodide using a sodium iodide oven or ^{11}C-Methyl Triflate using a silver triflate oven. The resulting products, ^{11}C-Methyl Iodide or ^{11}C-Methyl Triflate, are then available for tracer synthesis.

Key features

- Fully automated synthesis process with no user intervention necessary
- Fully automated cleaning routine after each process to help ensure minimum chemical contamination of the system
- Traceability of the complete process, including documentation of all process parameters and functions
- Short synthesis and pre-preparation time
- Turnaround time between successive batches of ^{11}C-Methyl Iodide: 20 to 30 minutes
- Computer for system control
- Modular-Lab Software Professional – GMP, GAMP5 and 21 CFR part 11 compliant
- Trapping of ^{11}C-CO_2 and controlled release for ^{11}C-Acetate

Benefits

- Higher yields and higher specific activity compared to the liquid-phase method
- Multiple batches (>6 runs per day) without need for apparatus replacement or setup
- No liquid nitrogen necessary for the process
- No air and moisture sensitive chemicals necessary

Onsite installation and training are provided by Eckert & Ziegler.

**The gas-phase ^{11}C-Methyl Iodide setup was developed and validated in close cooperation with Bruce H. Mock Ph.D., Associate Professor of Radiology at Indiana University (USA).*

E&Z Modular-Lab Methylation System

Product Description

The Modular-Lab Methylation system that is based upon the Modular-Lab PharmTracer synthesis technology allows for the easy and fully automated synthesis of ^{11}C-Methionine, ^{11}C-Choline, ^{11}C-Acetate and ^{11}C-Raclopride, as well as other radiopharmaceuticals, using disposable single-use cassettes. These cassettes guarantee a sterile fluid path and eliminate cross-contamination.

Key features

Modular-Lab Methylation system features

- Modular-Lab PharmTracer system – 4 fold cassette
- Heater module (Max 220°C + with air cooling)
- Syringe module with holder for 20 ml BD syringe
- Activity detector plug (activity max 5-Ci)
- Operates off the same computer as MeI/MeOTf system

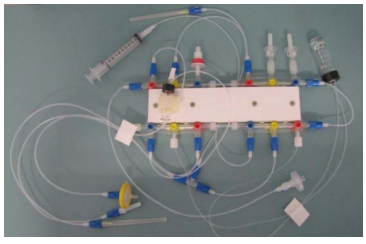
Onsite installation and training are provided by Eckert & Ziegler.

Modular-Lab PharmTracer cassettes

- Cassettes are assembled under GMP-compliant clean room conditions, sterilized with gamma-radiation and double vacuum-packed.
- All consumables used are chemical resistant and have been tested for their suitability with the specific syntheses. All materials are free of animal-derived ingredients.
- A shelf life of 12 months can be guaranteed. Due to the cassettes one-time use, no reconditioning and cleaning or sanitation routines are necessary.
- Sterile cassettes are available for ^{11}C-Choline, ^{11}C-Methione, ^{11}C-Raclopride and ^{11}C-Acetate

A vacuum-packed cassette unit consists of three components:

- Bag A with sterile cassette
- Bag B with sterile vials
- Bag C with sterile accessories (syringes, needles, etc.)



Bag A

Bag B

Bag C

E&Z Modular-Lab HPLC System

Product Description

The Modular-Lab HPLC system is designed to purify the reaction product of a radiopharmaceutical synthesis by semi-preparative HPLC (needed for ^{11}C-Raclopride). The system comprises integrated parts that include injection valve, a sample loop, a fluid detector and an activity detector.

Key features

- Knauer HPLC pump (10 ml pump head)
- Knauer HPLC UV-Detector (fixed wavelength)
- Analytical Flow Cell
- Operates off the same computer as MeI/MeOTf system

Onsite installation and training are provided by Eckert & Ziegler.

E&Z ^{11}C Modular-Lab Chemistry Solution

System Specifications

Compound	Synthesis Time (minutes)	Decay Corrected Yield	Uncorrected Yield	Radiochemical Purity
^{11}C-Methyl Iodide*	15	>67%	>40%	>95%
^{11}C-Methyl Triflate*	15	>60%	>30%	>95%
^{11}C-L-Methionine†	25	>35%	>21%	>95%
^{11}C-Choline†	25	>61%	>26%	>98%
^{11}C-Raclopride	35 + 20 min HPLC purification	>10%	>5%	>85%
^{11}C-Acetate*	17	>57%	>27%	>95%

Modular-Lab MeI/MeOTf System	
Dimensions	
Product Dimensions	19.7 in (50 cm) wide × 20.1 in (51 cm) high × 19.7 in (50 cm) deep
External support equipment	
Electrical Cabinet	11.8 in (30 cm) wide × 15.7 in (40 cm) high × 7.9 in (20 cm) deep; 11.8 in (30 cm) clearance at front, 5.9 in (15 cm) clearance above
Heat Exchanger	10.2 in (26 cm) wide × 14.6 in (37 cm) high × 14.2 in (36 cm) deep; 5.9 in (15 cm) clearance at back; should not be installed more than 1 meter height difference from system
Power Supply	115 or 230 VAC, 1000 W
Modular-Lab Methylation System and Modular-Lab HPLC System	
Dimensions	
Product Dimensions	15.7 in (40 cm) wide × 18.5 in (47 cm) high × 14.6 in (37 cm) deep
External support equipment (only with HPLC System)	
HPLC Pump	4.7 in (12 cm) wide × 3.9 in (10 cm) high × 8.7 in (22 cm) deep
UV Detector	8.9 in (22.6 cm) wide × 16.1 in (41 cm) high × 5.3 in (13.5 cm) deep, 6 kg
Power Supply	115 or 230 VAC, 1000 W

All modules are supplied with a one year manufacturer's warranty from Eckert & Ziegler.
Service and support are provided by Eckert & Ziegler.
Extended service contracts and additional consumables such as the synthesis cassettes can be purchased from Eckert & Ziegler.

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