Original Article

고정상 추출법을 이용한 효율적인 [^{11}C]methionine의 합성

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Simple and Highly Efficient Synthesis of [^{11}C]methionine Using Solid-Phase Extraction Method

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We developed simple and highly efficient synthesis method for [^{11}C]methionine using solid-phase extraction method. For synthesis, we used C18 cartridge. [^{11}C]methionine was synthesized on C18 cartridge according to the solid-phase [^{11}C]methylation of precursor L-homocysteine thiolactone hydrochloride. The radiochemical yields of [^{11}C]methionine was 48.9±7.93% decay corrected (results of 30 syntheses, mean±SD), with average production higher than 180 mCi. This procedure showed high yield and simple synthesis of [^{11}C]methionine. **(Korean J Nucl Med Technol 2008;12(3):181-183)**

Key Words : [^{11}C]methionine, Solid phase cartridge

INTRODUCTION

[^{11}C]methionine is a widely used compound for the diagnosis of brain tumors. Even though we do not fully understand the mechanism exactly how [^{11}C] methionine is taken to the tumor cells, but blood-brain barrier is known to be permeable to methionine as well as few other amino-acids such as phenylalanine, leucine and tyrosine. And, it was known that [^{11}C]methionine is more accurate than CT for diagnosis the tumor grade.

Production of [^{11}C]radiophamaceuticals has gained increasing importance in PET diagnostic.

And recently, human PET studies with [^{11}C]methionine have shown the effectiveness of this radiotracer for the imaging of brain tumors. This is the reason we have developed this [^{11}C]methionine synthesis method such a simple and efficient because [^{11}C]methionine is playing an important role for PET. And finally, we applied this to routine production of [^{11}C]methionine.

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METHODS

1. Preparation of Cartridges and Reagents

All reagents and solvents were commercially available and used without further purification. All cartridges (Sep-Pak C18, Accell Plus CM, QMA) were purchased from Waters.

For Synthesis, We used C18, CM and QMA cartridges. Activation of cartridges as followed. Sep-Pak C18 was eluted 10 mL ethanol and 10 mL water. Accell Plus CM was eluted 10 mL water. Accell Light QMA eluted 5 mL 1N NaOH and 10 mL water. After activation of

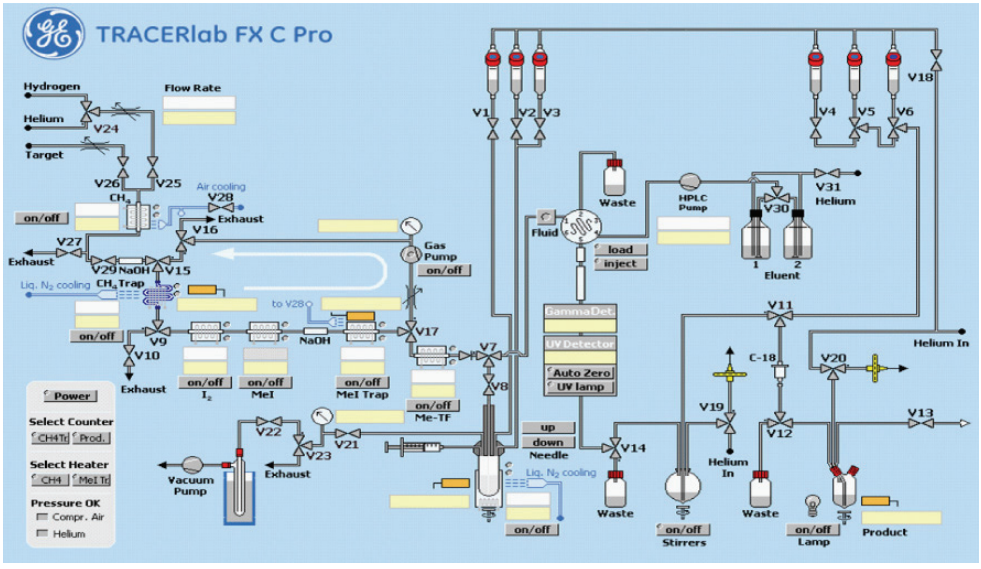


Fig. 1.

cartridges, we installed them to GE TracerLab FXc commercial module.

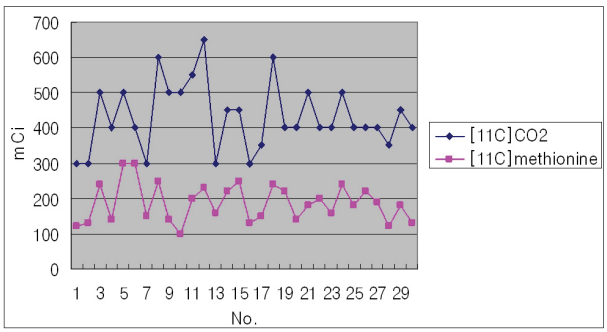
2. Preparation of Precursor

L-homocysteine hydrochloride were purchased from Fluka (Sigma Aldrich). We dissolved 6 mg of L-homocysteine hydrochloride in 1 mL of 0.1N NaOH. And, loaded 0.2 mL of this solution on C18 cartridge.

3. Synthesis of [^{11}C]methionine

GE Tracerlab FXc module was modified as depicted in the scheme shown in Fig. 1. As you can see, V8 is connected directly to V11.

[^{11}C]CO_2 was produced by the classical nuclear reaction 13N(p,α)^{11}C on a mixture of nitrogen and 0.5~1% oxygen in a IBA Cyclone 18/9. This means that the target gas is bombarded by high energetic protons. Produced [^{11}C]CO_2 was transferred within a target delivery gas stream to the GE Tracerlab FXc module. The [^{11}C]CO_2 activity is converted by Ni-catalyst (Shimalite-Ni) support, under continous addition of Hydrogen at 400℃ into [^{11}C]CH_4. Both unconverted [^{11}C]CO_2 and formed H_2O traped by Ascarite column. The produced [^{11}C]CH_4 is trapped on Carbosphere (60~80 mesh) under N_2 liquid cooling at -140℃ for purification. Purified [^{11}C]CH_4 was allowed to react with I^2 and AgOTf and the make [^{11}C]CH_3OTf in a gas circulationg system. Produced [^{11}C]CH_3OTf was transfered under stream of helium (50 mL/min) into a Sep-Pak C18 cartridge. [^{11}C]methionine is synthesized on C18 cartridge according to the solid-phase [^{11}C] methylation of precursor L-homocysteine thiolactone hydrochloride. Synthesized [^{11}C]methionine was eluted with 3 mL of 0.85% NaCl solution and collected in a vial. The solution was sterilized by 0.22 μm GS filter.



Graph 1.

RESULTS

Result of produced [^{11}C]CO_2 and [^{11}C]methionine were described on Graph 1. The radiosynthesis of [^{11}C] methionine through a solid supported [^{11}C]methylation

on a commercial Sep-Pak C18 cartridge has been successfully carried out in remarkable short synthesis time and good radiochemical yield. The radiochemical yields of [^{11}C]methionine was about 48%, with average production highly than 180 mCi.

CONCLUSION

We have described a modification of a commercial GE TracerLab FXc module for simple synthesis of [^{11}C]methionine. This procedure showed high yield without impurities. We have applied this procedure to our routine production of [^{11}C]methionine with high and reproducible radiochemical yield in short time of synthesis.

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