Applied Radiation and Isotopes 67 (2009) 1654–1660

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

Simple and rapid preparation of [^{11}C]DASB with high quality and reliability for routine applications

D. Haeusler [a,b], L.-K. Mien [a,b], L. Nics [a,c], J. Ungersboeck [a,d], C. Philippe [a,b], R.R. Lanzenberger [e], K. Kletter [a], R. Dudczak [a], M. Mitterhauser [a,b,f], W. Wadsak [a,d,*]

[a] Department of Nuclear Medicine, PET, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria
[b] Department of Pharmaceutical Technology and Biopharmaceutics, University of Vienna, A-1090 Vienna, Austria
[c] Department of Nutritional Sciences, University of Vienna, A-1090 Vienna, Austria
[d] Department of Inorganic Chemistry, University of Vienna, A-1090 Vienna, Austria
[e] Department of Psychiatry and Psychotherapy, Medical University of Vienna, A-1090 Vienna, Austria
[f] Hospital Pharmacy of the General Hospital of Vienna, A-1090 Vienna, Austria

ARTICLE INFO

Article history:
Received 29 October 2008
Received in revised form
12 February 2009
Accepted 10 March 2009

Keywords:
Serotonin
SERT
PET
Carbon-11
Radiosynthesis
DASB

ABSTRACT

[^{11}C]DASB combines all major prerequisites for a successful SERT-ligand, providing excellent biological properties and in-vivo behaviour. Thus, we aimed to establish a fully automated procedure for the synthesis and purification of [^{11}C]DASB with a high degree of reliability reducing the overall synthesis time while conserving high yields and purity. The optimized [^{11}C]DASB synthesis was applied in more than 60 applications with a very low failure rate (3.2%). We obtained yields up to 8.9 GBq (average 5.3 ± 1.6 GBq). Radiochemical yields based on [^{11}C]CH_3I, (corrected for decay) were 66.3 ± 6.9% with a specific radioactivity (A_s) of 86.8 ± 24.3 GBq/μmol (both at the end of synthesis, EOS). Time consumption was kept to a minimum, resulting in 43 min from end of bombardment to release of the product after quality control.

Form our data, it is evident that the presented method can be implemented for routine preparations of [^{11}C]DASB with high reliability.

1. Introduction

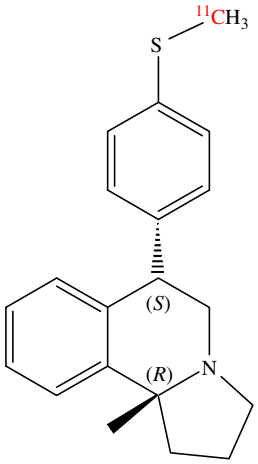
The serotonin transporter (SERT) influences and controls extracellular serotonin levels in the synaptic cleft by decreasing the serotonin level through reuptake and is involved in the pathophysiology of psychiatric disorders, e.g. schizophrenia (Joyce et al., 1993), mood disorders (Ichimiya et al., 2002), depression (Meyer et al., 2001, 2004a; Owens and Nemeroff, 1994; Parsey et al., 2006a; Reivich et al., 2004) and anxiety (Jarret et al., 2007). Hence, it is one of the main targets for antidepressant drugs, the so called SSRIs (selective serotonin reuptake inhibitors) (Meyer et al., 2001, 2004b; Reivich et al., 2004; Spindelegger et al., 2008). Consequently, the imaging of the SERT before and after medication with SSRIs would be of great value for a deeper and further understanding of psychiatric disorders (Hesse et al., 2004; Meyer, 2008), the way of action of newly developed anti-psychotics, and could help to improve diagnosis and the planning of treatment.

Imaging with positron emission tomography (PET) allows in vivo measurement of receptors and transporters in humans non-invasively. For the visualisation and quantification of the SERT, highly selective carbon-11 and fluorine-18 labelled PET-tracers have been developed and synthesised, such as [^{11}C]McN5256 (Suehiro et al., 1993), [^{11}C]DASB (Wilson et al., 2000b), [^{11}C]ADAM (Vercouillie et al., 2001) [^{11}C]MADAM (Tarkiainen et al., 2001), [^{11}C]DAPP (Wilson et al., 2000b), [^{11}C]DAPA (Huang et al., 2002), [^{11}C]AFM (Huang et al., 2004a), [^{11}C]AFA (Huang et al., 2004b), [^{11}C]AFE (Zhu et al., 2004), [^{18}F]ACF (Oya et al., 2002) and [^{18}F]F-ADAM (Shiue et al., 2003a, b), respectively. Structures are given in Fig. 1. So far, only, [^{11}C]McN5256 (Frankle et al., 2004; McCann et al., 2005; Parsey et al., 2000, 2006a; Szabo et al., 1995), [^{11}C]DASB (Frankle et al., 2004; Houle et al., 2000; McCann et al., 2005; Meyer et al., 2001, 2004b, 2007; Parsey et al., 2006b; Praschak-Rieder et al., 2008), [^{11}C]DAPP (Houle et al., 2000) and [^{11}C]MADAM (Chalon et al., 2003; Jovanovic et al., 2008; Lundberg et al., 2005, 2006, 2007a, b) have found their way into clinical measurements.

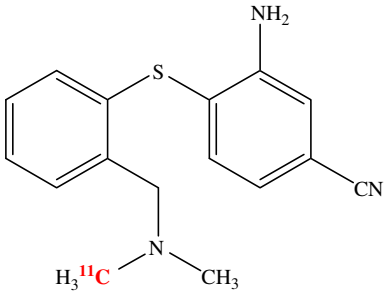
The best established and explored SERT ligand for PET-imaging is [^{11}C]DASB (3-amino-4-[N-methyl-N-[^{11}C]methyl-amino-methyl-phenylsulfanyl]-benzonitrile). It was firstly introduced and synthesised by Wilson et al. (2000a, b) and showed promising properties:

* Corresponding author at: Department of Nuclear Medicine, PET, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria.
Tel.: +43 1 40400 5255; fax: +43 1 40400 1559.
E-mail address: wolfgang.wadsak@meduniwien.ac.at (W. Wadsak).

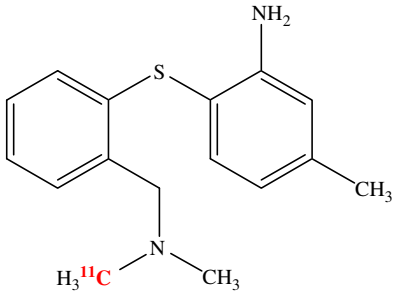
0969-8043/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.apradiso.2009.03.005



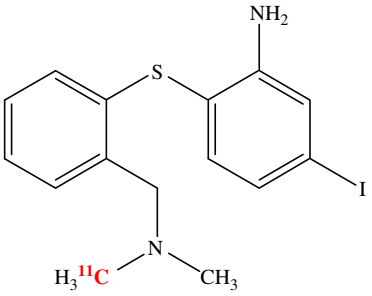
[11C]McN(+)5652



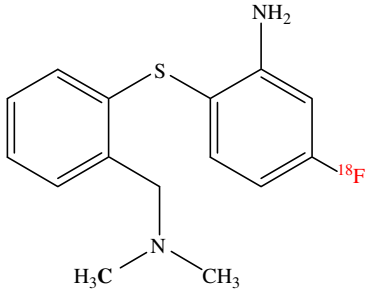
[11C]DASB



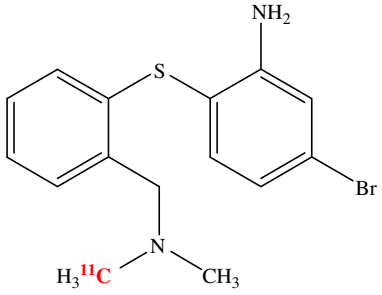
[11C]MADAM



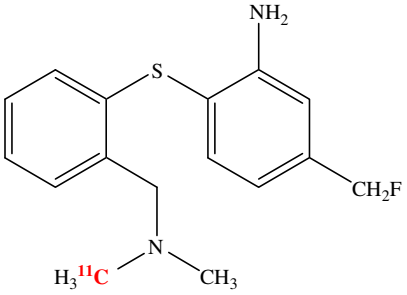
[11C]ADAM



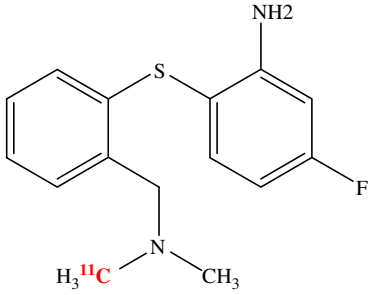
4-[18F]ADAM



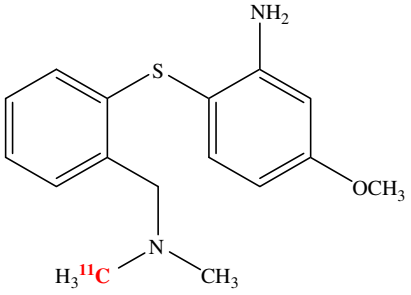
[11C]DAPA



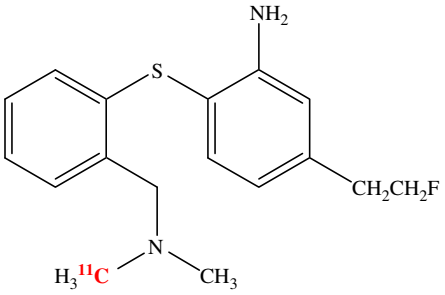
[11C]AFM



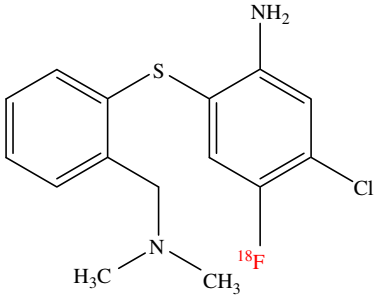
[11C]AFA



[11C]DAPP



[11C]AFE



[18F]ACF

Fig. 1. Chemical structures of various important SERT-tracers.

$K_i =$ 1.1 nM; signal/noise ratio 7.9 (hypothalamus–cerebellum/cerebellum ratio at 60 min p.i. in rats); cerebellar clearance 15.6 min; log $P^{7.4}$ 2.7 (Wilson et al., 2000b).

As revised recently by Meyer (2007), DASB is the SERT tracer of choice since it combines several advantages such as (1) high affinity (1.1 nM) (Wilson et al., 2000b); (2) excellent selectivity