Production of [123I]-*m*ZIENTfor Biodistribution and Dosimetry studies

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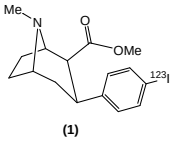
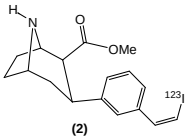
Background

[^{123}I]β-CIT (1) is the most commonly used radioligand for imaging the serotonin transporter (SERT) by SPECT and has been used in many neuroimaging studies. 1,2 However, it is not an ideal radioligand for measuring SERT as it also has affinity for the dopamine (DAT) and noradrenaline (NAT) transporters. [^{123}I]-*m*ZIENT (2) is a new radiotracer that is reported both to have a high affinity for SERT, and to have specificity for SERT over DAT and NAT. 3,4 We intend to perform a dosimetry and biodistribution of [^{123}I]-*m*ZIENT, to enable further future studies using this tracer.



(1)



(2)

Methods

Radiochemistry set up

- $Na^{123}I$ was supplied in 0.05M NaOH.
- The radioactivity was made up to 150µl with 0.05M NaOH.
- Water (45µl) and 0.8M H_3PO_4 (25µl) were added, followed by a solution of trimethylstannyl precursor (100µg in 50µl MeOH).
- Immediately after the addition of precursor (ie within 30 seconds), peracetic acid was added to oxidise the radioiodide.
- After 15mins the reaction was quenched and purified by preparative HPLC.

Radiochemistry: investigation methodology

- Radioiodide is supplied differently to the US and UK collaborators.
- Investigated pH of cold reaction mixture
  - Reaction mixture using 0.1M NaOH (as used by US)
  - Reaction mixture using 0.05M NaOH (supplied to Glasgow
- Compared different storage conditions for precursor
  - Stored dry in single synthesis aliquots
  - Stored in bulk followed by aliquoting single synthesis amount immediately before reaction.

Scanning Protocol

- 6 subjects: 3 control subjects and 3 on SSRI anti-depressant medication
- 150 MBq [^{123}I]-*m*ZIENT i.v. injection
- Whole body anterior and posterior gamma camera imaging, venous blood sample and urine collection over 48 hours
- SPECT brain scan at 4hrs p.i.

Results

- Small scale reactions gave adequate yields.
- Low HPLC yields of *m*ZIENT were observed when large scale clinical doses were attempted. This translated into insufficient [^{123}I]-*m*ZIENT being isolated for a patient dose.

	Reaction yield of [^{123}I]-*m*ZIENT/%
Small scale reaction (74MBq)	48.1 ± 1.8 (n=2)
Clinical scale reaction (>2GBq)	11.2 ± 11.1 (n=3)

Table 1: HPLC yields of [^{123}I]-*m*ZIENT for small scale and clinical scale reactions

Peracetic acid	vol 0.1M NaOH/µl[a]		vol 0.05M NaOH/µl[b]	
	50	200	50	200
1% v/v added	1.5	1.5	1.5	1.5
Post quench	9	8	8.5	9
10% v/v added	1.5	1.5	1.5	1.5
Post quench	9	8	8	8

[a]acid added: (µl 0.1M NaOH) x 0.2+10 µl; [b]acid added (µl 0.05M NaOH) x 0.1+10 µl

Table 2: Results of pH measurements for different reaction mixtures

	Reaction yield of [^{123}I]-*m*ZIENT/%
Reaction using precursor stored as dry, single synthesis aliquot	48.1 ± 1.8 (n=2)
Reaction using precursor stored in bulk	60.7 ± 6.6 (n=2)

Table 3: Reaction yields of [^{123}I]-*m*ZIENT for precursor batches stored as single synthesis aliquots vs. precursor stored in bulk from small scale reaction (74MBq)

- Mimics of large and small scale reactions using either 0.05M or 0.1M NaOH showed no difference in pH.
- Reaction yields were higher when precursor was freshly aliquoted from bulk storage immediately prior to synthesis.
- To date, one subject on SSRI medication has been scanned.

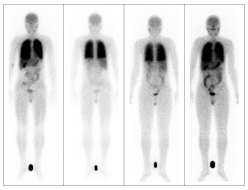


Figure 1: Whole body image of patient on SSRI medication at 2hrs and 6hrs

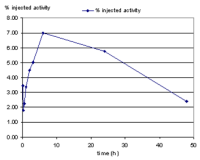


Figure 2: Percentage of injected activity in blood up to 48 hours

Conclusions

A problem with the storage conditions of the precursor has been identified and a new batch of precursor has been obtained.
Precursor should be stored in bulk, then a small amount taken immediately prior to reaction.
The remaining clinical scans for this study are being scheduled.

References

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2. Willeit et al; Biol. Psych 2000; 47: 482-489
3. Plisson *et al*; J. Med..Chem 2006; 49: 42-946
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