In one aspect, there is provided a pharmaceutical composition of ^{18}F-FACBC characterised in that said composition:

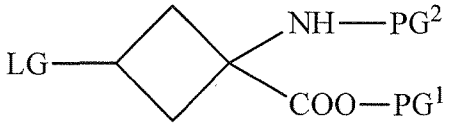
(i) comprises 50-100 mM citrate buffer; and,

(ii) has a pH of 4.0-5.0,

with the proviso that said composition does not comprise a sugar lactone or a sugar alcohol radiostabiliser.

In another aspect, there is provided a method to obtain a radiopharmaceutial composition wherein said composition is as defined above and wherein said method comprises:

(i) reacting with a suitable source of [^{18}F]fluoride a precursor compound of Formula I:



(I)

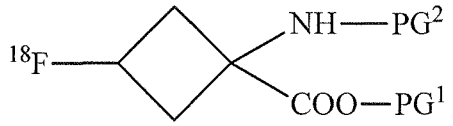
wherein:

LG is a leaving group selected from from methanesulfonic acid, toluenesulfonic acid, nitrobenzenesulfonic acid, benzenesulfonic acid, trifluoromethanesulfonic acid, fluorosulfonic acid, and perfluoroalkylsulfonic acid;

PG^1 is a carboxy protecting group selected from methyl, ethyl, t-butyl and phenyl; and,

PG^2 is an amine protecting group selected from t-butoxycarbonyl, allyloxycarbonyl, phthalimide, and N-benzylideneamine;

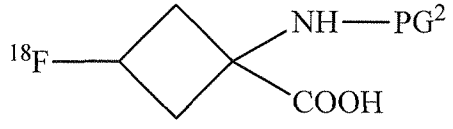
to obtain a compound of Formula II:



(II)

wherein PG^1 and PG^2 are as defined for Formula II;

(ii) reacting said compound of Formula II with a PG^1 deprotecting agent to obtain a compound of Formula III:



(III);

wherein PG^2 is as defined for Formula I;

(iii) reacting said compound of Formula III with a PG^2 deprotecting agent to obtain [^{18}F]FACBC;

(iv) formulating said [^{18}F]FACBC with citrate buffer to obtain said pharmaceutical composition.

Claims

(1) A pharmaceutical composition of ^{18}F-FACBC characterised in that said composition:

(i) comprises 50-100 mM citrate buffer; and,

(ii) has a pH of 4.0-5.0,

with the proviso that said composition does not comprise a sugar lactone or a sugar alcohol radiostabiliser.

(2) The pharmaceutical composition as defined in Claim 1 comprising 60-90 mM citrate buffer.

(3) The pharmaceutical composition as defined in either Claim 1 or Claim 2 comprising 75-85 mM citrate buffer.

(4) The pharmaceutical composition as defined in any one of Claims 1-3 that has a pH of 4.1-4.5.

(5) The pharmaceutical composition as defined in any one of Claims 1-4 that has an end of synthesis (EOS) radioactive concentration (RAC) of at least 1000 MBq/mL.

(6) The pharmaceutical composition as defined in any one of Claims 1-5 that has an end of synthesis (EOS) radioactive concentration (RAC) of at least 1500 MBq/ml.

(7) The pharmaceutical composition as defined in any one of Claims 1-6 which comprises not more than 150 µg/mL 1-amino-3-hydroxyl-cyclobutane-1-carboxylic acid (hydroxyl-ACBC).

(8) The pharmaceutical composition as defined in any one of Claims 1-7 which comprises not more than 80 µg/mL hydroxyl-ACBC.

(9) The pharmaceutical composition as defined in any one of Claims 1-8 which comprises not more than 0.15 µg/mL 1-amino-3-fluoro-cyclobutane-1-carboxylic acid (FACBC).

(10) The pharmaceutical composition as defined in any one of Claims 1-9 which

comprises not more than 0.10 μg/mL FACBC.

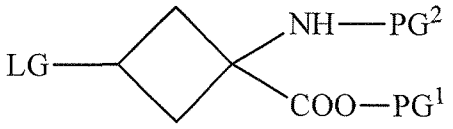
(11) The pharmaceutical composition as defined in any one of Claims 1-10 which comprises not more than 2.0 μg/mL 1-amino-3-chloro-cyclobutane-1-carboxylic acid (chloro-ACBC).

(12) The pharmaceutical composition as defined in any one of Claims 1-11 which comprises not more than 1.0 μg/mL chloro-ACBC.

~~(13) The pharmaceutical composition as defined in any one of Claims 1-12 with the proviso that said composition does not comprise a radiostabiliser, wherein said radiostabiliser is a sugar lactone or a sugar alcohol.~~

(~~14~~13) A method to obtain a radiopharmaceutial composition wherein said composition is as defined in any one of Claims 1-~~13~~12 and wherein said method comprises:

(i) reacting with a suitable source of [^{18}F]fluoride a precursor compound of Formula I:



(I)

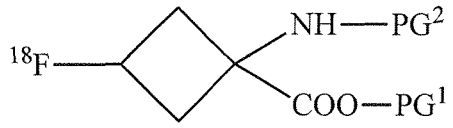
wherein:

LG is a leaving group selected from methanesulfonic acid, toluenesulfonic acid, nitrobenzenesulfonic acid, benzenesulfonic acid, trifluoromethanesulfonic acid, fluorosulfonic acid, and perfluoroalkylsulfonic acid;

PG^1 is a carboxy protecting group selected from methyl, ethyl, t-butyl and phenyl; and,

PG^2 is an amine protecting group selected from t-butoxycarbonyl, allyloxycarbonyl, phthalimide, and N-benzylideneamine;

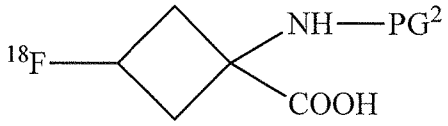
to obtain a compound of Formula II:



(II)

wherein PG^1 and PG^2 are as defined for Formula II;

(ii) reacting said compound of Formula II with a PG^1 deprotecting agent to obtain a compound of Formula III:



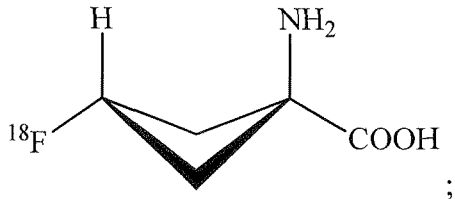
(III);

wherein PG^2 is as defined for Formula I;

(iii) reacting said compound of Formula III with a PG^2 deprotecting agent to obtain [^{18}F]FACBC;

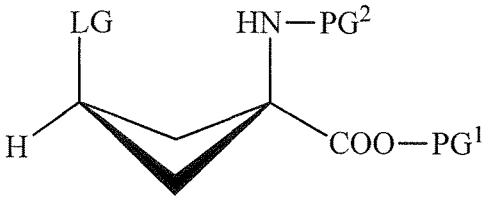
(iv) formulating said [^{18}F]FACBC with citrate buffer to obtain said pharmaceutical composition.

(~~15~~14) The method as defined in Claim ~~14~~13 wherein said [^{18}F]-FACBC is trans-1-amino-3-[^{18}F]-fluorocyclobutanecarboxylic acid (*anti*-[^{18}F]-FACBC):



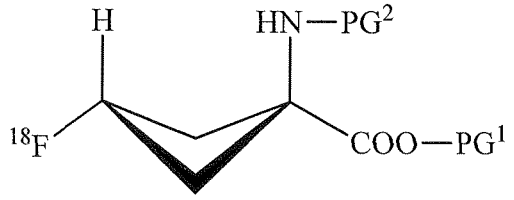
;

said compound of Formula I is a compound of Formula Ia:



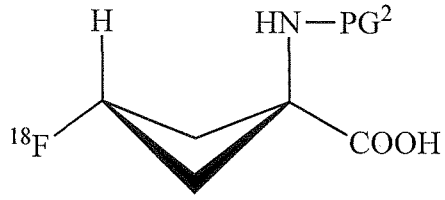
(Ia)

said compound of Formula II is a compound of Formula IIa:



(IIa); and,

said compound of Formula III is a compound of Formula IIIa:



(IIIa)

wherein PG^1 and PG^2 are as defined in Claim 14 for Formula I.

(~~16~~15) The method as defined in either Claim ~~14~~13 or Claim ~~15~~14 wherein PG^1 is ethyl.

(~~17~~16) The method as defined in any one of Claims ~~14~~13-~~16~~15 wherein PG^2 is t-butoxycarbonyl.

(~~18~~17) The method as defined in any one of Claims ~~14~~13-~~17~~16 wherein said PG^1 deprotecting agent is NaOH.

(~~19~~18) The method as defined in any one of Claims ~~14~~13-~~18~~17 wherein said PG^2 deprotecting agent is HCl.

(~~20~~19) The method as defined in any one of Claims ~~14~~13-~~19~~18 which is carried out on an automated synthesis apparatus.