SUMMARY ~~OF THE INVENTION~~

As [^{18}F]flutemetamol and its deprotected precursor, AH111832 (6-hydroxy-2-(4'-(N-methyl)amino-3'-nitro)phenylbenzothiazole) are physico-chemically very similar, preparative HPLC is required to separate them. However, Applicants have now found that it is possible to replace the preparative HPLC equipment in previous purification processes with low cost, single-use solid phase extraction (SPE) cartridges for purification of [^{18}F]flutemetamol.

In one aspect, there is provided ~~Accordingly, the present invention provides~~ a purification process comprising the following steps:

(a) passing a diluted crude product reaction mixture comprising flutemetamol through a first reverse phase SPE cartridge;

(b) washing said first reverse phase SPE cartridge with a water/acetonitrile, tetrahydrofuran(THF)/water, methanol(MeOH)/water or isopropanol/water mixture; preferably, a water/acetonitrile mixture;

(c) rinsing said first reverse phase SPE cartridge with water once step (b) is completed;

(d) eluting said first reverse phase SPE cartridge with acetonitrile or tetrahydrofuran; preferably, acetonitrile;

(e) directly passing the mixture from said eluting step (d) through a normal phase SPE cartridge to give an acetonitrile or tetrahydrofuran solution; preferably, an acetonitrile solution, comprising purified flutemetamol;

(f) diluting said acetonitrile or tetrahydrofuran solution; preferably, an acetonitrile solution, comprising purified flutemetamol, with water to form a diluted water/acetonitrile or a diluted water/tetrahydrofuran solution; preferably, a diluted water/acetonitrile solution, comprising purified flutemetamol, wherein said water/acetonitrile solution contains about 40-70% (v/v) water; preferably at least about 40% (v/v) water; more preferably at least about 50% (v/v) water;

(g) passing the diluted water/acetonitrile or diluted water/tetrahydrofuran solution; preferably, diluted water/acetonitrile solution, comprising purified flutemetamol of step (f)

through a second reverse phase SPE cartridge and trapping the flutemetamol on said cartridge second reverse phase SPE cartridge;

(h) rinsing said second reverse phase SPE cartridge with water; and

(i) eluting the trapped purified flutemetamol from second reverse phase SPE cartridge with an injectable organic solvent; preferably, ethanol or DMSO; preferably with ethanol.

According to the present disclosure~~invention~~, the purified flutemetamol can be collected after step (i).

The present ~~invention~~ disclosure also provides a purification process of the present ~~invention~~disclosure, wherein the process is automated.

The present ~~invention~~ disclosure also provides a cassette on which a purification process of the present ~~invention~~ disclosure can be performed.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 depicts hydrophilic precursor derivatives.

Figure 2 depicts the effect of ambient temperature and acetonitrile concentration on yield.

Figure 3 depicts the effect of ambient temperature and acetonitrile concentration on level of chemical impurities.

Figure 4 depicts a flow chart describing the production and formulation of Flutemetamol (^{18}F) Injection on a cassette of the present invention.

Figure 5 is a picture of a fully assembled cassette of the present invention for the production of Flutemetamol (^{18}F) Injection, showing all tubing and prefilled reagent vials and the SPE cartridge.

Figure 6 shows the numbering of each position of the cassette manifold of the present invention.