TADDEO
AUTOMATED MODULE FOR SYNTHESIS OF THERAPEUTIC RADIOPHARMACEUTICALS

Features

- Multipurpose synthesis module
- Open software for different synthesis procedures such as:
  - [^{60,61,64}Cu]-ATSM
  - [^{90}Y]-DOTATOC
  - [^{124,131}I]-MIBG
  - ^{68}Ge/^{69}Ga elution and [^{68}Ga]-DOTATOC synthesis
  - ^{188}W/^{188}Re elution, concentration and [^{188}Re]-Lipiodol synthesis
  - ZEVALIN™ preparation
- Disposable sterile cassette with 15 motorised zero dead volume valves
- Disposable 10 ml conical-bottom sterile reactor
- Two high precision syringe actuators
- Two heaters with cooling system for reactors or reagents
- High temperature resistant (150°C) disposable reactors
- Multiple scintillation crystal radioactivity detectors
- Human-Machine Interface on Laptop

Applications

The growing clinical demand of radiopharmaceuticals for Radio-metabolic Therapy, radio-labeled with ^{90}Y, ^{177}Lu, ^{188}Re, etc, combined with the severe operator's exposure for high activity routine handmade preparations, has prompted us to investigate the feasibility of an automated process combining the radioprotection issues and the GMP pharmaceutical requirements.

The result of our investigation has been Taddeo, a fully automated module for the preparation of therapeutic radiopharmaceuticals that guarantees high reproducibility synthesis with high yields and high radio-protection for the operators.

A prototype of the automated synthesis module has been investigated by using a typical ^{90}Y-radio-labeling of DOTATOC to evaluate its efficiency and flexibility; such investigation was performed in cooperation with a well-known radiopharmaceutical institution.

Materials and methods

A general purpose module (Taddeo) has been developed consisting of a "black box" equipped with:

Disposable sterile cassette with 15 motorised zero dead volume valves

Two high precision syringe actuators

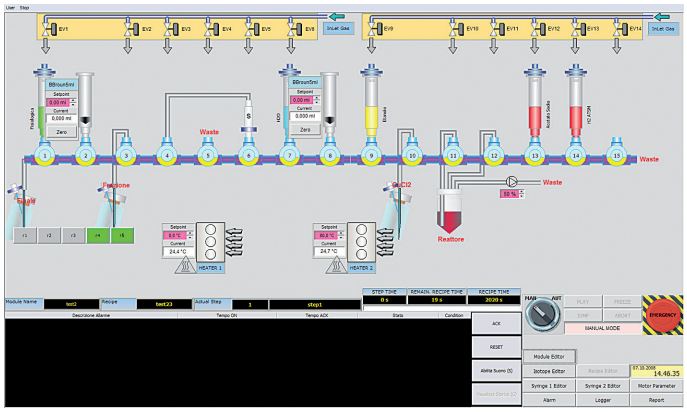
Two heaters with cooling system for reactors or reagents

- five radioactivity detectors
- a membrane vacuum pump
- ten inert gas supplies at low and high pressure

The module works with a sterile and easily removable valves manifold, used as "synthesis cassette" where the user can install his customisable labeling kit. (Comecer supplies the sterile cassette without any reagent; it is the customer's responsibility to provide the suitable reagents and accessories, such as cartridges, filters, needles, tubings, etc.).

The disposable cassette and the reactor are made of Polysulfone, a special polymer resistant to high concentration of solvents usually used in radiochemistry and resistant to high temperatures (until 150 °C).

Taddeo is controlled by a laptop computer via a dedicated PC-PLC interface. Its software aims to be user friendly and is completely open to let the user create his own cassette configuration and labeling procedure. It is in fact possible to introduce via software all the components that the operator may went to mount on his disposable cassette.



The software is able to save and easily recall at any moment all the personal cassette configurations created by the user. All the parametres of the radio-labeling sequence are also stored in a database (valves position, syringe type and position, heating parametres, step times...) and can be edited at any time via software or via Microsoft Access®. As an example, the following is our 90Y DOTATOC radio-labeling sequence:

- transfer of $^{90}YCl_3$ to the reactor
- recovery of residual $^{90}YCl_3$ with buffer pH 5.5 and transfer to the reactor
- transfer of peptide solution to the reactor
- labeling for 30 min at 90 °C
- activation of the C18 SepPak cartridge
- purification on the C18, using 100% ethanol as the elution solvent.

Conclusions

Taddeo has the capability to work with small reagent volumes and negligible losses, high yield and reproducibility. Moreover, the disposable 15-valve cassette offers the versatility to perform the radio-labeling and the purification steps in a fully-automated way.

This module allows you to perform the synthesis in accordance with GMP, drastically reducing the manipulation of radioactive reagents. The contamination of the module is avoided by the use of the disposable cassette, as well as Its cleaning validation (CIP-SIP).

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