Design and Construction of an Equipment for the Radiochemistry Process of Molecules Marked for the Sector Health

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Abstract: At the Plant of Production of Radioisotopes part of Nuclear Center of Mexico (ININ), weekly radiofarmaceutics of sodium iodohippurate and meta-iodobenzyl-guanidine are prepared, these compounds are known as marked molecules with iodine-131. Currently the processes for the preparation of these compounds are carried out individually and in manual form, in box of gloves, presenting radiological risks. To avoid these risks, this work, shows equipment that is inside a warm cell with the finality of minimizing the radiological risks. Also, this semi-automated equipment has the purpose of to reduce the radiation exposure of personnel involved in the process of marking molecules. The routine industrial production with this equipment starts with the preparation of 9 marked doses of sodium iodohippurate of 2.73 mCi of iodine-131, each of the vials with saline solution of 4.5 mL and the product that containing the marked molecules of 0.5 mL with a percentage of marked of 95.6%. The innovation of this work consists in presenting a new design of equipment, for marked molecules, formed by electrical, mechanical, vacuum systems, and air extraction system.

Key words: Construction, equipment, molecules marked, sector health.

1. Introduction

The ININ's (Mexico's Nuclear Research Center) Radioisotopes Production Plant is working on the development of radiopharmaceuticals that are sold in the area of medicine nationally as well as internationally.

The administration of a radiopharmaceutical to a patient enables the study of different organs of the human body through two-dimensional (scintigraphy) or three-dimensional (tomography) images.

This paper refers to the design, construction and installation of molecule marking equipment inside a hot cell used to prepare the radiopharmaceuticals: sodium iodohippurate and meta-iodobenzyl-guanidine

The equipment design is based on the study of the hot cell where it is located, thus determining the area where the equipment is to be set up and based on this area it was decided where to place the equipment to be utilized during the marking process and the mechanical components that were especially designed for this process.

Once the equipment was designed, it went on to the stage of construction of the mechanical pieces that were assembled in a base of 0.5 inch thick aluminum base. The functioning of the equipment is basically based on pneumatic pistons and automatic burettes that are activated from the outside of the cell during the molecule marking process, as well as automatic burettes for solution dosing. The process of marked, it is carried out inside a warm cell of the following way: preparation of the solutions for the process, selection

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of the isotope that will be used, the marking of the molecule and the preparation of the doses that are sold as product to the hospitals in the area of nuclear medicine.

2. Experimental

Formerly, the processes for the preparation of these radiopharmaceuticals were carried out in a glove box or in hot cells for radiopharmaceuticals production, which entailed radiological safety risks/hazards, difficulties in the process manipulation, or rather, the radioactive material, other chemical compounds and the laboratory material, like disposable syringes, lead shielding, vials containing reagents and other devices were manipulated manually and occasionally with the hot cell's manipulators. Therefore, from a radiological safety view point, the operator is exposed to radiation and radioactive contamination. In order to lessen these inconveniences, it is necessary to have an equipment with the semi-automated process, in order to reduce considerably the exposure to the radiation and the contamination of radioactive material of direct form.

The molecules marking process [1]:

The equipment design was accomplished taking into account 3 stages of the marking process for sodium iodohippurate and meta-iodobenzyl-guanidine, since the preparation characteristics were similar for both processes. For the equipment design, one process is considered, since they start from a common basis (trunk). In order to be able to begin with the equipment design, the authors divided it into three stages.

2.1 Preparation of the Copper Sulfate CuSO_4 Solution

(1) To the CuSO_4 in a 20 mL vial 2 mL of H_2O are added;

(2) From the solution above 100 μL are taken and used in the preparation of meta-iodobenzyl-guanidine;

(3) To the remaining solution 8 mL of H_2O are added;

(4) From the aforementioned solution (3) 1 mL is

taken for the preparation of sodium iodohippurate.

2.2 Preparation of Solutions for the Two Radiopharmaceuticals

Taking into account the previous stage, the marking process for sodium iodohippurate is developed, thus guaranteeing the subsequent design of the molecule marking equipment for the two radiopharmaceuticals, thanks to the similarity of the processes.

2.2.1 Solution 1

(1) The non-radioactive hippuran is placed in a 20 mL vial then 2 mL of ethylic alcohol are added and later 68.09 mCi of iodine-131 (it is topped with a rubber stopper and an aluminum cap);

(2) Then 1 mL of the abovementioned CuSO_4 solution from subsection (4) is added;

(3) It is put in an autoclave at 115 °C for 16 minutes.

2.2.2 Solution 2

In a disposable 10 mL syringe the buffer solution consists of a mixture of:

(1) Ammonium phosphate and;

(2) Two-phase phosphate.

2.2.3 Solution 3

In a 20 mL the following reagents are mixed:

(1) 4 mL of propylene glycol;

(2) 1 mL of EDTA (Ethylene Diamine Tetraacetic Acid);

(3) 1 mL of Sodium Citrate;

(4) 1 mL of NaCl Sodium Chloride.

2.3 Molecule Marking Equipment Design and Construction

The molecule marking equipment is designed and placed on an aluminum platform, then put inside a hot cell, thus we are able to assemble all the equipment components without damaging the surface of the hot cell itself and allows us to change components during maintenance procedures. The cell is equipped with 4 mechanical manipulators that handle the molecule marking process. The pneumatic pistons, basic components of the equipment, allow movements to be

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performed in a coordinated manner, for example, the adding and extracting of solutions from one container to another. The equipment has 5 automatic burettes: 2 burettes for the marking of the sodium iodohippurate and meta-iodobenzyl-guanidine molecules respectively and 2 burettes to dose each compound's final product (dose) and it also has 1 burette for dosing the saline

solution of the final dose. The equipment is designed to work with elevated doses up to 500 mCi. With the above considerations in mind, the authors continue with the marking process. The solutions are put into the hot cell and placed in the equipment, in order to perform the marking process for the sodium iodohippurate, using the following procedures (Fig. 1):

Fig. 1 Molecule marking equipment: sodium iodohippurate and meta-iodobenzyl-guanidine.

(1) To the solution 1, which contains the hippuran, the solution 2 is added, using the pistons, thus resulting in solution 4;

(2) The automatic burettes have an entry opening, where solutions are absorbed and an exit opening, where solutions are discharged;

(3) The solution 4 goes to the iodohippurate 1 burette in order to be discharged afterwards through a Millipore filter and mixed with solution 3;

(4) With the mixture of the solutions 3 and 4 the molecule is marked and the solution 5 is obtained;

(5) Solution 5 is placed in the horizontal piston and the iodohippurate 2 burette needle put in position to be absorbed. The burette exit opening handles the dosing of the amounts (doses) required in the vials that are located in a rack;

(6) Thus the final product is obtained in amber color vials.

3. Results and Discussion

This molecule marking equipment design and construction facilitates the manipulation of the molecule marking processes, thus reducing the radiological risks/hazards and the main advantage is to manage to obtain 2 compounds marked with major consumption in the market.

The mechanical pieces of the molecule marking equipment are made of aluminum, since this is a non-corrosive material, and easy to machine and the components of the pneumatic system are easily unassembled when equipment maintenance requires it. In order to operate this equipment, it is necessary for the conducts to be transparent and the hot cell to be well illuminated, since it is important to observe the liquids during the process, thus to obtain a better marking.

The injector needles of the automatic burettes must have exact measures of agreement to the design of the equipment, in order to guarantee the mixing of the solutions and thus guaranteeing a better molecule marking.

The Fig. 2 shows the molecule marking equipment that is installed inside the cell with all its mechanical parts visible.

The hot cell for the molecule marking equipment is located in the Radioisotope Production Plant and is set on a metallic structure of 80 cm in height, the cell's shape is cubic and its walls are 10 cm cubic lead bricks, covered with acrylics, which give the cell walls a thickness of 11 cm, sufficient for working with the doses required by the molecule marking process. It is located on the inside on top of a base structure. It is covered (lined) with a stainless steel sheet metal plate, inside of which the molecule marking equipment is located and there are also air extraction and vacuum systems in place. On the outside, two mechanical manipulators in form of tongs and two manipulators on the upper part that provide a greater range of movement when working in a larger area inside the cell. The Fig. 3 shows the hot cell and the peripheral equipment.

Located inside the cell are the devices that participate in the process: a shaker oven, a capper and decapper for containers, a radioactivity/radiation meter and the 8-piston-equipment. All these devices are activated from the outside, using the process control panel located on the front part of the cell (Fig. 4).

The system of dosing solution formed by the automatic burettes which is manipulated from the exterior of the cell, across automatic controls that dose the exact volume of solution, where the radioactive activity that is dosed is depending on the volume that contains every burette and this volume is depending on the accounts that there marks the electronic control (Fig. 5).

The third stage, which consisted in the utilization of the marking equipment based on a sodium iodohippurate trial marking, where 10 doses were obtained and offered on the business market for the medical area. The trial resulted in the following:

Taking into account solution 1, with 68.08 mCi of iodine-131 to begin the process of bearing molecule,

Fig. 2 Molecule marking equipment installed in the hot cell.

Fig. 3 Hot cell for molecule marking equipment.

Fig. 4 Control panel used in the marking process for sodium iodohippurate and meta-iodobenzyl-guanidine.

Fig. 5 Control system for automatic dosing burettes for the molecule marking process.

Table 1 Dose of sodium iodohippurate.

Volume of the product (mL)	volume of saline solution (mL)	activity mCi (mBq)
0.55	4.45	3.00 (0.11)
0.55	4.45	3.00 (0.11)
0.55	4.45	3.00 (0.11)
0.55	4.45	2.78 (0.10)
0.55	4.45	2.70 (0.10)
0.55	4.45	3.00 (0.11)
0.55	4.45	3.00 (0.11)
0.55	4.45	3.00 (0.11)
0.55	4.45	2.84 (0.11)
0.55	4.45	3.00 (0.11)
Total activity of dosed dose		29.32 (1.08)

of which 3 mCi for analyses of Quality Control. During the marking process 10.09 mCi are lost while going through process lines and laboratory material where it is trapped, which let the amount to be dosed

for the final doses come to 54.50 mCi. When the doses preparation was initiated we had 50 mCi with a specific activity 5 mCi/mL, which were used to prepare 10 doses. The Table 1 shows the results. We can see in the Table 1, that the total in dosed activity was 29.32 mCi and the remaining radioactive activity of 20.68 mCi could be used to make another 6 doses, nevertheless, the production batch was established with 10 doses and received the number 7,410. It was the first one produced with the molecule marking equipment.

4. Conclusions

The equipment facilitates achieving the molecule marking processes with the main advantage that this equipment enables the marking of the 2 compounds that are produced for the medical sector. Under consideration of the foregoing we can say that it is possible to considerably reduce the exposure to radiation when the marking processes are performed in semi-automatic equipment, which also guarantees the highest degree of prevention for contamination risks/hazards through radioactive substances.

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