EFFECT OF DIFFERENT GAMMA IRRADIATION DOSES ON THE DECREASE OF TROFIN POWDER BIOBURDEN

Lenay Barrera; Isabel Otero; Adriana Díaz; Dania Rodríguez; Juana Suárez
Centro de Estudios Aplicados al Desarrollo Nuclear
Calle 30 esq. 5ta # 502 Miramar Playa

ABSTRACT

Ionizant irradiation microbicide action is one of the most important effect in medical industry. It has been used for the sterilization and decontamination of medical devices, biological tissues, drugs and so on. Trofin is a natural nutritional supply principally used for children and old people. Because of its composition characteristics is not appropriate to use another sterilization methods. The decontamination dose for gamma radiation of Trofin batches 7001 and 6006 were determined using different doses. It was used an sterility assurance level (SAL) of 10^{--2} enough for this kind of product.

INTRODUCTION

There are not world agreement in relation to the standards related to sterilization by ionizing irradiation. This happens because of two reasons: The first one is that the control of the use of that kind of radiation is not joined to the national control of, drugs, medical devices, food and equipment production, the other one is that the assurance level of a product or item have some common principles to any kind of sterilization method and they are applied automatically [6].

The radiation process is a physical one, involving the exposure of a product to ionizing radiation. The product is exposed in specially designed equipment to gamma rays from a Cs^{137} or Co^{60} radionucleides, or to an electron or x-ray beam from an electron beam generator. When properly applied, radiation sterilization is safe and reliable industrial process [4].

Ionizing irradiation is the only kind of sterilization where it is necessary to demonstrate the no production of any toxic product after its application. Generally solids are less damaged by irradiation. This kind of toxicity should be distinguished from the toxicity derived from the agent like some chemicals. Up to now the medicaments radiosterilization is more used in dry solids, powder or some oils [3].

Substances sterilized by radiation may either lose some original properties or assume some new ones because radiation may induce significant molecular and structural changes. Aimed and undesired effects are subject to the criteria of applicability. Technology, radiation dose and radiation conditions should also follow this principle.

The following questions may be raised in connection with the radiation sterilization of pharmaceuticals and pharmaceutical basic materials.

- How the presence of pharmaceuticals influence the sterilizing efficiency of radiation;
- Whether the radiation induces undesirable changes in the quality pharmaceuticals.

Because of the destructive nature of ionizing radiation and of the difficulty in predicting its radiolytic effect, particulary in some more complex molecules, it is necessary to analyze each compound for molecular damage changes in quality, or for induction of toxic products[1].

The irradiation with low doses have advantage that low the damage in the product[2]. The doses required for treatment of pharmaceutical depend of the bioburden, microbial total count, radiosencibility of bioburden and chemical structure of the material.

The bioburden admitted in Trofin is $5x10^3$ ufc/g, by the administration way and its naturals was realized the bioburden variation studies with different irradiated doses. The doses aplicated to the batches were 1,2,3,4,5kGy. The product was irradiated in its finally bottle.

MATERIALS AND METHODS

Methods to determine the radiation doses for sterilization base in the inactivation of the bioburden when expose to this treatment.Over the bases of of the results obtained.Calculation are made to specify the necesirry doses to sterilize devices or products,the sterility assurrance level(SAL)required.

Bioburden determination

- Batches 6006 and 7001

It was took 5 samples randomly for each bacth. 1g from each one is added in 99ml of saline solution. From this dilution is made several dilutions 1:10 in saline solution. From each one were cultivated five plates with 1 ml of the dilution and 15-20 ml of Tryptone Soya Agar at 45 ± 2 ^{0}C. They were counted after 72 h of incubation [8].

Coliforms determination

Multiple tube method (most probable number) was used for each samples of each batch according to the standard ISO 9308-2 [8]. The incubation was during 48 hours at 35-37 ^{0}C.

- Confirmatory test

From positives tubes was taken 1 ml and added to Brilliant green-lactose broth with Durham tubes to determine gas production. The incubation was during 48 hours at 35-37 ^{0}C.

- Identification test

Positives tubes were cultivated in SS Agar, Mac Conkey Agar and aislated colonies from both mediums were cultivated in Kliger iron Agar to differentiate among species.

Irradiation

It was used a Co^{60} installation model PX-γ-30, located in Radiobiology and Irradiation Techniques Department belonging to Center of Applied Studies to Nuclear Development (CEADEN). The dose mapping of both installation and irradiation was made trough Fricke dosimetric system [7]. Batches were irradiated in the end baggage.

RESULTS AND DISCUSSION

Methods to determine the radiation doses for sterilization base in the inactivation of the bioburden when expose to this treatment. Over the basis of this results obtained calculation are made to specify the necesary doses to sterilize devices or products the sterility assurance level(SAL) required.

The International Atomic Energy Agency (IAEA) is an international organization with the objective "to accelerate and enlarge the contribution of atomic energy to peace, health and prosperity throughout the world". In keeping with these defined service objectives and with particular regard to the emphasis of the programs for the benefit of the developing Member States, the IAEA's activities in the current context aim to promote the applications of "microbicidal effects of ionizing radiation energy" to help achieve effective sterilization of indigenous medical supplies and to attenuate the risks of nosocomial disease during clinical interventions[5].

In figures 1,2 and 3 are shown results obtained in the experiments .In table 1 is shown values of bioburden of batches studied, where in batch 6006 the charge is bigger than the accepted for this natural nutritional

supply, so is necessary make it low for later uses and in batch 7001 the charge is $5x10^3$ which is admitted but coliforms can be found ,so is necessary decontamination.

Table 1. Value of bioburden

batch	Total count	COLIFORM
6006	10^5 ufc/g	not seen
7001	5×10^3 ufc/g	*Salmonella sp.*

In tables 2 and 3 are represented values of bioburden and the presence of coliforms in every batch for each dose used. In batch 6006 with a dose of 4 kGy reaches decontamination, In case of batch 7001 with a dose of 3 kGy kills all coliforms and low its charge till 200ufc/g.

Batch 6006.

Table 2. Values of bioburden de la irradiated sample

DOSES (kGy)	BIOBURDEN	COLIFORM
1	10^5 ufc/g	Not seen
2	10^5 ufc/g	Not seen
3	10^4 ufc/g	Not seen
4	1100 ufc/g	Not seen
5	200 ufc/g	Not seen

BATCH 7001:

Table 3. Values of bioburden de la irradiated sample

DOSES (kGy)	BIOBURDEN	COLIFORM
1	5×10^3 ufc/g	*Salmonella sp.*
2	1100 ufc/g	*Salmonella sp.*
3	200 ufc/g	Not seen
4	90 ufc/g	Not seen
5	90 ufc/g	Not seen

CONCLUSIONS

-With a dose of 4kGy is possible decontaminate batch 6006 of Tofin in powder for its use as a natural nutritional supply.

- For decontaminate batch 7001 was necessary a dose of 3 kGy.

REFERENCES

[1] Dám, A. (1988). Radiation Treatment Pharmaceutical. International Training Course on Radiation Technology and Engineering. Budapest, Hungría. 16 mayo-10 junio

[2] Gopal, N.G:S; (1978).Radiation Sterilization of Pharmaceutical and Polymer. Radiat. Phys. Chem.12, 35.

[3] Gazsó, L.G. Dám, A. M., Kaewpila, S. and Maschek, Y. (1996). Radiation Treatment of Pharmaceutical. Radiat. Phys. Chem. Vol 47, 3 pp515-517.

[4] ISO 11137."Esterilización de productos de uso médicos- Validación y control de rutina- Esterilización por radiación gamma y haces de electrones ". ISO,1995.

[5] Mukherjee, R.N. IAEA Standards Applicable for Sterilization. International Atomic Energy Association, Vienna, Austria.

[6] Outschoorn, A.S. (1978). Pharmacopeial bieufpoints on radiation sterilization, Sterilization by ionizing radiation ed Gaughram/Goudie, 1978 pp. 297-307.

[7] Prieto, E. F., Chávez, A. 1993. "Influencia de diferentes factores en la calibración de los dosímetros Perspex (Red and Clear). Nucleus No. 15; 16-19.

[8] Tallentire, A. (1996). Curso regional de capacitación sobre radioesterilización. Conceptos básicos de aseguramiento de la calidad y radiomicrobiología. Santiago de Chile.