

Importance of gamma radiation using sodium pertechnetate (TC 99m) and iodine 131 as a suggestion in the treatment of COVID-19

Importância da radiação gama utilizando o pertechnetato de sódio (TC 99m) e o iodo 131 como sugestão no tratamento da COVID-19

Importancia de la radiación gamma utilizando pertechnetato de sodio (TC 99m) y yodo 131 como sugerencia en el tratamiento del COVID-19

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Abstract

Objective: to point out the importance of nuclear medicine for the diagnosis and therapy of COVID-19, in addition to reporting the efficacy of treatment with radioisotopes (sodium pertechnetate and iodine 131) in individuals infected with SARS-CoV-2 causing viral sterility and preventing its mutagenesis and ensuring the absence of adverse reactions. **Methodology:** This is a review of the narrative-type literature, prepared between June and September 2020, using the following databases: PubMed, SciELO and Lilacs. Thus, there was the inclusion of articles published between 1971 and 2020. **Results and Discussion:** The use of gamma and neutron radiation for the purpose of eliminating viral pathogens has been extensively researched in American studies, initially focusing on H1N1. The substance of Sodium Pertechnetate, suggested in this study, and iodo 131 (designed to act as prevention in the cervical

region) have the potential for satisfactory responses in the therapeutic treatment of COVID-19 due to the innocuous, painless and free of any effect methodology therefore, offering greater security to the treatment. Inferring in the replication of the coronavirus through the electrolysis of its fatty structure, since with the sterilization of its RNA molecule there will be no replication. Final Consideration: Based on the effectiveness of this method in sterilization protocols and action on various types of microorganisms, especially other viruses that affect the respiratory system, it is suggested as a safe, low-cost and low-dose radioactivity method for the patient, when used doses similar to those of the diagnostic and therapeutic practice in Nuclear Medicine. It should be noted that the administration protocol must be in accordance with the standard already recommended clinically, with full guarantee of the absence of associated effects. For better clarification, there is a need for more specific research within the scope of SARS-CoV-2.

Keywords: Gamma radiation; Nuclear medicine; COVID-19; Radioactive therapy.

Resumo

Objetivo: apontar a importância da medicina nuclear para o diagnóstico e terapia do COVID-19, além de relatar a eficácia do tratamento com radioisótopos (pertecnato de sódio e iodo 131) em indivíduos infectados pelo SARS-CoV-2 causando esterilidade viral e prevenindo sua mutagênese e garantindo a ausência de reações adversas. **Metodologia:** Trata-se de uma revisão da literatura do tipo narrativa, elaborada entre junho e setembro de 2020, utilizando as seguintes bases de dados: PubMed, SciELO e Lilacs. Assim, houve a inclusão de artigos publicados entre 1971 e 2020. **Resultados e Discussão:** O uso da radiação gama e de nêutrons com a finalidade de eliminação de patógenos virais tem sido extensamente pesquisado em estudos americanos, inicialmente com foco no H1N1. A substância do Pertechnetato de Sódio, sugerida neste estudo, e o iodo 131 (desenvolvido para atuar como preventivo na região cervical) têm potencial para respostas satisfatórias no tratamento terapêutico da COVID-19 devido à inócua, indolor e isenta de qualquer efeito metodologia, portanto, oferecendo maior segurança ao tratamento. Inferindo na replicação do coronavírus por meio da eletrólise de sua estrutura gordurosa, já que com a esterilização de sua molécula de RNA não haverá replicação. **Considerações Finais:** Com base na eficácia deste método em protocolos de esterilização e ação sobre vários tipos de microrganismos, principalmente outros vírus que afetam o sistema respiratório, é sugerido como método seguro, de baixo custo e baixa dose de radioatividade para o paciente, quando usado em doses semelhantes às da prática diagnóstica e terapêutica em Medicina Nuclear. Ressalta-se que o protocolo de administração deve estar de acordo com o padrão já recomendado clinicamente, com total garantia da ausência de efeitos associados. Para melhor esclarecimento, há necessidade de pesquisas mais específicas no âmbito do SARS-CoV-2.

Palavras-chave: Radiação gama; Medicina nuclear; COVID-19; Terapia radioativa.

Resumen

Objetivo: señalar la importancia de la medicina nuclear para el diagnóstico y terapia del COVID-19, además de reportar la eficacia del tratamiento con radioisótopos (pertecnato de sodio y yodo 131) en individuos infectados con SARS-CoV-2 causando esterilidad viral y previniendo su mutagénesis y asegurando la ausencia de reacciones adversas. **Metodología:** Se trata de una revisión de la literatura de tipo narrativa, elaborada entre junio y septiembre de 2020, utilizando las siguientes bases de datos: PubMed, SciELO y Lilacs. Así, se incluyeron artículos publicados entre 1971 y 2020. **Resultados y Discusión:** El uso de radiación gamma y neutrónica con el propósito de eliminar patógenos virales ha sido ampliamente investigado en estudios estadounidenses, inicialmente enfocados en el H1N1. La sustancia de Pertechnetate de Sodio, sugerida en este estudio, y yodo 131 (diseñado para actuar como prevención en la región cervical) tienen el potencial de respuestas satisfactorias en el tratamiento terapéutico de COVID-19 debido a que es inocuo, indoloro y libre de cualquier efecto. metodología por tanto, ofreciendo mayor seguridad al tratamiento. Inferir en la replicación del coronavirus mediante la electrólisis de su estructura grasa, ya que con la esterilización de su molécula de ARN no habrá replicación. **Consideración final:** En base a la efectividad de este método en protocolos de esterilización y acción sobre diversos tipos de microorganismos, especialmente otros virus que afectan el sistema respiratorio, se sugiere como método seguro, de bajo costo y de baja dosis de radioactividad para el paciente. cuando se utilizan dosis similares a las de la práctica diagnóstica y terapéutica en Medicina Nuclear. Cabe destacar que el protocolo de administración debe estar de acuerdo con el estándar ya recomendado clínicamente, con total garantía de ausencia de efectos asociados. Para una mejor aclaración, es necesario realizar una investigación más específica dentro del alcance del SARS-CoV-2.

Palabras clave: Radiación gamma; Medicina nuclear; COVID-19; Terapia radiactiva.

1. Introduction

The coronavirus, classified as a zoonotic virus, belongs to the Order Nidovirales, Genus Betacoronavirus, Family Coronaviridae and subfamily Orthocoronavirinae. SARS (acute breathing syndrome) - CoV-2 is a new coronavirus that causes a respiratory infection called COVID-19. This microorganism has a single-stranded and positive sense RNA genome between 26 and 32 kilobases, its particles are spherical with a diameter of about 125 nm, covered by a phospholipid envelope

(Duarte, 2020; Gruber, 2020; Lima et al., 2020; Menezes et al., 2020).

The protein S contributes to the adhesion of the virus to the host cells, participating in the interiorization process. In the case of SARS-CoV-2, which causes the current pandemic of COVID-19, protein S recognizes the receptor ligand (RBD) domain ACE2 (angiotensin-converting enzyme 2). The clinical outcome, which depends on the viral load, can range from a simple cold to severe pneumonia. The initial condition is characterized as a flu-like syndrome. The patient has fever, fatigue, myalgia, sputum, nausea, headache, emesis, abdominal pain, body plaques, diarrhea, odynophagia and rhinorrhea (Gruber, 2020; Lima et al., 2020; Menezes et al., 2020).

Despite the absence of specific antiviral drugs to guarantee the timely treatment of this pathology, the area of bioimaging called Nuclear Medicine stands out because this domain, in addition to performing the diagnostic examination, enables treatment without any side effects. The examination is done from the temporary contamination of the patient, carried out in a controlled, safe way, with the application of a small amount of radioactivity, which is short-lived. It employs a very low dose of radiopharmaceutical or just radioisotopes (radioactivity), when compared to other diagnostic techniques that use contrast agents. The half-life of the radionuclide consists of the time necessary for it to halve the initial activity, dividing it into physical half-life (in vitro), without interaction with the patient, and biological half-life (in vivo), with interaction (Murphy, 1989; Gruber, 2020).

The radiopharmaceutical is a substance marked with radioactive material, and its production is carried out in the cyclotron machine, a particle accelerator, where the radioisotope is primarily obtained. Subsequently, it is linked to a molecule capable of carrying the radioactive element (radiopharmaceutical), the physicochemical characteristic of it, determines its pharmacokinetics, that is, its elimination, metabolism and fixation in the target organ. When treating some types of pathogens, radionuclides use gamma, beta-negative, alpha and Auger electron emission (Murphy, 1989; Oliveira et al., 2006).

The radioisotope most used today is Samarium-153 together with EDTMP (ethylenediaminetetramethylene diphosphoric acid), it has fast blood clearance, high uptake in bones and low in soft tissues, making it an excellent radiopharmaceutical in the location and palliative treatment of bone metastasis, still thus, sodium pertechnetate may also be used after eluate (Murphy, 1989).

The physical properties of Samarium-153 are beta and gamma emission, maximum beta energy of 0.805 (20%), 0.710 (49%) and 0.64MeV (30%), and gamma energy of 103KeV (29.8%), their average physical life of 46.27 hours⁷. The gamma energy used in the therapy makes it possible to perform scintigraphy after its use, following deposition in various metastatic sites, since the low beta energy ensures that there is no damage to the healthy tissues that are adjacent to the metastatic site, and is now being visualized as a great help in the treatment of COVID-19 (Suzuki, 2003; Etchebehere et al., 2004; Oliveira et al., 2006).

Radioactive therapy with Sodium and Iodine Pertechnetate 131, before being performed, requires a pre-dose assessment, this is limited to knowing the patient's history, analyzing whether the use is preventive or therapeutic⁶. The procedure is performed by injecting the radiopharmaceutical by intravenous or oral Pertechnetate and only oral when using Iodine 131, the dose is 0.5 to 3mCi / kg weight, administered orally diluted in serum or water, the rest is eliminated via body secretions, the most predominant being renal (Seber et al., 2013).

The aim of the present study was to point out the importance of nuclear medicine for the diagnosis and therapy of COVID-19, in addition to reporting the effectiveness of treatment with radioisotopes (sodium pertechnetate and iodine 131) in individuals infected with SARS-CoV-2 causing viral sterility and preventing its mutagenesis and ensuring the absence of adverse reactions.

2. Methodology

This is a review of the narrative-type literature and qualitative, which was elaborated between June and September of the year 2020, using the following databases: PubMed, SciELO and Lilacs. The search process was used in isolation or in combination with the respective descriptors: Gamma radiation; Nuclear medicine; COVID-19; Radioactive therapy. Thus, there was the inclusion of articles published between 1971 and 2020, these, described in English and Portuguese.

For the synthesis of this study, inclusion and exclusion criteria were pre-included. With regard to inclusion, content was selected that addressed the theme of objective, with publishing within the stipulated period. The exclusion criteria were identified in materials with information content in duplicate, as well as those that do not fit the time frame.

For selection, the following criteria were applied: exploratory reading, selective reading and selection of material in accordance with the objectives of the study. As a result of the search, 43 files were found, of which 21 were selected for the contemplation of this article.

3. Results and Discussion

The authors Duarte (2020), Gruber (2020) and Lima et al., (2020), states that in the case of SARS-CoV-2, which causes the current COVID-19 pandemic, protein S recognizes the ACE2 receptor (angiotensin-converting enzyme 2) through its receptor binding domain (RBD) of the cell. The particles have projections emanating from the envelope in the form of spikes, formed by trimers of protein S (Spike protein = spider protein). These projections generate a crown aspect, hence the name coronavirus. The Protein S is responsible for the adhesion of the virus to the host cells, participating in the interiorization process, which occurs through the fusion between the viral membranes and the host cell, allowing the virus to enter the cytoplasm.

For Lima et al., (2020), SARS-CoV-2 is a virus that managed to adapt and migrate from one species to another, this is what happened with this infectious agent. Bats and pangolins are considered to be one of the main reservoirs for the virus, potentially terrible to humans. The coronavirus is not an exception, it is a solution before, that someone thinks about exterminating it, one must respect its habitat more. Pandemics caused by zoonoses are nothing more than a reflection of man's interventions in the environment. In the desire to expand, humanity invades other people's land, causing an imbalance in the ecological niche, causing problems in the animal's natural habitat.

Transmission occurs through respiratory droplets, either by people who transmit or by contaminated surfaces. Contagion can happen in both courted or asymptomatic patients, and the incubation time varies from 12 to 14 days. The initial symptoms can vary from: cough, fever, fatigue, lack of ophthalmology and taste, dyspnoea, to complications that include pneumonia and acute respiratory distress syndrome. The diagnostic confirmation of COVID-19 is done through the collection of respiratory material (aspiration of airways or sputum induction). At the laboratory level, the virus is identified using the Real Time Polymerase Chain Reaction (RT-PCR) technique and partial or total sequencing of the viral genome. The collection of nasopharyngeal aspirate or combined swab (nasal / oral) or a sample of lower respiratory secretion (sputum or tracheal lavage or bronchoalveolar lavage is recommended). Still, other tests can be performed with the detection of IgM and IgG immunoglobulins (serology and immunochromatography). Currently, severe cases should be referred to a referral hospital, where isolation and treatment will be performed. Mild cases should be accompanied by primary health care and home precautionary measures instituted (Lima et al., 2020; Menezes et al., 2020).

Regarding computed tomography (CT), Lima et al., (2020) defines that the most common aspects reported by this technique were ground-glass opacity and consolidation areas, sometimes with rounded morphology and peripheral distribution. Chest CT shows the most extensive disease approximately 10 days after the onset of symptoms. The chest X-ray study is often essential to assess patients with suspected COVID-19. Immediate recognition of the disease is fundamental to

ensure timely treatment, and from the point of view of public health, the rapid isolation of the infected patient is crucial to contain this transmissible disease.

By using the method described there is the possibility of examining various organs of the body, which are specific because the compounds used follow functional or metabolic paths, specific to the patient, showing how different and unique this type of exam is, since a single radionuclide evaluates and studies macroscopic and molecular aspects of the same system or organ (Suzuki, 2003).

Gamma emission is described by Murphy (1989) as having low linear energy transfer, using it for the detection of tumor masses in computerized topography by single photon emission (PETCT). Beta-negatives, on the other hand, are the radioisotopes most used in treatment, when combined with various types of carrier substances. Alpha emitters, due to their very ionizing capacity, deposit a large amount of energy during their journey, thus being useful in oncology, since alpha particles travel in a straight line and because they can remain in tumor or residual cells (Papillary Carcinomas Cervical Region) for a relatively long time, making our thesis of preventing the virus in the cervical region viable.

Accordingly, Suzuki (2003), states that primary malignant bone lesions and metastases cause a lot of pain to patients, disabling them, so, when there is no success in external radiotherapy, they act on healthy tissues of great extent and obtain short duration and little results efficient, after confirmed by scintigraphy with ^{99m}Tc -MDP (Technetium-99 metastable methylene diphosphonate) the use of samarium153 has been proving increasingly effective in relieving pain, it accumulates mainly in regions where there is osteoblastic activity, some recent evidence shows that samarium153-EDTMP has cytotoxic activity. Samarium153-EDTMP is used when the patient no longer responds to palliative treatment with analgesics, with analogy to the method we will use other drugs with tropism to facilitate molecular acceptance.

For Etchebehere (2004) and Pretti (2011) pain therapy aims to relieve pain in patients who no longer have a social life due to advanced cancer (bone metastasis), the isotope used goes away and the drug is linked to these specific cells, making the anesthetic effect. In 1935 metabolic studies of bone tissue with radionuclides were initiated, Chievtz and Hevesy used orthophosphate (^{32}P), being expanded in 1940 with the use of fluorine-18 and over the years with calcium-45 and strontium-89, however there was occurrence of myelotoxicity at a higher level than desired and the high cost related to the import of radiopharmaceuticals. Still, Murphy (1989) reports that renio-186 was also used, but its role in palliating pain in bone metastases lasts for up to five weeks.

For the assessment of the response to therapy and the possible side effects, Etchebehere (2004), it explains the relevance of medical follow-up, which allows for the early detection of hematological changes. It is important to note that systematic exposure to ionizing radiation can cause damage, but they are not fully known when the method is Nuclear Medicine. Because of this, the fundamental importance of radioprotection for the applicator of the technique, highlighting the justification which is limited to the use of ionizing radiation only in a situation that may have a positive balance for society (Radiológica, 2002; Castro, 2005).

Therefore, in the health sector, it is extremely important to consider the inevitable social and economic impacts due to the implementation of the social distance measures that it may cause. Therefore, due to these reasons, it is necessary that a very careful assessment of the epidemiological moment takes place and that it is more appropriate in the application of these measures, such as their validity, objectively maximizing the desirable effects on health while minimizing both social and economic (Cowling & Aiello, 2020; Nicola et al., 2020).

Table 1. Summary of previously reported D10 values.

	Genome	Titer assay	Temperature media (°C)	Radiation source	D ₁₀ (kGy)	Literature citation
Adenovirus	ds DNA	Plaque	RT? 2% serum/MEM	Cobalt 60	4.1–4.9	Sullivan et al., 1971
Coxsackievirus	ss RNA	Plaque	RT? 2% serum/MEM	Cobalt 60	4.1–4.8	Sullivan et al., 1971
Echovirus	ss RNA	Plaque	RT? 2% serum/MEM	Cobalt 60	4.4–5.1	Sullivan et al., 1971
Herpes simplex virus	ds DNA	Plaque	RT? 2% serum/MEM	Cobalt 60	4.8–5.2	Sullivan et al., 1971
Influenza A	ss RNA	Plaque	RT? 2%	Cobalt 60	4.9	Sullivan et al., 1971
Newcastle Disease	ss RNA	Plaque	RT? 2% serum/MEM	Cobalt 60	5.2	Sullivan et al., 1971
Poliovirus	ss RNA	Plaque	RT? 2% serum/MEM	Cobalt 60	4.9–5.2	Sullivan et al., 1971
Reovirus I	ds DNA	Plaque	RT? 2% serum/MEM	Cobalt 60	4.2	Sullivan et al., 1971
Simian virus	ds DNA	Plaque	RT? 2% serum/MEM	Cobalt 60	4.5	Sullivan et al., 1971
Coxsackievirus	ss RNA	Plaque	RT? Water	Cobalt 60	1.2	Sullivan et al., 1971
Echovirus	ss RNA	Plaque	RT? Water	Cobalt 60	1.4	Sullivan et al., 1971
Influenza A	ss RNA	Plaque	RT? Water	Cobalt 60	1	Sullivan et al., 1971
Poliovirus	ss RNA	Plaque	RT? Water	Cobalt 60	1.1	Sullivan et al., 1971
Pseudorabies	ss RNA	TCID	– 70 °C	Cobalt 60	5	Sun et al., 1978
Ebola Zaire	ss RNA	Plaque	Frozen	Cobalt 60	2.3	Lupton, 1981
Akabane	ss RNA	Plaque	RT?	Cobalt 60	<2.0	Thomas et al., 1981
African Swine Fever	ds DNA	HA	RT?	Cobalt 60	<2.0	Thomas et al., 1981
Avian Adenovirus	ds DNA	Plaque	RT?	Cobalt 60	4.8	Thomas et al., 1981
Avian pox	ds DNA	Plaque	RT?	Cobalt 60	2.2	Thomas et al., 1981
Bovine Diarrhea Virus.	ss RNA	Plaque	RT?	Cobalt 60	<2.0	Thomas et al., 1981
Infect. bovine rhino	ds DNA	Plaque	RT?	Cobalt 60	<2.0	Thomas et al., 1981
Bluetongue	ds RNA	Plaque	RT?	Cobalt 60	<2.0	Thomas et al., 1981
Maedi-visna	ss RNA	Plaque	RT?	Cobalt 60	3.5	Thomas et al., 1981
Newcastle disease	ss RNA	Eggs	RT?	Cobalt 60	2	Thomas et al., 1981
Porcine parvovirus	ss DNA	HA	RT?	Cobalt 60	4	Thomas et al., 1981
Pseudorabies	ds DNA	Plaque	RT?	Cobalt 60	<2.0	Thomas et al., 1981
Swine vasc. Disease	ss RNA	Plaque	RT?	Cobalt 60	5.5	Thomas et al., 1981
Teschen	ss RNA	Plaque	RT?	Cobalt 60	2.8	Thomas et al., 1981
Transm. gastroent.	ss RNA	Plaque	RT?	Cobalt 60	<2.0	Thomas et al., 1981
Ebola	ss RNA	TCID	– 60 °C/culture media?	Cobalt 60	2.2	Elliott et al., 1992
Ebola	ss RNA	TCID	4 °C/culture media?	Cobalt 60	1.4	Elliott et al., 1992
Lassa	ss RNA	TCID	– 60 °C/culture media?	Cobalt 60	3.1	Elliott et al., 1992

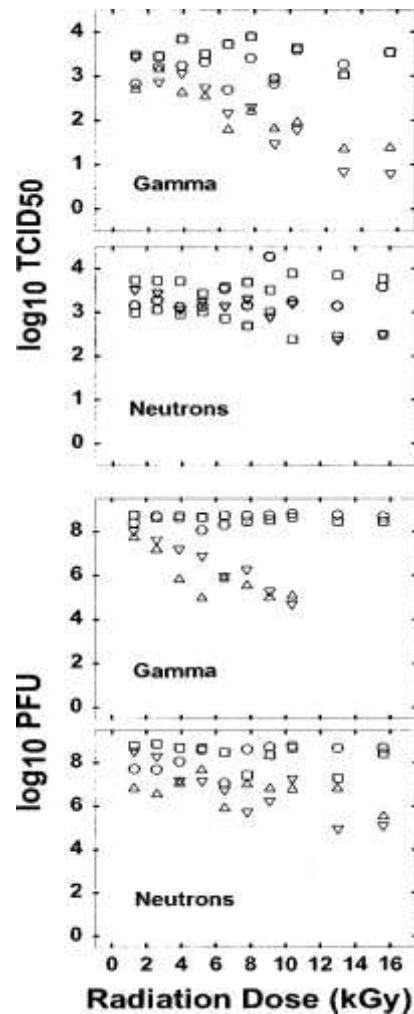
Marburg	ss RNA	TCID	-60 °C/culture media?	Cobalt 60	2.1	Elliott et al., 1992
Marburg	ss RNA	TCID	4 °C/culture media?	Cobalt 60	1.2	Elliott et al., 1992
HSV	ds DNA	Plaque	-75 °C 5% serum/MEM	Cobalt 60	1.0	Zamansky and Little, 1982
HSV	ds DNA	Plaque	4 °C 5% serum/MEM	Cobalt 60	0.4	Zamansky and Little, 1982
HSV 1 Theta	ds DNA	Plaque	-80 °C/water	Cobalt 60	3.3	Rosen et al., 1987
HSV 1 Ang	ds DNA	Plaque	-80 °C/water	Cobalt 60	4.3	Rosen et al., 1987
HSV 1 Kos	ds DNA	Plaque	-80 °C/water	Cobalt 60	2.7	Rosen et al., 1987
HSV 1 Muller	ds DNA	Plaque	-80 °C/water	Cobalt 60	4.3	Rosen et al., 1987
Akbane	ss RNA	TCID	-68 °C	Cobalt 60	2.5	House et al., 1990
Aino	ss RNA	TCID	-68 °C	Cobalt 60	3.5	House et al., 1990
Bovine ephem. fever	ss RNA	TCID	-68 °C	Cobalt 60	2.9	House et al., 1990
Bluetongue	ds RNA	TCID	-68 °C	Cobalt 60	8.3	House et al., 1990
Foot-mouth disease	ss RNA	TCID	-68 °C	Cobalt 60	5.3	House et al., 1990
Hog Cholera	ss RNA	TCID	-68 °C	Cobalt 60	5.5	House et al., 1990
Minut. virus of mice	ss DNA	TCID	-68 °C	Cobalt 60	10.7	House et al., 1990
Swine vesicular fever	ss RNA	TCID	-68 °C	Cobalt 60	5	House et al., 1990
Bacteriophage M13	ss DNA	Plaque	RT?	Gamma-particle accelerator	0.090	Singh et al., 1990
Bacteriophage M13	ss DNA	Plaque	RT?	Neutron-particle accelerator	0.015	Singh et al., 1990
Hepatitis A	ss RNA	Plaque	RT	Cobalt 60	2.9	Bidawid et al., 2000

Source: Lowy et al., (2001).

The tables were assembled with the grouping of data, first by author being in chronological order and then viruses in alphabetical order. From the published methods, the exposure conditions are provided according to the possibility. There was no description for the temperature condition, just as there was no report to keep the temperature below the environment. In some cases, the D10 values were calculated from the D37 values, estimating the values from the slopes of the published survival curves.

Tables 1, 2 and 3 shows the means for cross-comparisons within this study, as well as for other studies using a single parameter. Being able to observe REB, which is the proportion of neutron inactivation (efficacy) in relation to gamma photons. There is an inspection on the data curve of qualitative impressions that confirms the magnitudes of the D10 values.

Figure 1. Comparison of the titer values for irradiated A / PR8 and A / X31 virus samples and control. Control samples (circles and squares) and irradiated (triangles) of the influenza virus (A / X31, circles and vertical triangle; A / PR8, squares and inverted triangles) exposed to gamma photons or neutrons. The titre values for the plaque-forming unit (PFU per ml) and infectious tissue culture dose (TCID50) assays are shown for irradiated and matched control samples. The data shown are means with no error limits. The symbols were generally much larger than those of the S.E.M. values.



Source: Lowy et al., (2001).

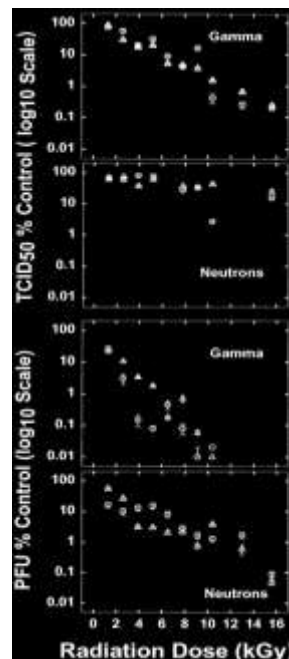
Figure 1 shows the values of titers that were obtained, for the control samples and exposed to viruses A / PR8 and A / X31, being for all combinations of radiation assay and for the titers that were used in this study. The radiation dose does not change the control title values reliably, this indicates that there were no major systemic errors in the titration tests. For several months in section 2, doses of radiation were spread and in trials of different strains.

With the exception of some determinations, the values, whether they are considered to be control or experimental samples, are quite reasonable along the same trend lines. The errors for each title determination were small, being within the dimensions of the symbols. In addition, the survival curves are log-linear. Unique exponential inactivation curves were observed for a wide variety of virus types where they have been reported in most of the literature. Incomplete inactivation at high doses was observed, which indicated a refractory response to increased radiation, in the same way that has been reported for cells, cell lines and bacteria.

If the inactivation plateaus existed in a demonstration, they would be difficult due to the extremely low titers, a high precision measurement would be necessary, and may therefore be necessary for total doses of 50-100 kGy.3.2. in a comparison made between neutrons with gamma photons, the most remarkable result was obtained, where neutrons were much less effective in activating the influenza A virus compared to gamma photons. Thus, having an easily illustrated result for the TCID50 values and the neutron values decrease much less quickly with dose, which can be seen for both strains of virus, which can remain in magnitude close to the controls (Lowy et al., 2001).

There is an indication of the greater effectiveness of gamma photons, due to the slope of the survival curve that there was a greater exposure for gamma than for neutrons. It is noted that the qualitative impressions of the data curve inspection can be confirmed by the magnitudes of the D10 values, which were also shown in Table 1. Regardless of the virus strain or the titer method, the D10 values for neutron exposure were consistently larger than gamma photons.

Figure 2. Comparisons of the percentage of control values for radiation inactivation of influenza A / PR8 and A / X31 viruses. The title values for A / PR8 (triangles) and A / X31 (circles) were normalized by the paired control values. The data are shown on a semi-logarithmic axis with the same scale for all combinations of radiation title-method to facilitate comparison of results. Data are mean S.E.M. plotted as open symbols to display error estimates. The D10 values, the radiation doses necessary for a reduction of the unit log₁₀, were determined from these data and are presented.



Source: Lowy et al., (2001).

In Figure 2 there is an elucidation that for both strains of the influenza virus, the title data normalized by the respective paired control values can be observed. These absolute title data for both strains were very similar in magnitudes, being identical, essentially in the response pattern, occurring for each radiation quality, gamma photons and neutrons, as well as for the two different titles of the test methods. D10 values were used to determine the inactivation curves of normalized data. The radiation dose in kGy is D10, which is necessary for a reduction of a log in the title, being effectively the parameter that gives the slope of these survival curves, being convenient the D10 values. A graphic representation used open symbols, so that the magnitudes that present errors, could be observed. Making the survival curves log-linear.

Reports in most of the literature have been observed in a wide variety of virus types showing a unique exponential inactivation curve. A difference in the effects of radiation measured by the PFU title data may be easier to observe. As in Table 1 it showed the D10 value, they were also confirmed by its magnitudes. D10 values when exposed to neutrons, were consistently higher than gamma photons, being independent of the virus strain or the titer method.

They were compared with photons between 0.4 and 0.6 relative effective dose of neutrons. Trials or strain 3.3 does not appear to be dependent on the RBE values. Comparisons were made between D10 and 6 values that were previously reported. Under exact conditions of exposure for many of the reports, they have not been fully described. The authors would have to have declared that frozen samples were used. Coming to a conclusion that only the materials that have been defrosted have been irradiated. Where no reports were found using dry material.

In some cases, the radiation doses and quality used in this study cannot be compared. As an example, when some viruses are exposed to gamma radiation in appropriate metal safety containers. However, the dose corrections that were made for attenuation and for changing the quality of gamma radiation to secondary X-rays were unclear. The D10 values were reported by researchers, in some cases, the D10 values were estimated based on published inactivation curves or else by D0 conversions, in which 37% of inactivation occurred.

D10 values all fall within the range of values reported for gamma activation cited in that study. The attack of hydrated free radicals can be reduced by frozen samples, hoping that exposure, even to ice temperatures, has resulted in very different sensitivities to radiation, being possible even in the order of magnitude changes. It had no effect on the samples that were aggregated, the frozen and thawed data were very similar in the range of values. Using two sets of experiments, direct comparisons were made on frozen samples and ice temperatures for the Lassa and Marburg ss RNA viruses and the HSV DNA virus at ds (Elliott et al., 1982; Zamansky & Little, 1982).

There was a difference in D10 values by factors of 1.6-1.8 for ss RNA viruses and approaching 2.8 for DNA ds viruses, as expected, requiring the low radiation dose for the thawed material. This factor was taken into account 2-3 times, based on the data from the PFU assay that there were D10 values of 2 and 3, thus corresponding quite reasonable to the previously reported values of 4.9 kGy for the thawed influenza A virus (Sullivan et al., 1971).

The reported D10 values are in the upper range of the neutron data in this study, where it was determined from the TCID50 titles that there was a high peculiarity. Another study on neutrons could be used for the DNA bacteriophage ss M13m11. Comparison with gamma photons was also performed with an RBE of 6. Unlike the results that were reported in the present study, the gamma photons that have been shown to show that they are less effective than neutrons for inactivating the virus (Elliott et al., 1982; Singh et al., 1990).

Samples that were in buffered saline were not exposed to any temperature provided, but apparently close to room temperature, and were air-cooled to expose neutrons to avoid overheating.

The reported D10 values were a concern to interpret in these findings, as they were 1-2 in orders of magnitudes lower than other values that were reported to be 15 Gy (neutrons) and 90 Gy (range). The low D10 values may be a not very likely explanation for the target size of the genome, as it is one of the smaller viruses, it has a lower molecular weight than the flu virus. The title method used with those for the PFU assay. this study depended on the magnitude of the D10 values, being consistently lower. The importance of observing the differences between the D10 values did not depend on the absolute magnitudes of the raw title data, so these D10 values started to be derived from normalized proportional survival curves.

PFU assays were determinant for most literature titles, however, two reports, TCID50 assays were used (Elliott et al., 1982; House et al., 1990). Other studies for radiation inactivation, unfortunately, were not found to directly compare the titration methods. For SS RNA data the averages were aggregated to show a fast upward trend for D10 which determined from TCID50 data (3,490.52) versus PFU (1.5 90.21) for thawed samples, having a little difference for frozen material,

3,090.45 and 3.3 90.60, TCID50 and PFU data, with respective.

The D10 values have a possibility of interfering depending on the title assay method in which important implications, considering the total gamma dose necessary for virus inactivation. The gamma D10 values used for example in this study were 25 kGy which would result in a 10-12 log reduction in the title, as predicted by the D10 based on the PFU assay, but only a 3-4 log reduction, as expected by the D10 test based on the TCID50 test.

For this reason, it is important to demonstrate in a study that the essentially complete loss of viability of the virus by radiation, as well as the preparation of biological products or antigens for vaccination, in a single type of titration assay may not be so rigorous enough.

In particular, radiation is an advantageous method to inactivate in the case of viral pathogens, being important in the preparation of vaccines or for positive controls in analytical methods. There may be a possibility of damage to the auxiliary protein, which combined with unwanted residual immunological activity needs attention in monitoring for some applications.

4. Final Considerations

Knowing that Gamma Radiation is being widely used in several studies in the world, in industry, agriculture, sterilization of surgical materials, elimination of microorganisms (bacteria and viruses), treatment and therapy of cancerous pathogens with 100% proven accuracy. Thus, the suggestion of using the method is necessary for the viability of yet another viral inactivation tool, with low cost, without side effects for the patient and, consequently, opening the window of possibilities in the cure of COVID-19. This requires further studies to elucidate the statements.

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