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EFFECT OF GAMMA RADIATION COBALT-60 ON CAFFEINE

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ABSTRACT

Objective: The objective of the study was to evaluate the effects of the incidence of gamma radiation of Cobalt-60 on caffeine. **Material and Methods:** The samples were studied in aqueous solution and powdered form after irradiation at doses: 2, 4, 8, 16 and 32 kGy by ionizing radiation source of ^{60}Co. After wards, they were analyzed by differential scanning calorimetry (DSC), thermogravimetry (TG), and high performance liquid chromatography (HPLC). **Results and Discussion:** For the DSC technique no changes were observed in the curves after irradiation, which could witness changes in physicochemical properties after irradiation. The TG corroborated with the expected mass loss of caffeine, independent of the action of ionizing radiation. Furthermore, the results obtained by the chromatographic analysis did not show a percentage of caffeine degradation in the dose of the applied radiation when compared to the non-irradiated caffeine. **Conclusion:** In view of the results obtained, it was possible to observe the stability of caffeine on the influence of gamma radiation on the Cobalt-60 source.

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INTRODUCTION

The caffeine (1,3,7-trimethylpurine-2,6-dione), Fig. 1, is an alkaloid belonging to the methylxanthine family. This alkaloid is found in large amounts in coffee seeds, and also in tea leaves in general (De Maria e Moreira, 2007). As an active dermatological agent, it exerts action on subcutaneous adipose tissue through the inhibition of phosphodiesterase, causing adipocyte lipolysis (Treffel *et al*., 1992; Van De Sandt *et al*., 2004; Wilkinson *et al*., 2006), which degrades cyclic adenosine monophosphate (AMPc), as well as the adenosine receptor, blocking its anti-lipolytic effect (Wisher, 2012).In addition, it has been studied for its antioxidant and anticancer effects, with great photoprotective potential, as it has been shown to be a potentially bioactive molecule that induces pre-neoplastic cellular apoptosis (Lu, 2007). Several animal studies have shown that caffeine has inhibited the appearance of non-melanoma skin cancer because it is a UV-induced skin cancer (Conney *et al*., 2013). Commercially available topical formulations of caffeine typically contain from 1 to 3% (Byun; Hamishehkar *et al*., 2015).

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The use of antioxidant formulas and/or cosmetics in combination with photoprotectors have demonstrated improved protection against UV rays, significantly reducing epidermal damage, as well as reducing the appearance of cancers (Masnec, 2010). The ionizing radiation consists of electromagnetic waves with high enough energy to cause the electrons to detach themselves from atoms and molecules, changing their structure in a process known as ionization (Silindir, 2009). When transposing a material, there is an energetic transference to the atoms that have been found in its path. If the transferred energy is greater than the bonding energy of the electron, it is ejected from its orbit. Taking into account that biological systems are formed basically by atoms, these, after being irradiated will have their electrons removed from their orbit. The consequence of an irradiated molecule (water, protein, sugar, DNA, RNA, etc.) will have effects that should be evaluated according to their biological role. In parallel, the genesis of new by-products in the body should be examined because of the direct impact suffered by the irradiated way (Nouailhetas, 2005). The objective of this work was to evaluate the effects of the incidence of Cobalt-60 gamma radiation on caffeine.

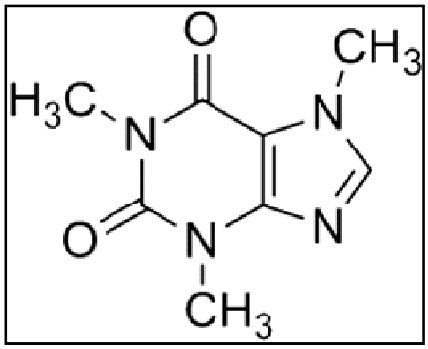

Figure 1. Caffeinemolecule. Source: Adapted: (De Maria e Moreira, 2007)

MATERIALS AND METHODS

In the development of this work caffeine (1,3,7 trimethylxanthine) and deionized water were used. The samples were analyzed and characterized in aqueous solution and powder form after irradiation at the doses: 2, 4, 8, 16 and 32 kGy by ionizing radiation source of ^{60}Co.

Differential Scanning Calorimetry (DSC): The characterization was done in the model Mettler-Toledo DSC822^e e apparatus were allocated in standard sealed aluminum pans. Samples were heated from 30°C to 265°C with a heating rate of 20°C / min. The apparatus was checked with indium of melting point 156°C 24.75 J g^{-1}, and the enthalpic events and changes in the crosslinking processes were verified.

Thermogravimetry (TG): The caffeine powder was lyophilized and subjected to TGA / DTGA thermogravimetric analysis in the Mettler-Toledo SDTA / 851 apparatus (heating rate: 10°C min^{-1} at 25-60°C under N_2 flow (10 mL .min^{-1}) Records of temperature variations from beginning to end of decomposition.

High Performance Liquid Chromatography (HPLC): It is a technique used in the separation of the various components of a mixture of substances, for the purpose of identification, quantification or purification (Siqueira, 2003). An aqueous solution of caffeine at a concentration of 0.45 mg L^{-1} was prepared, the solution was stirred for 1 hour for complete solubilization on ultrasound apparatus. After 5 mL aliquots were transferred to glass tubes and after being closed were irradiated at different doses, 2, 4, 8, 16 and 32 kGy in Cobalt-60 source. The Agilent 1100 + API 2000 model coupled to a mass spectrometry detector of the triplequadrupole type (MS / MS) was used to perform the analysis. Column: Restek Ultra Aqueuos C_{18} (150 x 2.1 mm 3 um). MovingPhase: 65% H_2O / 35% ACN + 0.1% Ac. Formic. MRM Transition (Quantification): 195> 138. MRM Transition (Confirmation): 195> 110. Analytical Curve Linearity Range: 100 to 800 µg L^{-1}, allocated at the Center of Applied Mass Spectrometry - CEMSA.

RESULTS AND DISCUSSION

The Fig. 2 shows the DSC of the irradiated and non-irradiated caffeine powder. No changes were observed in the character of the curves after irradiation, which could show the presence of radiolysis products or changes in the physicochemical properties of the compound studied. Since DSC for the drugs of low radiochemical stability demonstrates peaks of radio degradation or impurities (Oliveira *et al*., 2011). Studies with biological effects showed the influence of caffeine in the irradiation process, where a delay in the G2 phase of the cell cycle corresponding to the interval between the end of DNA replication and the beginning of glioblastomas mitosis (brain tumors) was observed after the incidence of gamma radiation due to, caffeine acts as an inhibitor of two protein kinases, the ATM and ATR that are directly linked in the process of accelerated and uncontrolled replication of malignant tumor cells (Godoy *et al*., 2013).

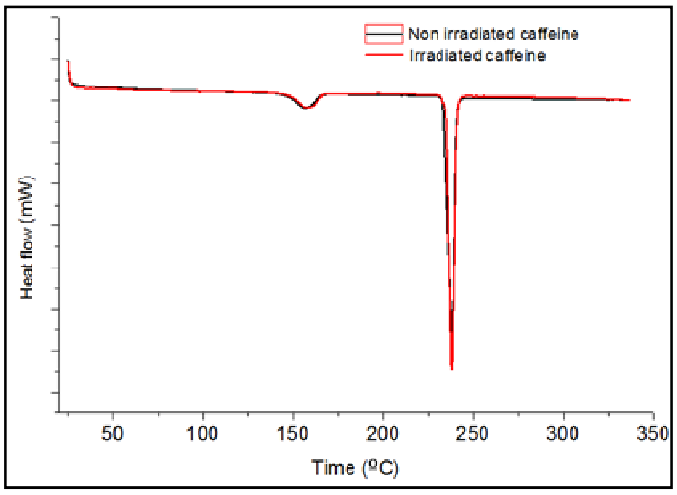

Figure 2. DSC of the caffeine powder not irradiated and irradiated at 25 kGy

The TG is a tool used to measure mass loss as a function of temperature in an atmosphere. For pharmaceutical purposes, its use is proposed for determination of purity and humidity, identification of false polymorphisms, in the evaluation of substance stability and degradation kinetics (Oliveira *et al*., 2011). The Fig.3 confirms the loss of caffeine mass around 207°C independent of the action of ionizing radiation.

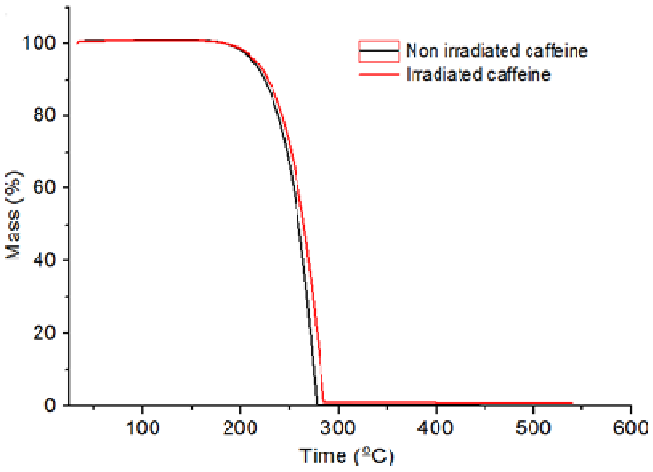

Figure 3. TGA curves of irradiated and non-irradiated caffeine powder at 25 kGy

Repolês (2015) investigated possible differences in the responses to DNA double-strand breaks caused by exposure to ionizing radiation from different *Trypanosoma cruzi* strains, concluding that previous treatment with caffeine was able to delay response to DNA damage mediated by 25 hours by the ATR and ATM proteins. Considering the results obtained by the chromatographic analysis, the percentage of caffeine degradation in the radiation dose applied was not verified when compared to non-irradiated caffeine. In the below chromatograms it can be seen that the retention time of the caffeine irradiated at 32 kGy and the non-irradiated caffeine was approximately 2.66 minutes, with very near peak intensity. This analysis could witness by-products from the water radiolysis, as observed in Fig.4. A study carried out by Silva (2012) which analyzed seeds of arabica coffee and *conillon* irradiated at a dose of 5 kGy and 10 kGy, concluded

that there were no deleterious effects in the seeds, being similar to the control group that did not suffer from ionizing radiation.

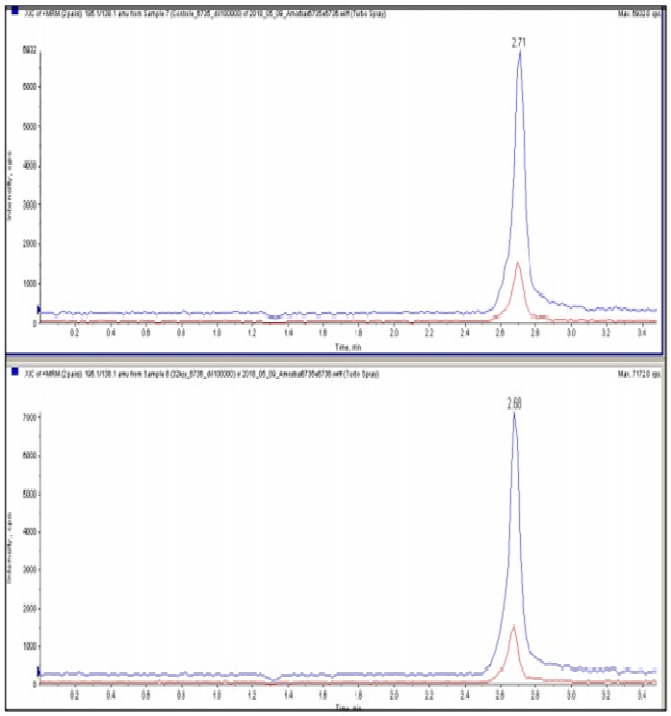

Figure 4. Chromatogram of the non-irradiated control sample (above) and chromatrogram of the sample irradiated at 32 kGy (below)

CONCLUSION

According to the results, it was possible to observe the stability of the caffeine when irradiated by gamma radiation in the Cobalt-60 source. However, this finding becomes important for future work, which can explore areas such as radiation protection and thus minimize problems arising from its use.

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Author Contributions

- **Conceptualization:** Tiago César dos Santos Maia, Ademar Benévolo Lugão, Maria José Alves de Oliveira.
- **Formal analysis:** Tiago César dos Santos Maia, Maria José Alves de Oliveira.
- **Investigation:** Tiago César dos Santos Maia, Ademar Benévolo Lugão, Maria José Alves de Oliveira.
- **Methodology:** Tiago César dos Santos Maia, Ademar Benévolo Lugão, Maria José Alves de Oliveira.
- **Resources:** Tiago César dos Santos Maia, Maria José Alves de Oliveira.
- **Writing – original draft:** Tiago César dos Santos Maia, Ademar Benévolo Lugão, Roberta Azoubel, Marcos Túlio Raposo, Maria José Alves de Oliveira.
- **Writing – review &editing:** Tiago César dos Santos Maia, Ademar Benévolo Lugão, Roberta Azoubel, Marcos Túlio Raposo, Maria José Alves de Oliveira.

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