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GREEN SYNTHESIS OF MAGNETIC NANOPARTICLES OF COBALT FERRITE WITH KIWI (*Actinidia delicious*) AND ITS ACTIVITY AGAINST THE PROLIFERATION OF *Trypanosoma cruzi*

Giani Christie Rodrigues
Universidade Federal do Rio de Janeiro. Núcleo Multidisciplinar de Pesquisas, NUMPEX, Campus Prof. Geraldo Cidade Duque de Caxias, RJ, Brasil

Alessandra Catarina Chagas de Lima
Universidade Federal do Rio de Janeiro. Núcleo Multidisciplinar de Pesquisas, NUMPEX, Campus Prof. Geraldo Cidade Duque de Caxias, RJ, Brasil

Georgia Correa Atella
Laboratório de Lipídios e lipoproteínas. Instituto Bioquímica Médica Leopoldo de Meis, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil

Robson Roney Bernardo
Universidade Federal do Rio de Janeiro. Núcleo Multidisciplinar de Pesquisas, NUMPEX, Campus Prof. Geraldo Cidade Duque de Caxias, RJ, Brasil

Abstract: Protagonist of a wide range of technological applications, nanoparticles (NPs) for reaching dimensions between 1 and 100 nm, provide characteristics and properties that stand out mainly in the pharmacological and biomedical areas. Skills such as hyperthermia and medication delivery system are examples of versatility, which has been the subject of many studies. The present work aims at the synthesis of cobalt ferrite nanoparticles, seeking the principles of green chemistry; characterize the nanoparticles produced and observe their antiproliferative behavior and activity in the culture medium of the protozoan *T. cruzi*,. To synthesize the nanoparticles respecting the principles of green chemistry, we use as raw material a fruit found in the Brazilian biodiversity: kiwi *(Actinidia delicious*), acquired in the local market. The components present in this fruit such as ascorbic acid, potassium, proteins, enzymes such as actinin, carbohydrates, among others, function as important structures for the interaction between elements with different charges, enabling the electrostatic effect through Coulomb's Law, as well as for the stabilization of the produced NPs. The cobalt ferrite NPs were synthesized by the sol-gel method, using MiliQ water as the solvent, where iron nitrate and cobalt were dissolved, which were subjected to heating to form cobalt ferrite ($COFe_2O_4$). The samples were centrifuged, dried in an oven (100ºC) and calcified in a muffle furnace (600ºC) for one hour. The characteristics related to the surfaces of the nanoparticles were analyzed using Scanning Electron Microscopy (SEM), which showed heterogeneity of particle sizes (5µm at 200 nm) as well as their aggregation. The crystallography analysis of X-Ray Diffraction, demonstrated the success in the formation of cobalt ferrite through the characteristic peaks present in the spectrum, and good crystallinity of the NPs, that is, a relatively organized internal structure. Subsequently, the sample was submitted to a biological assay study, in which the NPs were distributed in four different aliquots, which comprised four different concentrations (10, 20 and 50µg / mL), in which the 1mL of culture with T cruzi was added. This biological test was followed up for eight consecutive days, providing us with enough data to analyze the behavior of the protozoan in the presence of NPs. The biological assay showed significant antiproliferative activity for the 50µg / ml concentration. Which allows us to conclude that the aggregation confirmed by SEM, and the size of the NPs estimated by the DRX, did not prevent the antiproliferative activity of *T. cruzi*.

Keywords: Ferrite, *Trypanossoma Cruzi*, *Actinidia delicious*, nanoparticles.

INTRODUCTION

NANOPARTICLES

Nanotechnology has been revolutionizing over the past few years, and adding a new perspective in the form of doing science. Of the several areas that stand out are the nanoparticles (NPs). These are particles that reach the dimension between 1 to 100nm, and thus configuring an important relationship between the volume and surface area, so that the reduction in size of NP is related to the increase in the total of atoms on its surface, a region considered unstable and with a series of peculiarities (Singh A. K, 2016). With this, the NPs present numerous characteristics mainly according to their composition and organization, to mention the morphology and physicochemical properties, that the make protagonists of intensive studies mainly in the pharmacological and biomedical areas (Laurent S., Boutry S. and Muller R. N, 2018), standing out in the scope of cancer treatment, where biological-based NPs use two variables targeting to tumor cells known as passive segment (which uses the characteristic permeability and retention effect of cancerous tissues) and active (directed direction is induced by functionality as in the case of polymeric NPs) (Gherasim O. et al, 2019). There is still hyperthermia, a technique that warms NPs through a magnetic field (Laurent S., Boutry S. and Muller R. N, 2018; Long NV et al, 2014) and drug manipulation, the most common being drug delivery technique, where there is delivery directed to direct cells (Stark WJ, Stoessel PR, Wohlleben W. and Hafner A., 2015; Laurent S., Boutry S. and Muller R. N, 2018) in addition to effects inhibitory against microbial development (Gherasim O. et al, 2019). Such examples justify or increase investment in research involving nanostructured materials, more specific such as metallic nanoparticles, which has revolutionized therapeutic strategies.

METAL NANOPARTICLES

Due to the size of nanostructured materials, they exhibit physical and chemical properties of great interest for several areas of applications. In the biomedical area, they stand out as a contrast for MRI exams, and as therapeutic agents through hyperthermia (Cotin et al, 2018). Many of the nanostructured materials manufactured today are composed of metal oxide such as nanoparticles (Laurent S., Boutry S. and Muller R. N, 2018), which in the case of the present work, were synthesized from the iron nitrate and cobalt salts , in liquid medium through the sol-gel process which will be explained later. Nanoparticles composed of metal oxide have electronic and magnetic properties, determined by the orientation of the number of spins of their electrons, leading to show for example different magnetic fields and different magnetic responses when exposed to an external magnetic field (Laurent S., Boutry S. and Muller R. N, 2018). To explore these characteristics, we opted for the synthesis of nanoparticles of cobalt ferrite, a metallic oxide.

COBALT FERRITE

Within the vast group of metallic NPs is Cobalt Ferrite being a metallic oxide, whose synthesis is represented by the following equation: Co (NO_3) 2. $6H_2O$ + 2Fe (NO_3) 2. $5H_2O$ -> $CoFe_2O_4$ + 15 H_2O + $7NO_3$ The main properties of cobalt ferrite are magnetic, magneto-optical, and electrical properties (Ristic M., et al 2017). The atoms that make up the ferrite structure can be organized in different ways, giving it different properties. Such properties are directly related to the particle size, the degree of crystallinity, the purity of the phase diagram, and its shape (Ristic M., et al 2017). Also according to the organization of atoms, ferrite can be subdivided into groups, one of which is called episnelium (Ristic M., et al 2017), a structure synthesized in the present study. The episnelium is basically composed of two sites called tetrahedral and octahedral, whose cations interact strongly leading to the so-called super-exchange, influenced by the accommodation of cobalt ions in the structure, which is linked to the distribution of electrons in the valence d layer (Satpute SS et al , 2019). Such characteristics give cobalt ferrite: good chemical stability, good mechanical hardness, magnetic anisotropy and good magnetization saturation (Pineda X., Quintana GC, Herrera AP and Sánchez J. H, 2020), thus being one of the most studied magnetic materials .

SYNTHESIS OF NPS

Numerous NP synthesis methodologies are currently described, basically branching out from two groups: Top-down and Bottom-up (Pal G et al, 2019). In the first, NPs are generated by reducing the size, so that the source material decomposes into fine particles, usually by grinding or spraying, and in the second, NPs are generated from small entities such as atoms and molecules, so that there is a process called self-assembly in new nuclei, causing nanoscopic materials to increase in size, that is, we have that the first approach is the opposite of the second (Pal G et al, 2019). Both methodologies mainly describe three approaches: chemical ones, for example the sol-gel, microemulsion, hydrothermal co-precipitation and chemical vapor methods; the biological ones, whose synthesis of NPs involves the use of microorganisms such as bacteria and fungi, in addition to plants, and the physical ones through processes such as laser ablation, electro-spraying, evaporation-condensation and laser pyrolysis (Pal G et al, 2019). In the present work, we opted for chemical synthesis using a process called sol-gel.

SOL-GEL PROCESS

It corresponds to the transition from the liquid aspect of a solution to the viscous one, with subsequent gelatinization of the sample, until a solid state and a final powdery appearance are achieved. . This transition is due to the heating of the sample, which leads to the formation of structures called lacunar aggregates, within the solution (sol) (Boilot J. P., Gaicoin T. and Perruchas S, 2010). The evaporation of the solvent leads to the percolation of these aggregates giving a more solid state, corresponding to the sol-gel transition. When drying occurs at low densities, the airgel is formed and when it occurs at a higher density and done slowly at low temperatures (20 - 100 ° C), the xerogel is obtained, leading to the final powder aspect. (Boilot JP, Gaicoin T. and Perruchas S, 2010)

GREEN CHEMISTRY AND SYNTHESIS

The chemical approach to the synthesis of NPs generally involves the use of substances that are harmful to the environment, in view of this concern in the present study, we opted for the synthesis route called "green chemistry", also called "green nanotechnology", which according to Pal G., Rai P. and Pandey A, 2019, are chemical syntheses with a lower amount of toxic chemicals, the environment and animal and human health, being ecologically correct. (Boilot J. P. et al 2019). In view of this principle, we sought to use natural means to obtain interesting precursors for the synthesis of NPs. Kiwi (Actinidia delicious) was the chosen fruit, since according to the Brazilian Food Composition Table (TBC), 2011, Kiwi has in its composition a large percentage of ascorbic acid (Vitamin C) and polyphenol compounds that together expand the antioxidant capacity of the fruit (Du G., Li M., Ma F. and Liang D, 2009). Also according to TBC, Kiwi also has a high concentration of potassium, minerals, and to a lesser extent proteins and actinin, a proteolytic enzyme.

BIOLOGICAL ASSAY

Once the methodology, the approach and the synthesis route of the cobalt ferrite NPs were selected, we proceeded to the biological test in order to observe the behavior of the NPs in the T. cruzi protozoan culture medium.

CHAGAS DISEASE

The protozoan Trypanossoma cruzi is responsible for causing Chagas disease. T. cruzi is found basically in three forms: amastigotes, trypomastigotes and epimastigotes. Transmission generally occurs through the bite of an insect known as a barber, where T. cruzi lodges in its intestine (Health Surveillance Guide, 2019). Once infected, the mosquito (triatomine) when biting vertebrates, defecates, eliminating infectious forms of the parasite. When scratching the site, the skin lesion occurs, facilitating its penetration through the injured orifice, in its trypomastigote form. Within the infected organism, the protozoan takes different forms until it reaches the bloodstream, gaining other regions and organs (Health Surveillance Guide, 2019). According to CONITEC (National Commission for the Incorporation of Technologies in the SUS, 2018), Chagas disease is an infectious condition that presents the acute and chronic phases. The first one starts one to two weeks after the infection and lasts between eight to twelve weeks. Due to the high characteristic parasitemia at this stage, a classic symptom is prolonged febrile syndrome. The second can take two forms: the indeterminate (without symptoms) and the determined that can affect the heart, digestive system or both, and rarely neurological. Chagas disease is classified as one of the Neglected Tropical Diseases (DNT), which affects millions of people in low-income countries, (Islan G. A et al, 2017) and unfortunately currently used drugs (Nifurtimox and Benznidazole) are criticized due to low efficacy and serious side effects (Romero EL and Morilla MJ, 2010). Given this scenario, nanoscience can add a new therapeutic form to so many of these neglected diseases, and bring a new look to their treatments, and one of these alternatives may be the cobalt ferrite nanoparticle.

The present work aims at the synthesis of cobalt ferrite nanoparticles, seeking the principles of green chemistry; characterize the produced nanoparticles and observe their antiproliferative behavior and activity in a T. cruzi culture medium.

MATERIALS AND METHODS

THE KIWI SAMPLE

The Kiwi sample was purchased from local stores and was washed and sanitized. This was macerated, crushed and strained to form a pulp to be used in the synthesis of Cobalt Ferrite.

SYNTHESIS OF COBALT FERRITE

The Cobalt Ferrite nanoparticles were synthesized from a solution of Iron Nitrate III (1.2 g) and Cobalt Nitrate II (1.0 g) in 100 ml of ultrapure water each in separate beakers, in a ratio of 2 ; 1, respectively.

The solutions were combined and 50 ml of the Kiwi pulp was added. Subsequently, the sample was subjected to magnetic stirring and heated to 100 C for approximately 4 hours through a process called sol-gel (Boilot JP, Gaicoin T. and Perruchas S, 2010) where it presented itself at the end of this reaction appearance of dark colored powder. After this reaction, the sample was submitted to an oven at 100 ° C for 24h.

PURIFICATION OF IRON NANOPARTICLES

After removal from the oven and reaching room temperature, the iron nanoparticles were packed in falcon tubes with ultra pure water and subjected to centrifugation for 15 minutes at 3600 rpm. The supernatant was discarded and this repeated process was repeated three times. After the centrifugation step, the Nps produced were placed in the oven at 100 C for 48 hours. Subsequently, the previously dried sample was taken to the Mufla oven, with calcination at 600ºC for 1 hour.

CHARACTERIZATION OF COBALT FERRITE

To characterize these nanoparticles, the Scanning Electron Microscopy (SEM) techniques were used. at the National Institute of Metrology, Quality and Technology (Inmetro) on the Magalhães 400 microscope, using a voltage of 10 kV with a current of 0.4 nA. For X-ray diffraction, the samples were submitted to the Zeiss diffractometer (model HZG), located at the Brazilian Center for Physical Research (CBPF), equipped with a graphite monochromator and a rotating copper anode, operating at 40 kV and 40 bad. The analyzes were carried out in a range of 2 ° -80 °, with a step of 0.05 degrees / s, with Cu-Ka radiation. Diffractograms were analyzed and compared with the JCPDS database (Joint Committee on Powder Diffraction Standards) (Bayliss P, 1976)

BIOLOGICAL ASSAY

The samples were tested for their antiproliferative activity by the parasite. The Trypanosoma cruzi protozoan was grown, whose Y strain was supplied by the UFRJ Medical Biochemistry Institute - IBqM, installed at the Health Sciences Center, at UFRJ. The non-infectious form, epimastigote, was chosen to receive the NPs, which were introduced in LIT culture medium (from the liver in a triptonium fusion) supplemented with 10% fetal bovine serum (FBS). In the exponential phase (48 hours), with a minimum concentration of 1x10 parasite / mL. The parasites were treated with 10, 20 and 50µg / mL of nanoparticles. The LIT medium was supplemented with 10% SFB (Bovine Fetal Serum) and 25µl of DMSO, added as a vehicle. For the treatments, a solution was made that we call "solution N" containing 41µl of DMSO, 8,959 ml of LIT medium and 900µg of NPs. For the respective concentrations, the following protocol was followed: 10µg / mL - addition of 1 mL of N solution, 1 mL of culture, 7 mL of LIT medium and 1 mL of SFB; 20 µg / mL - addition of 2 mL of N solution, 1 mL of culture, 6 mL of LIT medium and 1 mL of SFB and 50 µg / mL - addition of 5 mL of N solution, 1 mL of culture, 3 mL of medium LIT and 1 mL of SFB. The aliquots were cultured in a final volume of 10 ml, in a 15mL sterile Falcon tube, containing 5mL of the aerial column. An incubator with a constant temperature of 28ºC was used. To determine the proliferation rate of a 0.01 ml aliquot of culture, it was made and diluted in 4% formaldehyde over eight days. The estimate was made using the Neubauer camera. The statistical test used for the analysis was the ANOVA (Analysis of Variance) in the ONE-WAY model so that the calculation of global variation involved the variation between treatments, and the variation within treatments. (Jacques M. C, 2013). In the present study, the variation between treatments was feasible because the monitoring of the growth curve of the protozoan for eight consecutive days was performed three times, providing data from three different curves. And with regard to variation within treatments, we compared four aliquots with different concentrations of NPs.

RESULTS AND DISCUSSION

COMPOSITIONAL ANALYSIS OF DELICIOUS ACTINIDIA

Originating in Asia, one of the fruits that became popular worldwide for its sensory and nutritional properties, the Kiwi, is part of the great genus Actinidia composed of more than 60 species (Wojdyło A., Nowicka P., Oszmianski J. and Golis T ., 2017). In general, Actinidia has in its composition: fibers, organic acids, phytochemicals, carotenoids, sugars, proteins and vitamins (Padmanabhan P. and Paliyath G., 2016). Of all species, Actinidia delicious is one of those that have had their cultivation successfully domesticated (Wojdyło A., Nowicka P., Oszmianski J. and Golis T., 2017). The properties of the kiwi are due to its nutritional composition, detailed by the USDA (US Department of Agriculture) National Nutrient Database, 2019, demonstrating that the kiwi mainly contains substances such as vitamin C, which prevents the formation of nitrous compounds, classified as reactive species oxygen (ROS) responsible for the oxidation of several different situations in the body, leading to conditions such as cancer, and cardio and cerebrovascular diseases (Du G., Li M., Ma F. and Liang D, 2009). The compounds called polyphenols such as flavonoids, also act as antioxidants neutralizing free radicals that can oxidize cell proteins, DNA, carbohydrates and membrane lipids, being responsible as well as ROS, for pathological conditions such as inflammation and infection (Jiao Y., Kilmartin PA, Fan M., and Quek SY, 2018). Another component described is a new form of vitamin E, alpha-tocomonoenol, which also has antioxidant activity in kiwis. (Drummond L., 2013). Another element that makes up the kiwi is actinidine, a proteolytic enzyme that catalyzes the hydrolysis of peptide bonds of proteins, amides and simple esters (Boland M., 2013) Its structure is globular, with a single polypeptide chain, and has two domains whose nuclei are hydrophobic and the interface between the two domains has a catalytic site composed of hydrophilic side chains. In its internal organization, actinidine also has three disulfide bonds, configuring a well-stabilized structure. (Boland M., 2013). Minerals, on the other hand, still have the contribution of elements with different electrical charges, which enhances the ability of electrostatic interaction, according to Coulomb's Law (Corradi W. et al, 2010). There are also non-starch polysaccharides (KPS) in the composition of kiwi, whose antioxidant activity has also been studied and partially attributed to non-methylated galacturonic acids (Wu D. T. et al, 2019). It is important to note that the composition of phytonutrients varies according to the cultivar and various conditions including growth and maturation of the fruits (Padmanabhan P. and Paliyath G., 2016). Remembering that phytonutrients, also called phytochemicals or secondary metabolites that fight oxidative stress and their classification depends on the chemical structure or functional attributes are they polyphenols (flavonoids, anthocyanins, phenolic acids), carotenoids, alkaloids, steroids among others (Belwal T et al, 2010). In general, studies show that daily consumption of one to three kiwis increases resistance to oxidative DNA damage in lymphocytes and reduces lipid peroxidation in humans (Padmanabhan P. and Paliyath G, 2016).

With the knowledge of all these elements, we have in kiwi a great candidate to provide stability to NPs through a set of items that can synergize their antioxidant activity, and may even contribute to the reduction of $Fe + 3$ in $Fe + 2$ in the reaction of formation of the cobalt ferrite already mentioned, in addition to possibly providing elements capable of interacting electrostatically providing a microenvironment that enables the formation of NPs, since the interactions between the particles can involve the weak forces of Van der Waals, covalent interactions as well as stronger polar and electrostatic. (Hong N.H., 2019). In addition, both the aggregation and the agglomeration of particles are influenced by the polarization and viscosity of the liquid since they determine interaction between the nanoparticles through attractive and repulsive forces that govern the individual and collective movement of NPs (Hong N.H., 2019).

MORPHOLOGICAL CHARACTERIZATION OF COBALT FERRITES

One of the techniques used for the morphological characterization and analysis of metallic NPs was Scanning Electron Microscopy (SEM), which demonstrated heterogeneity in the sample sizes so that apparently there was a visual variation from 200 nm to 5µm, also showing the aggregation of the same . It can be seen in figure 1 that the nanoparticles also had an apparently predominant geometric shape. According to Roca A. G. et al, 2019, the properties of the particles are dependent on the surface-volume relationship, and on the faces that the crystal takes on whose surface can confer different reactivities. In addition, the morphology is also influenced by the synthesis route, responsible for conducting thermodynamic and kinetic aspects, which are the ones that control the reactions, determining in addition to the geometric shape, the size and chemistry of the surface of the particles, characteristics that confer their properties (Roca AG et al, 2019) Cobalt ferrite generally takes the form of episnelium, a type of crystalline structure that takes on a cubic shape, with the general formula XY2O4 where the metal cations are positioned in two different crystallographic locations, the tetrahedral (represented by X) and octahedral (represented by Y) (Kefeni KK,. Msagati TAM, Nkambule TT, Mamba B. B, 2020). At these sites ions of different oxidation states that interact and cations are reorganized but in different ways, the composition of which, their distribution and interaction being determinant for the particle's geometric shape and directly influencing its properties (Kefeni KK ,. Msagati TAM , Nkambule TT, Mamba B. Bl, 2020)

The other technique used for the study of NPMs was X-ray diffraction. It is known that crystalline structures are composed of atoms organized periodically, once the X-ray beam interacts with the sample, there is a spreading of these beams that respects Bragg's Law, described by the equation $n\ \lambda = 2\ d\ sen\theta$, whose analysis was carried out by the Rietveld method and through the FullProf program (Kumar L., Kumar P., Narayan A. and Kar M., 2013) showing that the synthesized sample produced a similar pattern of cobalt ferrite, demonstrated by the signs presented and according to the coincident position of the characteristic peaks that respect Bragg's Law It is also observed that the peak intensity reached 2200 intensity (arbitrary unit), showing good crystallinity of the sample, allowing us to conclude that its crystalline structure it presents an interesting degree of organization, and as mentioned earlier, organization of cations as well as their interaction influence the geometric shape. As we saw earlier, the kiwi has in its composition different elements that provide its high antioxidant potential and possible participation in the reduction of Fe + 3 in Fe + 2 contributing to the interaction of cations between the tetra and octahedral sites, enabling the stability of the structure it had its geometric shape reasonably predominant comparing the images in figure 1. According to previous studies such as Coelho et al, 2019, fruits such as lemon, okra and açaí showed different structural characteristics such as geometric shape (evidenced by SEM) and crystalline structure (evidenced by DRX) of its nanoparticles, also synthesized with cobalt ferrite and using the same sol-gel method. This allows us to conclude that the participation of the raw material of each fruit directly influences not only the stability but also the geometric shape, which can be attributed to the different cations and electrons present in the tetra and octahedral sites, as detailed previously.

In the diffractograms below we have that the red line refers to the sample, that is, the result of the synthesis and in the blue sign, the difference pattern between our sample and in black, the alignment between our sample and the cobalt ferrite pattern., being represented in figure 2.

PROLIFERATION CURVES

The sample was exposed to the anti-proliferation assay of T. cruzi, in concentrations ranging from 10μg /mL to 50μg / mL, we observed an anti-proliferative characteristic in all concentrations, however the greater effectiveness of this action was demonstrated in the concentration of 50μg / mL , leading us to conclude that we need

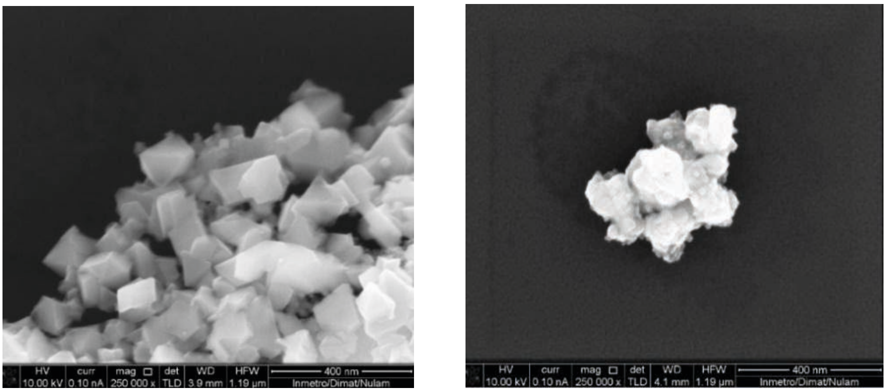

Figure 1: Scanning Electron Microscopy of the Kiwi NPM

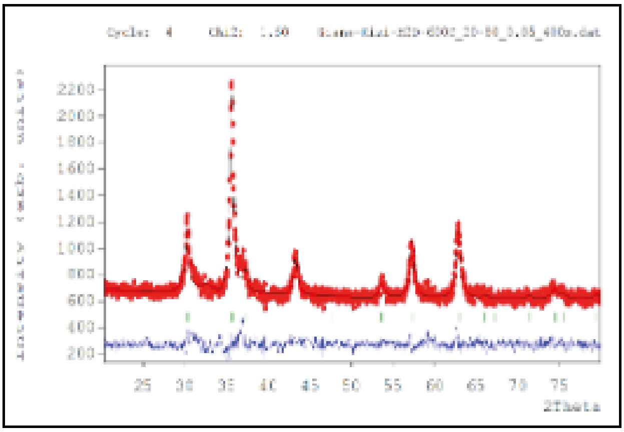

Figure 2: XRD of kiwi NPMs

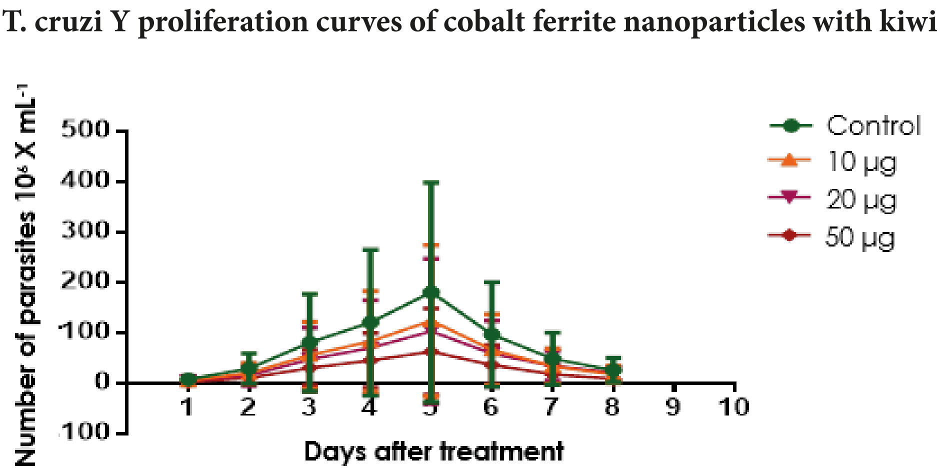

Figure 3: T. cruzi proliferation in kiwi NPMs

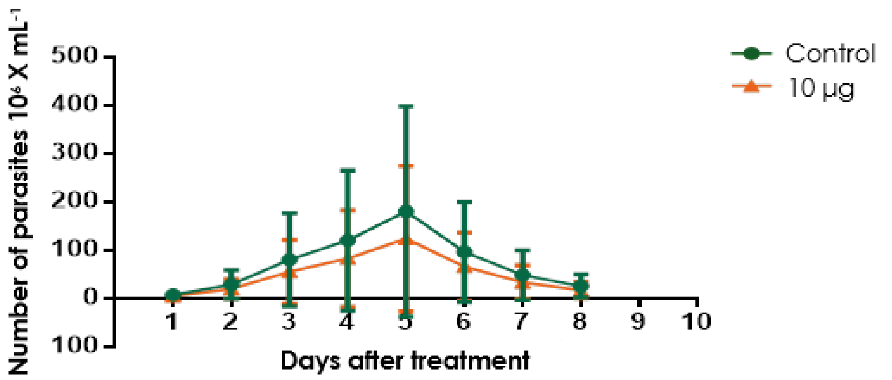

Figure 3.1: Individual comparison between the control and 10µg /mL concentration

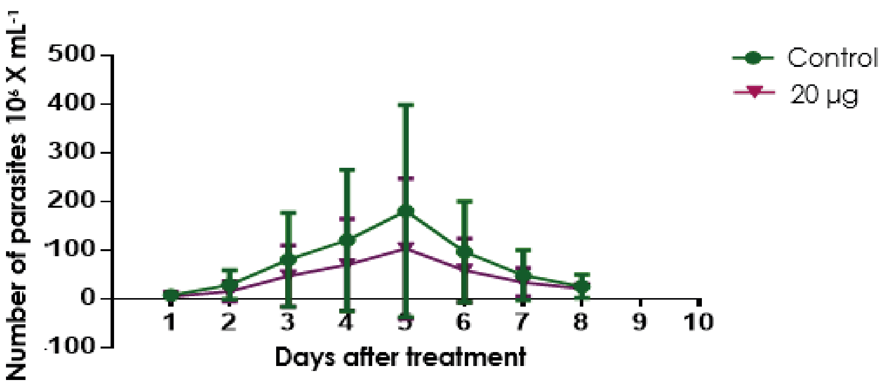

Figure 3.2: Individual comparison between the control and 20µg /mL concentration

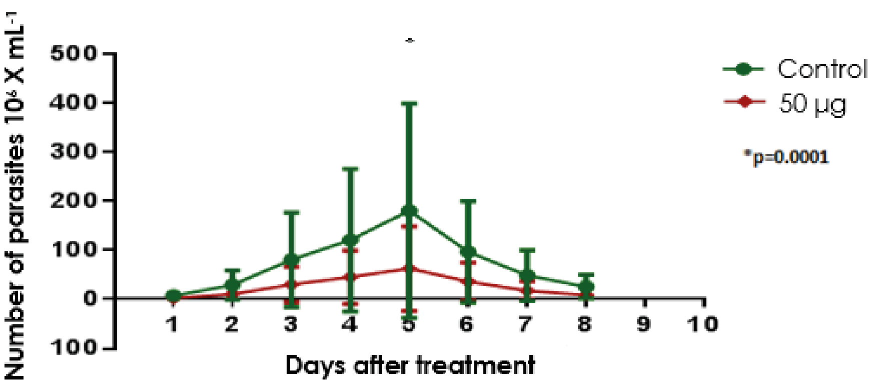

Figure 3.3: Individual comparison between the control and 50µg /mL concentration

a higher concentration of nanoparticles coated with kiwi to achieve significant anti-proliferative action. Several mechanisms of antiparasitic action are described in the literature, as some of the properties of NPs, among which are: inhibition of the proliferation of promastigotes, inactivation of oocysts, ionic release of NPs, interaction of NPs with the parasite surface, NPs can harm structures of lipophosphoglycan molecules and glycoproteins found on the surface of the parasite responsible for infection and DNA disturbance, can also diffuse in three different ways such as through the pores present in the parasite's membrane, or through ion channels, by carrier proteins or by endocytosis (Khezerlou A., Sani MA, Lalabadi MA and Ehsani A, 2018) We were also able to show that, although we have not reached the the expected particle size, this fact did not influence the antiproliferative activity of the protozoan, as shown in figures 3 to 3.3.

According to the behavior of the proliferation curves, in view of the anti-proliferative action of NPs, corroborates the information in the literature (Khezerlou A., Sani MA, Lalabadi MA and Ehsani A, 2018) regarding the antiparasitic property of NPs, the that enables us to contemplate an effective suggestion for a possible treatment of Chagas' disease. Currently, Chagas disease, caused by T. cruzi, is part of the group of neglected diseases that affect about millions of individuals worldwide and mainly Latin America and Africa (Islan G. A, 2017), however, counting only two drugs for treatment, which present issues of concern, such as low efficacy, making it necessary to increase the dosage and thus cause toxicity and side effects (Romero EL and Morilla MJ, 2010)

CONCLUSION

New strategies in the field of nanomedicine combined with biotechnology, project a prosperous future for the development of intelligent and effective solutions, gradually involving less aggressive methods for the organism and using increasingly smaller doses, optimizing the prognosis. In the present study, we can conclude that the synthesis of cobalt ferrite nanoparticles was successfully carried out before confirmation by means of XRD analysis. We can also rely on the literature to suggest that the synthesis of the cobalt ferrite nanoparticle shows effectiveness in one of its properties of great interest, the antiparasitic action, confirmed by analyzing the growth curves. In addition, we also observed that the constituent elements of the kiwi served as important precursors that possibly participated in the interactions inherent to the cobalt ferrite synthesis process, participating as contributors to Van der Waals forces, ionic and electrostatic interactions, as well as its spinel geometric structure. cubic with the interaction between the ions present in the two sites (tetra and octahedral) even before the aggregation of NPs evidenced in the SEM analysis. The green synthesis of NPMs, demonstrated in the present work, that it could be an alternative in the search for new therapeutic methods, because in addition to involving low-cost production, using accessible raw material and not generating toxic waste for the environment, it glimpses a a viable alternative both biologically and financially, being an attractive solution not only for Chagas disease, but for so many other diseases neglected by the large pharmaceutical industries.

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