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Study Of The Toxicological Effects Of Pentostam And Silver Nanoparticles On Liver And Spleen Tissue In Albino Mice Infected With Cutaneous Leishmaniasis

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ABSTRACT

Cutaneous Leishmaniasis (CL) is a parasitic disease that has been known to humans for centuries, and which are called by many local names and were causing suffering and death to people infected with it**,** The results also showed that pentostam (Sb), silver nanoparticles (AgNPs) and loaded drug (AgNPs + Sb) had different toxic effects on liver and spleen tissue, as it was higher on liver and spleen tissues when using pentostam compared with free silver nanoparticles and loaded silver nanoparticles .The drug Pentostam, which did not show clear pathological effects on the tissues of the liver and spleen.

INTRODUCTION

Cutaneous Leishmaniasis (CL) is a parasitic disease that has been known to humans for centuries, and which are called by many local names and were causing suffering and death to people infected with it (WHO, 2000). Cutaneous Leishmaniasis, which is caused by two types, is considered Leishmania major, Leishmania tropica is the most common parasite that causes skin lesions mainly ulcers on the exposed parts of the body and differs from one another in clinical and immunological aspects (WHO,2020). Studies have shown that recent anti-leishmanial chemotherapy applications are far from effective (Sundar et al., 2014). As for the effect of Pentostam treatment, which is one of the most common and effective medicines used. Sometimes the use of this group of drugs is associated with a combination of problems such as drug resistance, toxicity, increased failure rate, and prolonged treatment course. In addition, some patients have experienced some types of heart or kidney failure as side effects of these drug compounds. However, pentostam remains the drug of choice for the treatment of leishmaniasis in its various forms. In the early 1980s, some reports of patients who did not receive treatment with these drugs were announced, but unfortunately, there is still no development in the production of a new anti-leishmanial drug (Mendonça- Filho et al., 2004). Nanotechnology has been developed using nano-sized particles to treat many diseases including human tumors, as new functions and properties of the byproduct have been observed in a wide range of applications, nanotechnology provides important new tools that are expected to have the greatest impact on many areas in the world. Medical sciences, where polymer-coated metallic NPs have recently been demonstrated as an active and new field of advanced research, for example, are an important accessible adsorbent and AgNPs outperform other secondary metal particles for their antimicrobial effects. However, its stability is a serious problem with polar groups such as hydroxyl or amine groups and is usually used for stabilization (Prasad 2008), Nano carriers are nano-materials in the form of inorganic compounds that have their own ability to carry drugs and deliver them to the target and reduce the side effects of drugs due to their high capacity in unlimited ion exchange, and as it was shown to load many organic pharmaceutical treatments in these compounds After that, nanodrugs became a new idea or called smart drugs that revolutionized the treatment of

many diseases and reduced the negative effects and toxicity on bodily tissues (Alshawwa et al., 2022) .

MATERIALS AND METHODS

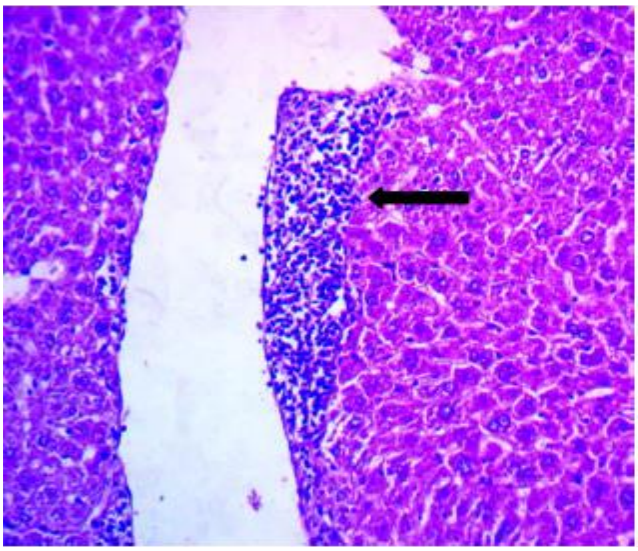
Used RPMI-1640 medium, which was obtained ready-made from ABI (America), where 10% of Fetal Bovine Serum, antibiotics of penicillin and streptomycin were added to develop promastigotes phase of Leishmania parasite. Silver nanoparticles were prepared by dissolving 0.0285. g of (sodium borohydride) in 10 ml of deionized water in an ice bath, then 0.4 mg of (polyvinyl pyrrolidone) is added as a reaction stabilizer, then 0.0214 g of (silver nitrate) is dissolved in 10 ml of distilled water and then mixed. Magnetic stirrer and stirred at 1500 rpm for one hour at 50-60 °C until the resulting solution turns blackish-brown in color and then dried in an electric furnace (Zhu et al., 2011). Several methods were used to measure secondary particles, including X - ray diffraction, Fourier transform infrared, Atomic Force Microscope, Scanning Election Microscope. It was used in the experiment of white male mice that were divided into 11 groups, each group contains 8 mice, and the concentrations ng/ml 100,200,300 pentostam and silver nanoparticles (AgNPs) and loader were prepared as follows: The first group (positive control) was injected each 1 mL animal subcutaneously from anterior flagella and left untreated, group II (negative control), group III pentostam (Sb) at 100 µg /ml, group IV (AgNPs) at 100 µg /ml, and group V (Sb + AgNPs). 100 µg / ml, group VII pentostam (Sb) at a concentration of 200 µg / ml, group VIII (AgNPs) at a concentration of 200 µg / ml , group VIII (Sb + AgNPs) at a concentration of 200 µg / ml, group IX pentostam (Sb) at a concentration of 300 µg / ml, group The tenth group (AgNPs) at a concentration of 300 µg/ml, the eleventh group (Sb+AgNP5) at a concentration of 300 µg /ml, Histological slides were prepared according to Bancroft and Stevens (2008) method in Al-Sadr Teaching Hospital laboratory affiliated to Najaf Health Department.

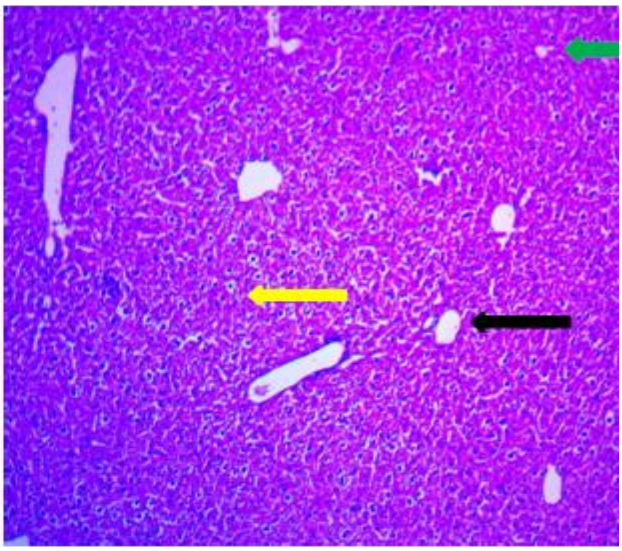
RESULTS AND DISCUSSION

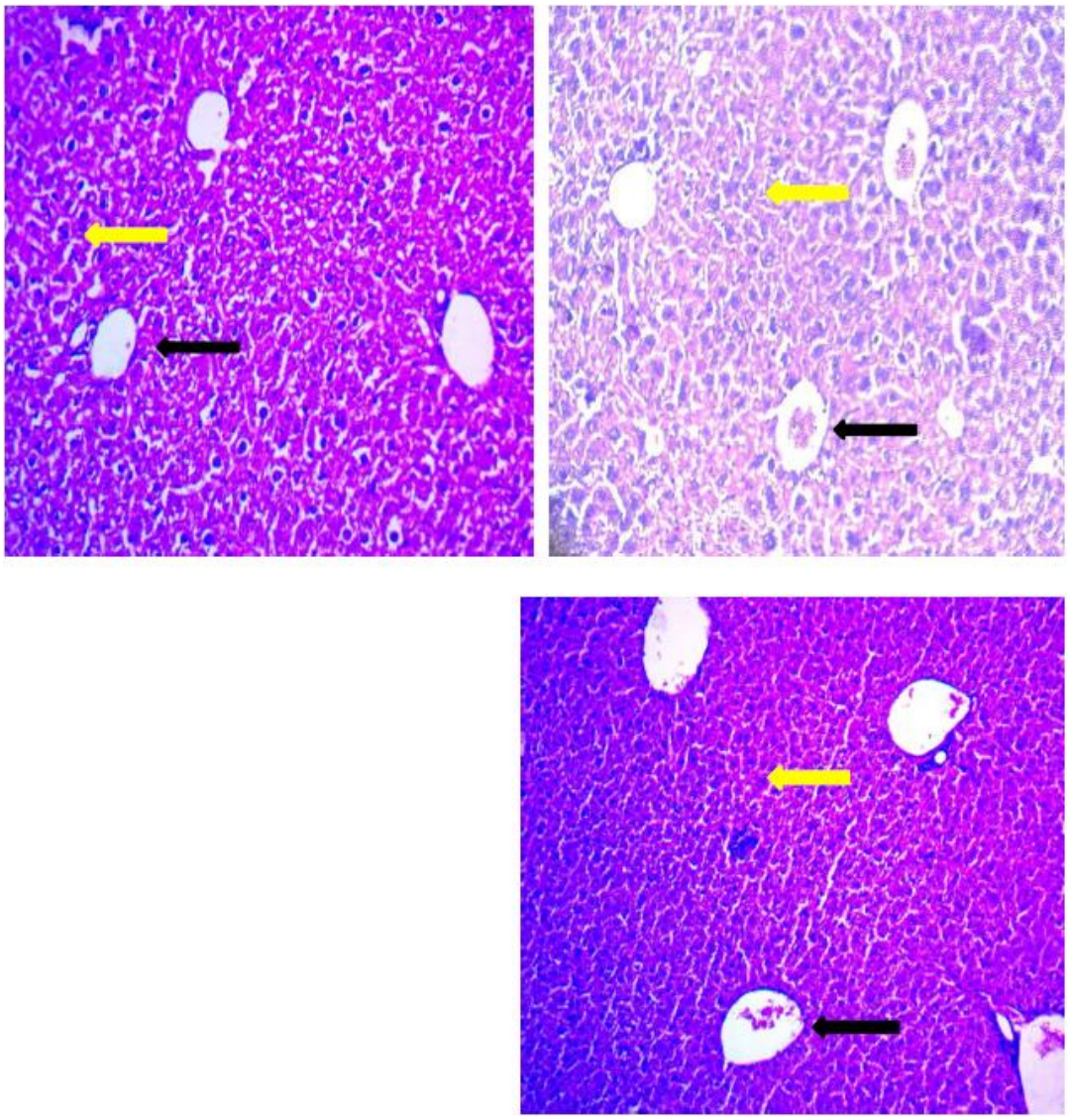
The toxic effects of nanoparticles on normal cells and organs is one of the factors that hinder their use in the treatment of some clinical medical conditions, depending on the diversity of nanopower sources and their physical and chemical properties, including shape, size, surface area and scattering factor, which is the main factor that has a decisive influence on its behavior and safety in the organism (Ajdary et al,. 2018). Where the images of No . (1) represent the liver tissue, where we notice in the image (a) a section of the liver tissue (the second group, negative control) and it appeared normally showing the hepatocytes arranged normally as well as the normal nuclei and the central vein indicated by the black arrow while the arrow indicates The yellow refers to the hepatic lobules and the green arrow indicates the bile duct, while the image (b) represents a section in the cells of the liver tissue infected with cutaneous leishmaniasis and untreated (the positive control group), where we notice congestion and infiltration in the inflammatory lymphoid cells of the liver tissue, as we note in the image (c) A section of liver tissue infected with cutaneous leishmaniasis treated with pentostam, where the black arrow indicates congestion in the central vein and portal blood vessels, The yellow arrow indicates necrosis of hepatocytes. This indicates the toxic effect of pentostam on liver tissue. This was confirmed by the results of (Elammari and Sariti 2021) and (Saad et al., 2022) through his study on the toxic effect of pentostam on liver tissue and kidneys in laboratory mice. The study showed that pentostam has toxic effects on liver tissue upon anatomical evaluation as a result of the role played by the liver in metabolizing toxic substances that enter the body of the organism. Picture (d) shows a section of the liver tissue affected by cutaneous leishmaniasis treated with free secondary silver particles, where the black arrow indicates the presence of the central vein and the portal blood vessels begin to return to their normal state and the yellow arrow indicates the presence of inflammatory cells in a lower percentage than in the group treated with pentostam And the cellular arrangement returns to normal, and this indicates that the toxic effect of free silver nanoparticles is less than when using the drug pentostam on the liver tissue. The results also showed that the treatment with silver nanoparticles depends on the size of the particles and the amount of dose given to the organism, as the smaller the size

of the particles, the less the toxic effect on the body tissues. This was confirmed by the results of (Hyun et al., 2008) by studying the effect of silver nanoparticles on body tissues in albino mice and showing that the use of low concentrations of silver nanoparticles for a period of 28 days does not cause harmful effects on liver tissue. It is also consistent with another study conducted by researchers (Mao et al., 2022) on the toxic effect of silver nanoparticles outside and inside the body such as the liver, spleen and kidneys, and noted that silver nanoparticles exert a degree of toxicity depending on the dose and type of target cell or organ, As it was found (Almansour et al., 2015), when he studied the histological changes that resulted when giving doses of free silver nanoparticles for a period of 35 days, no deaths occurred during the dosing period and no histological changes were observed compared to the control group, there were no histological changes in Liver and spleen tissue, which is applicable to the results of the current study. Also, picture (e) shows a section of the liver tissue infected with cutaneous leishmaniasis treated with pentostam loaded with silver nanoparticles, where we observe normal liver regardless of mild vascular congestion and moderate lymphocyte infiltration. The black arrow indicates the presence of the central vein and the portal blood vessels appear normal. With the presence of light congestion and the yellow arrow indicates the presence of moderate lymphocytes, and this indicates that the silver nanocompounds loaded with the drug reduce the toxic effect of the drug on the liver better than when using the drug freely. This was confirmed by the results of researcher (Saeed, 2021) in his study on the effect of biosynthetic silver nanoparticles from the plant on white mice, as confirmed (Korani et al., 2014) that the size and concentration of the given dose of silver nanoparticles is responsible for the side effects. On the body, as shown by exposure to large doses that change the tissue and destroy its cells and may cause some of them to necrosis, especially in the liver tissue as a result of the accumulation of nanoparticles as well as the spleen tissue. Also, images No. (2) represent the spleen tissue, where image (a) represents a section of the spleen tissue (the second group, negative control), and it appeared normally, in which the red pulp and white pulp appear naturally, where the black arrow indicates the red pulp while the yellow arrow indicates the pulp white and lymphatic sinuses appear naturally. Also, picture (b) shows a section in cells of spleen tissue infected with cutaneous leishmaniasis and untreated (positive control group), where we notice infiltration or infiltration in the inflammatory lymphocytes of the spleen tissue. Whereas in figure (c) we notice a section of the spleen tissue infected with cutaneous leishmaniasis and treated with Pentostam drug, where we notice dissolution of the spleen tissue with the presence of giant cells where the black arrow indicates hemorrhage outside the pulp and infiltration in the inflammatory lymphoid cells of the tissue, and the yellow arrow indicates the pulp white and the green arrow to the lymphoid giant cells, and this is due to the toxic effect of pentostam on the spleen tissue. These results are in agreement with (Otavio et al., 2008) Through his study on cutaneous leishmaniasis in mice, he observed inflammatory reactions in the liver, spleen and kidneys due to the deposition of the drug in tissues, which leads to their swell it up. The study also showed in figure (d) a section of the spleen tissue infected with cutaneous leishmaniasis treated with free silver nanoparticles, where the black arrow indicates the red pulp and the yellow arrow indicates the white pulp. It indicates that the toxic effect of free silver nanoparticles is less than in the study groups, and the results also showed that treatment with silver nanoparticles depends on the size of the particles and the amount of dose given to the organism. carried out by researchers (Mao et al., 2022) about the toxic effect of silver nanoparticles outside and inside the body such as the liver , spleen and kidneys and note that the secondary silver particles exert a degree of toxicity dependent on the dose and type of target cell or organ. A study (Cho et al., 2018) on the toxic effect of silver nanoparticles in the spleen of female laboratory mice at exposure from 60-100 nm, showed no obvious changes in the tissue of the liver, spleen and adrenal cortex. The image (e) also shows a section of the spleen tissue infected with cutaneous leishmaniasis and treated with Pentostam drug loaded on silver nanoparticles, where we note the spleen is normal regardless of the

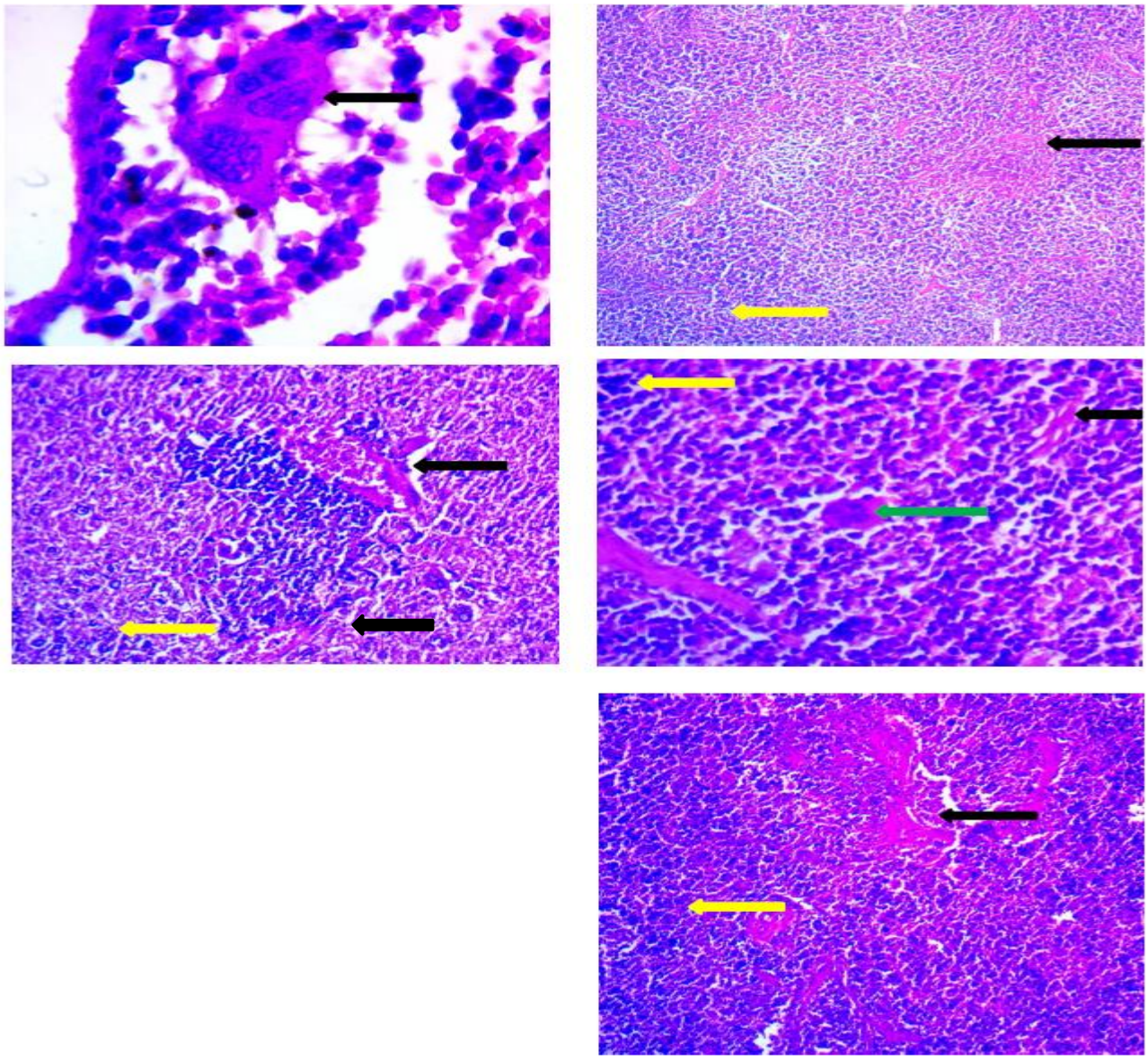
presence of moderate lymphocyte infiltration indicating the red pulp where we notice, a slight blood infiltration and the yellow arrow indicates the presence of The white pulp and the lymphocytes are moderate, and this indicates that the secondary silver compounds on which the drug is loaded succeed in delivering the treatment to the target organ, which reduces its toxic effect on tissues, especially the spleen, on the liver better than it is when using the drug freely. This was confirmed by researchers (Korani et al., 2014) that the size and concentration of the given dose of secondary silver particles is responsible for the side effects on the body, and exposure to large doses that changes tissue and destroys its cells and may cause some of them to necrosis, especially in liver tissue as a result of accumulation nanoparticles as well as hyperplasia of the spleen tissue. The study conducted by (Ansari et al., 2016) also showed that when high doses of secondary silver particles were given, the concentrations (500, 1000, 3000, 5000 mg/kg) were used to evaluate the potential toxicity in albino mice for 28 days when injected into a chelate. Peritoneal, the results of the effect are high and that the high concentration, especially 3000-5000, has an effect on cell degeneration, and obvious changes in the liver, spleen and kidneys, and low concentrations are good when using low doses.







Picture (1) a- Normal liver tissue b- Liver tissue of an infected and untreated rat c- Liver tissue of an infected rat treated with pentostam d- Liver tissue of an infected rat treated with silver nanoparticles e- Liver tissue of an infected mice treated with loaded silver nanoparticles pentostam drug.



Picture (2) a- spleen tissue of a normal mice b- spleen tissue of an infected and untreated mice c- spleen tissue of an infected mice treated with Pentostam d- spleen tissue of an infected mice treated with silver nanoparticles e- spleen tissue of an infected mice treated with loaded silver nanoparticles Pentostam drug.

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