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In Vitro Cytotoxicity Test of Nano Silver Medical Devices

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Abstract: *Nano silver is a single silver particle between certain chemical means and physical means. Its particle size is between 1-100nm. Nano silver is easy to enter the body of pathogens, so as to control infection and promote wound healing. Therefore, nano silver medical devices such as nano silver and nano silver dressing are widely used in clinical medicine. At the same time, nano silver materials also have certain biological characteristics, which may lead to the biological effects of nano silver materials, but so far, no complete conclusion has been reached. In recent years, a large number of cytotoxicity experiments have been carried out on silver nanoparticles in vitro. Therefore, this paper studies and discusses the in vitro cytotoxicity test of nano silver and its pharmaceutical products through the in vitro cytotoxicity test of nano materials, and provides the basis and support for the in vitro cytotoxicity test of nano materials by using the key project indicators in MTT test and LDH test. The selection of MTT test and LDH test is due to the characteristics of MTT method and the cytotoxicity of silver nanoparticles in vitro. The combination of MTT test and LDH test can evaluate the cytotoxicity of nano materials more comprehensively and study the in vitro toxicity of silver nanoparticles to mammalian cells. According to the experimental results in this paper, we can infer the toxicity mechanism of nano silver materials, which has a certain idea for the application of nano silver and nano silver materials. Through the discovery of in vitro cytotoxicity mechanism of nano silver medical devices, nano silver and its medical devices can be used more comprehensively and safely.*

Keywords: *Nano Silver, Cytotoxicity in Vitro, MTT Test, LDH Test*

1. Introduction

In recent years, with the continuous development of chemical research and the research and discovery of chemical substances, nano silver as a new functional material [1], has some specific properties, because nano silver has a strong role in sterilization, tissue repair and wound healing. More importantly, in terms of antibacterial effect, nano silver and its products are relative to other anti-bacterial materials Bacteria products have significant effect. Therefore, nano silver and its medical products are widely used in clinical medicine. In recent years, researchers have developed many medical products related to nano silver. In general, the types and application scope of nano silver products are expanding, and gradually applied in various fields. With the increasing contact between nano silver and nano silver related products and human body, we need to know and balance their biological safety in use. Therefore, the biological safety of nano silver has been studied in vitro and in vivo. However, for the current level of scientific research, the research on the in vitro cytotoxicity of nano silver materials [2-4] still has some great certainty, and there are some disputes. This topic has also attracted a large number of scholars to carry out the relevant tests of in vitro cytotoxicity test of nano silver materials. The diameter of silver nanoparticles is very small. It is only about 10-100nm. At the same time, small size effect and surface effect are important characteristics of nano silver. Moreover, nano silver is easy to enter the pathogen, which makes it easy to make nano silver and thiol sh contained in enzyme protein of bacteria. In addition, nano silver and its medical products also have the function of treating and preventing bacterial and fungal infections. At present, nano silver related medical devices are widely used as antibacterial materials [5] in wound dressings, skin topical use and surgical instruments. However, there are some problems in the application process. The biosafety of

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these nano silver products has not been determined, and the relevant research reports are inconsistent. Therefore, it is very important to study the biological safety of silver nanoparticles. In this paper, we will test the cytotoxicity of mammalian cells in vitro by MTT test and LDT test. In order to infer the cytotoxicity test of nano silver medical devices in vitro.

Cytotoxicity test [6] is to observe and evaluate the potential cytotoxicity of biomaterials, medical devices or leachable components by in vitro cell culture. moreover, cytotoxicity test is one of the more important detection indicators in the biosafety evaluation system. All kinds of medical devices and medical materials are almost inseparable from it in clinical application. One of them is called tetramethyl lazozolyl salt colorimetry, referred to as MTT test [7], which is more sensitive, and the results of this test method are more objective and reproducible. Therefore, MTT test can be used to understand the cytotoxicity of nano silver related products produced by some manufacturers in vitro. It provides more accurate test data and results for safety evaluation and standard formulation of nano silver related products in vitro. Another test method, LH detection, is involved in LDH detection, which is a cytoplasmic enzyme. However, the change of cell membrane permeability and membrane breakage may lead to LDH leakage outside the cell, so LDH test is suitable for testing the integrity of cell membrane. the principle of LDH test is to oxidize pyruvic acid from lactic acid with LDH and convert pyruvic acid formed by tetrazolium salt into methyl. The methylene dyes are soluble in water and can be detected by microplate spectrophotometer. However, the presence of serum in the cell culture medium may interfere with the test results, which may be due to the presence of more proteins in the serum, which can act as catalysts to help the formation of nail Zan crystals. Therefore, we have a reasonable reason to explore whether different concentrations of serum have a certain impact on the experimental results. In order to reduce the interference of some factors on the test results and improve the reliability of the test data and results, we mainly use MTT test and LDH test two test methods for research and discussion, in order to enhance the test results more comprehensive and more reliable.

We know that any biomaterial should be evaluated before it is used in human body to ensure its safety. at present, the research results show that the related evaluation of the cytotoxicity of biomaterials to cells and the safety standards are the first issues to be considered. It is very important and significant for us to study the cytotoxicity test of nano materials. If we can test the toxicity and side effects of nano materials in cells in a short time, and carry out in vitro cytotoxicity test on nano silver and its nano silver materials, we can easily, economically and quickly screen the parts that may have effects on human body by a large number of nano materials By testing different experimental conditions and different equipment, we can provide the basis for the safety of nano materials in vivo, and reduce unnecessary tests. At present, some scholars have studied the related test of cytotoxicity test in vitro by nano silver bone cement. According to the experimental results, compared with the control group, the experiment in the experimental group will not have a related impact on human osteoblasts. At the same time, it can also be proved that nano silver bone cement has a certain role in resisting a variety of drug-resistant bacteria, and nano silver bone cement is a kind of drug-resistant bacteria. But at the same time, there are other experiments to study the toxicity of nano silver and nano silver in cells, which can reduce the survival rate of cells and induce the generation of reactive oxygen species. Studies on the cytotoxicity of nano silver show that some cytotoxicity is related to the concentration of nano silver, but the cytotoxicity of nano silver is relatively small in a certain concentration range. In the related experiments, Xiong Ling compared the cytotoxicity of silver particles with different particle sizes in vitro, compared the relative cell proliferation rate, and compared the cytotoxicity of micron silver and nano silver. According to the results, the toxicity of silver nanoparticles was greater than that of silver nanoparticles at the same dose. In animal experiments, the acute oral toxicity of nano silver was not found in vitro, but it had cytotoxicity in a certain concentration range. although it has not been verified that nano silver does not have obvious toxicity, it has been verified by experiments that after trauma, the surface of nano silver will be absorbed and distributed in various tissues and organs, especially when applied to human body, the situation is relatively complex. Therefore, we should comprehensively consider the risks and benefits of nano silver when using nano silver and its related medical device products.

Therefore, in this paper, we will study and discuss the cytotoxicity test of nano silver in vitro, and in the research and discussion, we will use MTT and LDT two test methods, and apply the relevant key project indicators to provide the relevant basis for our research on the in vitro cytotoxicity test of nano silver cells, to test the relationship between the cytotoxicity of nano silver cells in vitro and nano silver So as to make the inspection more comprehensive and accurate.

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2. In Vitro Cytotoxic Test

Cytotoxicity evaluation in series of standards for biological evaluation of medical devices [8] is a routine evaluation item. Xiong Ling and other scholars conducted an experiment on the cytotoxicity of silver particles with different particle sizes in vitro. She compared the cytotoxicity of micron silver and nano silver according to the relative cell value-added rate. The results showed that the toxicity of nano silver was greater than that of micron silver at the same dose. When the concentration of nano silver is in the range of 3.5-35 μ g / ml, the nano silver particles with the particle size of 1-100nm may have slight cytotoxicity, and the cytotoxicity is grade 0-2. We can infer from the experimental results of the researchers that there is a correlation between RGR and silver content; as the concentration increases to more than 100 μ g / ml, the cells cultured with nano silver will be in shape In addition, it will show obvious cytotoxicity, and at the same time, the dose-response correlation will disappear. However, in the smaller size of micron silver, the particle size is in the range of 0.50-1.67 μ M. when the concentration of nano silver reaches 350 μ g / ml, it will show obvious city. In addition, the two groups of silver particles with relatively large particle size were in the range of 1.43-7.14 μ m and 1.74-45 μ M. under the same concentration of all experiments, the cultured cells grew well without obvious cytotoxicity.

Some scholars have shown that the cytotoxicity of nano silver is related to Ag +, and the accumulation of Ag + in the cells during the dissolution and release of nano silver may lead to cell apoptosis. But at the same time, some studies think that a small amount of Ag + will not react with the internal structure of cells when it circulates rapidly. Moreover, after the cells are treated with nano silver, the cell nucleus, mitochondria and other organelles interact with nano silver, which may even disrupt the normal function of organelles, thus further accelerating cell death. However, the sensitive target of cytotoxicity may also be mitochondria, and the loss of normal mitochondrial function is the beginning of cell apoptosis. Therefore, silver nanoparticles may damage the stem cells of mouse embryos, or damage the function of mitochondria, and then destroy the cells, so as to infer that silver nanoparticles have strong toxicity. Some scholars have carried out experimental research on the cytotoxicity of these two kinds of nano silver materials related to different particles. They found that these two kinds of nano silver materials can damage mouse embryonic liver cells, so as to change the shape of cells and produce shrinkage. Through this process, the function of mitochondria in cells can be significantly reduced, and the concentration of LDH in the culture medium can be greatly increased It is suggested that nano silver may damage cell membrane. At the same time, silver nanoparticles can induce oxidative stress and cytotoxicity. But at the same time, there are also other scholars' research shows that patients with chronic myeloid leukemia can be treated by nano silver materials, and affect the release of ROS in the cell membrane of patients with chronic myeloid leukemia, which leads to oxidative stress, and eventually leads to cell death. This experiment proves that nano silver particles can effectively inhibit chronic myeloid condition worsened.L929 cells exposed to nano silver environment will significantly enhance the gene level of metal binding protein family of ROS related products, and activate NF KB and JAK-STAT signaling pathways, which may lead to changes in L929 cells, or the cells show genotoxicity after treatment with nano silver.

The toxicity of silver nanoparticles in mammals. In recent years, there have been many studies on the cytotoxicity of nano silver in vitro, and the related biological distribution and toxicological research data of nano silver are also increasing. A large number of experimental studies in vivo have proved that nano silver can be absorbed through a variety of ways, including inhalation, oral and skin, so as to enter the body, and constantly flow in the body, and interact with different organs, thus causing damage to the main target organs including liver, lung and kidney. It is understood that some scholars have inhaled and dripped 15 nm silver particles into rats, and discussed and studied the distribution of silver particles in the lungs and even the whole body. It can be found that with the continuous increase of inhalation time, the deposition of particles in the lungs is constantly reduced, and the silver particles found in the blood and other organs. for example, the kidney deposition concentration of silver particles in female rats is higher than that in male rats. However, the mechanism of this gender difference is still uncertain, and the cause of this result is still under study. et al. Reported on the distribution and toxicity of nano silver implanted subcutaneously in rats. This experiment found that nano silver could migrate to the circulatory system and eventually flow to multiple target organs. In addition, it was also able to cause neuronal degeneration caused by the destruction of blood-brain barrier. In the study of inhalation toxicity in rats, no significant changes were found in the nasal cavity and lung, and no blood was found the biochemical indexes of fluid and blood changed greatly, and the specificity or histology also changed. the main toxic target organs were lung and liver. The decrease of tidal volume and volume per minute was the toxic reaction of lung. The inflammatory reaction was mainly caused by the lung, such

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as the infiltration of mixed inflammatory cells and chronic alveolar inflammation. In addition, there was dose-dependent increase in bile duct near the central vein of liver. After 30 days, the expression of inflammatory mediators and cytokines in the lung increased a lot, and the distribution of B cells increased continuously in the experiment.

3. MTT Test and LDH Test

The main content of MTT test is to evaluate the mitochondrial dysfunction caused by medical devices and extracts. MTT is a yellow water-soluble tetrazolium dye [9-10], which can be reduced by living cells to purple non water-soluble methionine.

3.1 MTT Test

1) Test purpose: in MTT test, it is very important to select the test reference material. In this test, AP was selected as the positive control of nano related materials, and the dosage and storage conditions of nano silver were observed. At the same time, the differences between the test conditions in the test and the main methods in ASTM standard of the United States were compared and analyzed; In the observation, PBS MTT solution was used for dilution and MTT solution was diluted by cell culture medium. In addition, glycine buffer was detected by adding or not adding DMSO after DMSO was dissolved. The stability and sensitivity of the experimental results were observed, and the appropriate detection wavelength was used.

2) Methods: in the experiment, the culture medium was collected to 85% confluence state, the condition of logarithmic long-term cells was observed, and the cell culture medium was diluted to 1 × 106 cells ·ML-2. In each well, 105 μ l of the above cell suspension was added, and 6 cells were seeded in each sample.it is because some nano related materials, such as silver nanoparticles, can interfere with the determination of absorbance to a certain extent. Therefore, in the last well of each column, the cell culture medium without cell suspension was used as the control substance for nanoparticle experiment. In the treatment group with cells, the background data of nano material group should be deducted. The seeded cells were cultured for 26 h at 38 ℃, 15% CO2 and more than 80% humidity, and the cells grew to 85%.In the 96 well plates taken out of the growth cells, the sample design was carried out in the corresponding holes, and the positive control solution (APAP), negative control solution (PE), and blank control solution (cell culture medium) and nano silver gel solution were added in the corresponding holes, and the culture was continued for 26 H.98 well plates were taken out from the incubator, and the liquid in the pores of Triton X-200 positive control group was removed, and then 2% Triton X-200 300 μ l was added and placed at room temperature for 20 min;800 g, centrifuged for 5 min, and then take 60 μ l liquid from each well and place it in another 98 pore plate. Pay attention to the transfer process, it is necessary to transfer according to the distribution of the original template samples, and the storage temperature is temporarily maintained at about 4 ℃, so as to prepare for LDH test.

MTT test: remove all liquid from the initial 98 plates.

Method a: 90 μ l PBS and 20 μ l MTT solution prepared with PBS were added into each well, incubated at 378 ℃ for 6 h, and then the liquid was discharged. Then, 200 μ l DMSO was added into each well, and the mixture was evenly mixed on an oscillator for 10 min, and then detected by enzyme-linked immunosorbent assay. In the process of experiment, we need to pay attention to the detection, scan the whole wavelength to determine the detection wavelength. Then continue to determine the absorbance value and calculate the relative proliferation rate according to the formula [11]:

$$RGR = A / B \times 100\% \quad (1)$$

Where: RGR is the relative proliferation rate, A is the average absorbance value of the test sample group; B is the average absorbance value of the blank control group.

Method B: 300 μ l of cell culture medium and 100 μ l of MTT solution prepared by culturing cells with Buha serum in each well were incubated at 37 ℃ for 6 h; 800 g was centrifuged for 5 min, and then the liquid in the well was aspirated, and then 300 μ l DMSO was added into each well and placed on the oscillator for 20 min;25 UL glycine buffer was added or not added into each well, and then the mixture was continuously mixed on the oscillator for 20 min. the detection method was acid standard

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analyzer, and then the detection wavelength was determined by full wavelength scanning, and then the absorbance value was determined, and the relative increment rate RGR was calculated according to the formula.

3) In different test methods: under the same APAP concentration, the absorbance values of different methods are also different. In the above experiments, method a used PBS to dilute the MTT solution, which needed to be incubated for 6 h after adding cells, but in method B, we used cell culture medium without serum to dilute the MTT solution, and the cells were incubated for 6 h after addition. It can be concluded from the experiment that the absorbance value of method B diluted with cell culture medium is much higher than that of method BT he method a of PBS dilution, especially in the low toxicity experiment of APAP, suggests that cells can keep their cell activity well in cell culture medium, so as to effectively absorb MTT solution, so as to ensure that succinate dehydrogenase can fully react with MTT related solutions. It can be observed in method B above that the absorbance value will be higher after the glycine buffer is added, and glycine buffer can increase the pH value to accelerate the dissolution of methyl in crystal, but for low concentration of APAP, it may promote crystal dissolution more obviously.

3.2 LDT Test

LDH involved in Lgh test is a kind of cytoplasmic enzyme, and the change of cell membrane permeability and membrane damage may lead to LDH leakage outside the cell. Therefore, LDH test can be used to test the integrity of cell membrane to make up for the deficiency of MTT test. As for the principle of LDT test, the LDT test principle is that the pyruvate formed by the oxidation of lactic acid by LDT; the converted from pyruvate and tetrazolium salt can be dissolved in water, and can be detected by microplate. The existence of serum in the cell culture medium may cause some interference to the detection results, which may be due to the presence of some proteins in the serum, which can be used as a catalyst to accelerate the formation of nail Zan crystal. Therefore, it is necessary to further explore the influence of different concentrations of serum on the experimental results.

1) Objective: To investigate the cell culture medium containing different concentrations of serum, such as 20%, 10%, 5%, which has a certain impact on the background of LDH test.

2) Test method: the cell culture test method and MTT test are the same. After the positive control solution is added, the culture can continue for 26 h. 98 well plates are taken out from the incubator to prepare as the pore liquid of Triton X-200 group. Then, 2% Triton X-200 containing 20%, 10% and 5% 300 μ L respectively is added. The cells are placed at room temperature for 20 min, and 800 g are centrifuged at the same time After 3 min, 100 μ l liquid was taken from each hole and transferred to another plate. In the transfer process, the samples were transferred according to the original template distribution. After the transfer was successful, 100 μ l of LDH reaction mixture was added into each well, and it was evenly mixed in the vortex mixer. The LDH was incubated at room temperature for 40 min, and then LDH was detected. in the detection wavelength, the full wavelength scanning should be carried out to determine the detection wavelength, and then continue to determine the absorbance value. The LDH release rate [12, 13] was calculated as follows:

$$LDH \quad leakage = (A - BC - B) \times 100\% \tag{2}$$

Where: A is the average absorption value of the sample group in the test, B is the average absorption value of the blank control group, and C is the average absorption value of the Triton X-200 control group [14-15].

3) Material characteristics: transmission electron microscopy and dynamic light scattering were used to characterize the size and distribution of nano silver gel. the cytotoxicity evaluation of nano silver gel products was carried out by using the optimized MTT test and LDH test.

4. Results Analysis

The first experiment in this paper is: passages of 50h-74h are in logarithmic growth period, and the number of cells adjusted after digestion is 200000 /ml, evenly inoculated into 24 orifice plates, each orifice plate. After the cells adhered to the wall, the original culture medium was discarded, and the nano silver powder and micron silver powder were sterilized and added to the cell culture medium. After contacting and culturing L929 cells for 26 hours, the morphology of cells was observed by inverted phase contrast microscope, and the cytotoxicity of cells was quantified by MTT colorimetry,

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and the relative value-added rate was calculated at the same time, the toxicity evaluation was carried out. According to the appeal experiment method, the experiment was repeated three times to improve the accuracy and reliability of the data.

There was no significant difference in RGR value between the experimental group and the control group after various concentrations of silver nanoparticles (see Figure 1). The RGR value was more than 4%, and the toxicity was grade 1-4. As shown in Figure 2, there was no significant difference in RGR values between the cells treated with different concentrations of nano silver in the experimental group and those in the control group. The toxicity was 0-2 grade ($P > 0.05$), $RGR > 85\%$.

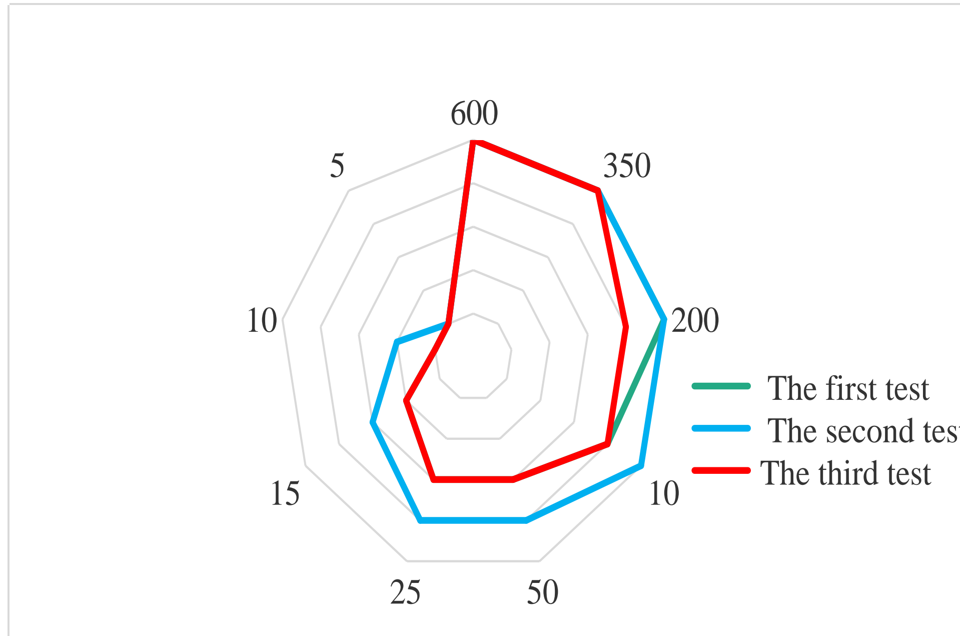

Figure 1: Results of MTT test of nano silver group

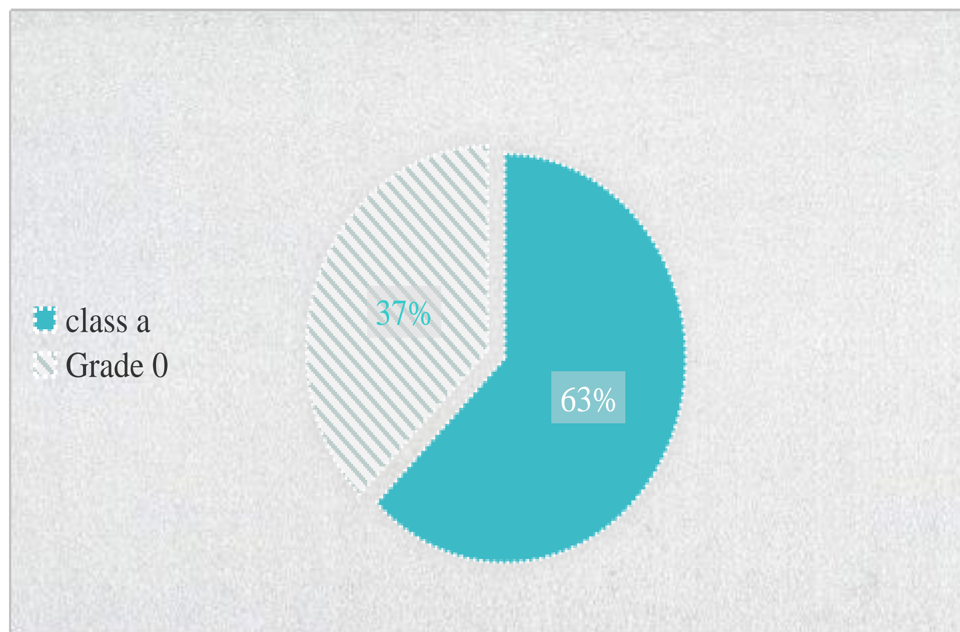

Figure 2: MTT results of micron silver group

By comparing the MTT test results of nano silver group with that of micron silver group, it can be concluded that the toxicity rating of nano silver is higher than that of micron silver. Therefore, this experiment has certain reference significance for us to study the cytotoxicity of nano silver products and its materials in vitro.

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In this paper, MTT method was used to compare the in vitro cytotoxicity of 18 kinds of nano silver medical products (as shown in Table 1), which were all registered test samples before clinical trial. according to the test results, the types of nano silver products have a certain impact on the cytotoxicity test in vitro. The cytotoxicity of different nano silver products is different in vitro. Some nano silver products have a cytotoxicity rating of up to a level. Relatively speaking, such nano silver products have higher biological safety, while some other nano silver products, such as nano silver antibacterial hydrogel and other products, have a cytotoxicity rating of up to four. Relatively speaking, the biological safety of such products is low, and in the process of application, cytotoxicity may occur in vitro, which is not conducive to nanoscale products. the use of rice silver products.

Table1. Relative proliferation rate and cytotoxicity of different silver nanoparticles in vitro

Product name	Relative value-added rate	Cytotoxicity rating
Positive control	8-14	4
Negative control	87-99	2
Anionic healing powder	7-9	4
Antibacterial dressing	6-8	4
Nano silver medical antibacterial dressing	6-7	4
Nano silver antibacterial application	37-39	2
Nano silver antibacterial hydrogel lotion	4-8	4
Nano silver antibacterial hydrogel	10-20	4
Nano silver antibacterial gel	9-19	4
Nano silver lady gel antibacterial device	3-5	3
Nano silver antibacterial hydrogel nano-silver Fu Yan Jing No. 1	10-24	4
Nanoscale silver gel	7-9	4
Nano silver antibacterial hydrogel nasal cavity rinse liquid	4-6	4
Nano silver antibacterial hydrogel spray	4-8	4
Nano silver external antibacterial spray	4-8	4
Nano silver antibacterial hydrogel - Biyan Jing	50-60	2
Nano silver antibacterial hydrogel - Acne net	48-60	1
Nano silver antibacterial hydrogel - Ke ringjing	54-62	2
Nano silver antibacterial hydrogel - hemorrhoid Jing	8-14	4
Nano silver prostate suppository	16-28	4

At the same time, MTT test was also used to test the cytotoxicity of nano silver materials in vitro. The results of MTT test showed that methylzan was dissolved by DMSO in routine detection, and the maximum peak value of APAP 20 mmol ·L - 2 was at 620 ～After methylzan was dissolved by DMSO and added with appropriate amount of glycine buffer, methylzan could be dissolved more fully. The maximum value of positive control was 640 nm-Similarly, in the PE group, the maximum peak value of DMSO was 620-670nm, and the lowest value was about 780nm. After methylzan was completely dissolved by DMSO solution, the maximum peak value was at 630 nm-From the results of the appeal experiment, it can be concluded that the dual wavelength should be set at 640-670 / 680 nm when determining the absorbance value of MTT test method. The test wavelength is set at 570nm in the international standard cytotoxicity standard, and the reference wavelength is 650nm, while the test wavelength is 570nm and the reference wavelength is 680nm in the American ASTM cytotoxicity test standard. In order to improve the accuracy and reliability of the experiment, the experiment was repeated three times, as shown in Figure 3. the reference standards of different studies, we can find that the reference wavelengths are different. Therefore, the optimal wavelength should be selected according to the experimental system. The error of experiment can be reduced by choosing a better wavelength.

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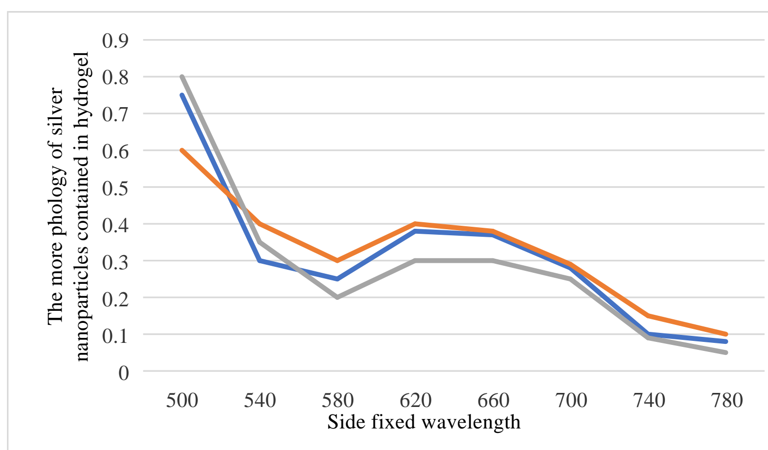

Figure 3: A Pap (positive control) treatment group 400-700 nm wavelength scanning

This paper also adopts the method of LDH test. The experimental results show that when the concentration of APAP is 35 mmol ·L - 1, the maximum peak value of LDH is about 590 nm, and the lowest value is about 780 nm. According to the experimental results, the maximum absorbance peak of 2% Triton X-200 LDH is at 590 nm. Similarly, in order to improve the reliability and accuracy of the experimental data, the same experiment was conducted three times, as shown in Figure 4. By observing the fixed wavelength of the three experiments, we can conclude that the fixed wavelength is not completely the same under different conditions. therefore, through comparison, it is convenient for us to choose a better fixed wavelength and reduce the error of the experiment.

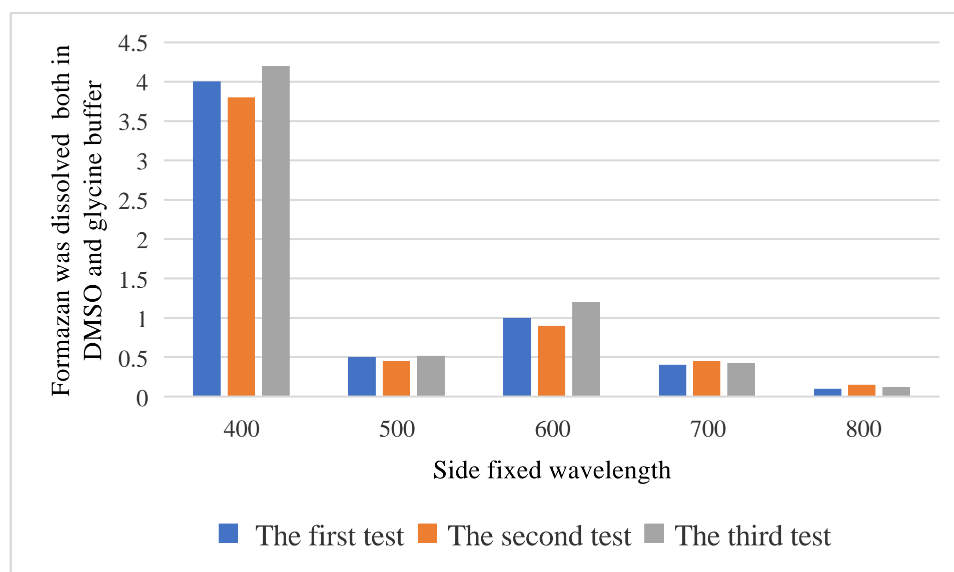

Figure 4: ldh300-700 wavelength scanning map

In this paper, we combine the MTT experiment and LDH experiment, choose the best wavelength under the contrast of different experiments to increase the accuracy of the experiment. Under the above optimized experimental conditions, we can reduce the interference of the serum to the absorbance and evaluate the cytotoxicity of the nano silver gel products. According to the above experimental process and results, we can deduce the cytotoxicity of nano silver gel. the mechanism is mainly due to the function of mitochondria. therefore, we infer that the in vitro cells of nano silver medical devices have a certain toxic mechanism.

5. Conclusions

Nano silver has strong bactericidal and antibacterial properties, and the bactericidal ability of this kind of nano silver is hundreds of times that of ordinary silver. The reason for this situation is that nano silver can release silver ions slowly and for a long time in cells, and then continue to play the

antibacterial effect of nano silver. Therefore, it is widely used in a variety of medical products, but at the same time, we also need to evaluate its biological safety. Some literatures have indicated that nano silver materials are safe and low toxicity, but others indicate that nano silver has certain toxicity rating. This paper lists and discusses the related nano silver and its material products, calculates the nano silver and its material products through the relative value-added rate. Through the analysis of the characteristics of nano silver, the analysis and thinking of in vitro cytotoxicity, the use of MTT test and LDH experiment to test the toxic cells in mammalian (rat as the experimental object), we can infer the nano silver and its nano silver materials However, different nano silver materials have different toxicity ratings. Moreover, the toxicity rating of nano silver is related to its dose and has potential toxicity. Therefore, when using nano silver and nano silver medical devices, we should pay attention to the toxicity rating of nano silver materials to ensure the biological safety of nano silver and nano silver materials.

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