British Journal of Healthcare and Medical Research - Vol. 9, No. 2
Publication Date: April, 25, 2022
DOI:10.14738/jbemi.92.11851.
Yehia, H. M. A., & Said, S. M. (2022). The Effectiveness of Silica Nanocomposites in the Treatment of Breast and Liver Cancer Through a Natural Physical Field. British Journal of Healthcare and Medical Research, 9(2). 11-21.

The Effectiveness of Silica Nanocomposites in the Treatment of Breast and Liver Cancer Through a Natural Physical Field

Hesham Mohamed Abdal-Salam Yehia
Department of Biotechnology, HST Company, Cairo, Egypt

Said Mahmoud Said
Department of Biotechnology, HST Company, Cairo, Egypt

ABSTRACT

Cancer survival rates, or survival statistics, show you the percentage of people who survive a specific type of cancer for a specific period of time. Cancer statistics use a five-year survival rate. Survival rates are usually given as percentages. For example, the five-year survival rate for breast or liver cancer is 77 percent. This means that, of all people diagnosed with breast or liver cancer, 77 out of 100 live to five years after being diagnosed with cancer. In contrast, 23 out of every 100 people die within five years of being diagnosed with breast or liver cancer. Despite the development of diagnostic and treatment methods, there is a significant meaning with chemotherapy, and a low cure rate. The current research aims to reveal the effectiveness of the impact of heat-treated silica nanoparticles with the addition of titanium dioxide on breast and liver cancer cells. The tests were carried out at the National Cancer Institute in the Arab Republic of Egypt, and the results showed a significant improvement in the rate of infection, as the percentage of tumors decreased by about 71%, which contributes significantly to the development of the patient's treatment condition.

Keywords: Silica nanocomposites; Cancer; Liver cancer; Breast cancer; Titanium dioxide.

INTRODUCTION

Cancer is a general term that includes a wide range of diseases that can affect any part of the body. Other terms used are malignant tumors and neoplasms. A hallmark of cancer is the rapid generation of abnormal cells that grow outside their usual boundaries and can then invade neighboring parts of the body and spread to other parts of the body [1]. The last operation is called metastasis, and metastases are the most important cause of death from cancer. Each person's cancer may be caused by a number of distinct factors. Despite advancements in detection and therapy, scientists still have a lot to learn about what causes cells to become malignant and why some cancer patients perform better than others. Furthermore, cancer is an ever-changing target. Throughout the course of the disease, cancer cells continue to transform and evolve. This may lead the cancer cells to become resistant to the chemotherapy medications or radiation therapies that the patient was first administered [2].

There are currently three main ways to treat cancerous diseases with drugs: immunotherapy, chemotherapy, and targeted therapy [3]. While chemotherapy targets both the healthy cell and the cancer cell, targeted therapy attacks the cancer cells alone and does not harm healthy cells.

That's why the negative side effects of this latter treatment are different from those of chemotherapy. In contrast to both, immunotherapy does not directly target the cancerous cell, but rather targets the patient's immune system and strengthens this system in a way that makes it able to recognize the cancer cell as a foreign aggressor, attacking and destroying it. Anticancer T-cell therapies, which involve removing and modifying immune cells and returning them to a patient's blood to search for and destroy cancer cells, are the latest model in advanced cancer therapies. The most widely used type, CAR-T, is customized for each patient, but it targets a limited number of cancers and has not been successful in treating solid tumors that make up the majority of cancers. Conventional T cells scan the surface of other cells to find what appears to be abnormal to kill cancer cells, ignoring cells that contain only "normal" proteins, and the scanning recognizes small fragments of cellular proteins attached to cell surface molecules called human leukocyte antigen (HLA), which allows killer T cells to see what's going on inside the cells by scanning their surface. as illustrated in figure 1.

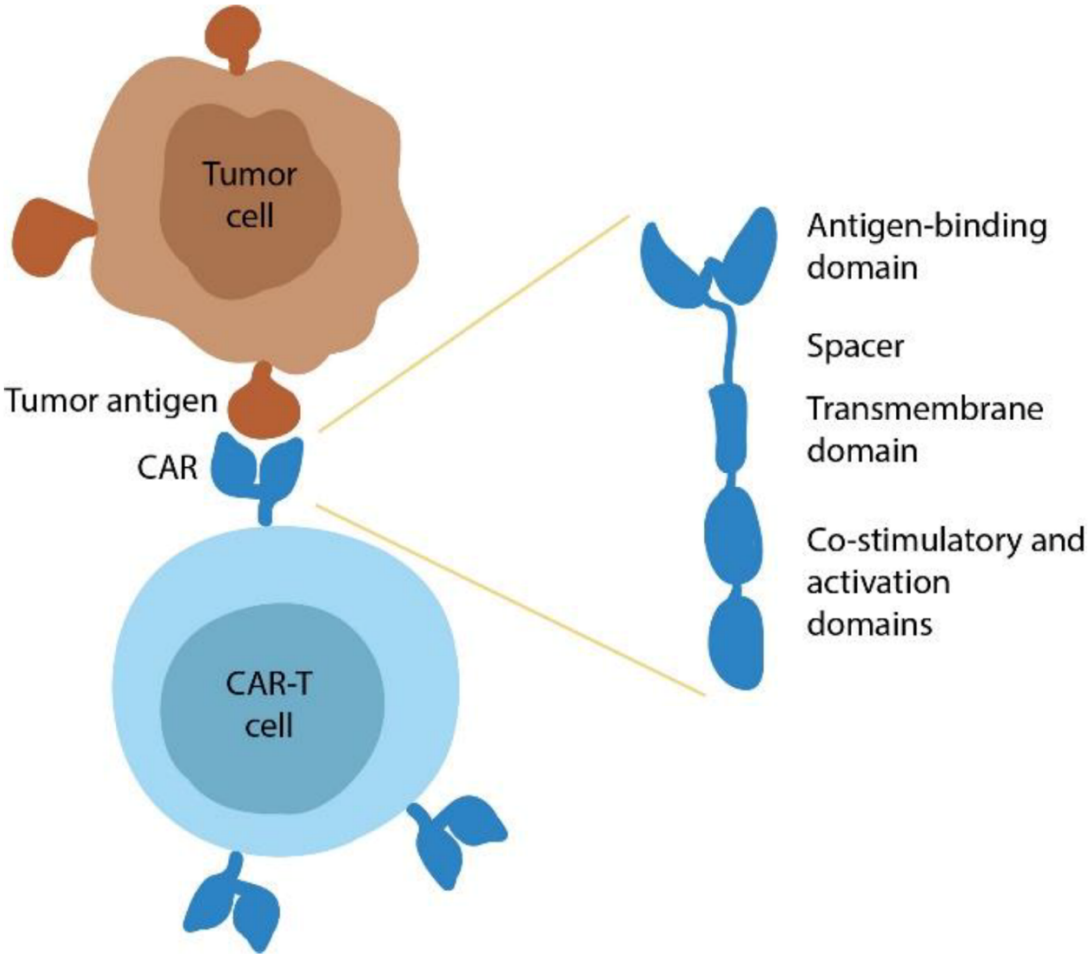

Figure1. Schematic representation of a chimeric antigen receptor (CAR) T-cell and its interaction with the tumor cell. The CAR contains two primary functional components: an antigen-binding domain (derived from variable region of the monoclonal antibody to an antigen) and an intracellular activation domain (derived from immunoreceptor tyrosine-based activation motifs (ITAMs) of CD3ζ and often also including one or more co-stimulatory domains, e.g., CD28, 4-1BB) for signal transduction. Antigen-binding and transmembrane domains are connected via a flexible spacer that partially contributes to the efficiency of target recognition [4,5]

The new type recognizes a molecule called MR1 found on the surface of a wide range of cancer cells and normal cells and is able to distinguish between healthy and cancerous cells, killing only the latter, making it a target for more immunotherapies. Researchers have discovered that this type of T-cell found in the blood can recognize and destroy many types of cancer cells and attack many types of cancer. In order to acquire the receptor capable of detecting cancer, the modified cells would then be cultured in copious numbers in the laboratory before being reinjected into the patient. It's the same technique used in Chimeric Receptor T-cell Therapy (CAR-T), a cancer immunotherapy that involves genetic modification of T cells to activate the immune system to recognize and destroy specific cancers [6].

Despite the positive results of the above-mentioned methods, but more than 4 years after their diagnosis of cancer, 14% of survivors were dissatisfied with the persistent and long-term side effects of cancer treatment, according to a recent study. Moreover, despite medical progress and an increase in the number of cancer survivors in recent decades, the side effects of anticancer chemotherapy continue to be a major source of concern for both patients and clinicians. Chemotherapy can have minor to severe side effects, depending on the type and quantity of treatment. These side effects can have a substantial impact on the quality of life of cancer patients. Chemotherapy often destroys rapidly dividing cells. Different parts of the body where normal healthy cells divide frequently are more likely to be affected by chemotherapy. The hair, mouth, skin, intestines, and bone marrow are usually affected by chemotherapy drugs [7].

With the extensive use of chemotherapies in various groups of cancer patients, the toxicities associated with such well-established chemotherapies as platinum-based chemotherapies continue to increase [8]. Thus, despite all the medical advances, most cancer survivors end up dealing with the long-term side effects of these chemotherapy treatments, even after several years of treatment. According to the National Children's Cancer Foundation, it is estimated that more than 95% of childhood cancer survivors will have a significant health problem by the time they reach the age of 45, which may be a result of their early cancer treatment. In light of the foregoing, it is clear that there is an urgent and necessarily need to develop a new method for treating cancer, or at least that helps speed recovery without experiencing the aforementioned side effects, so the main objective of the current research was to verify the effectiveness of heat-treated silica nanoparticles with the addition of titanium. Dioxide in reducing the growth of cancer cells and trying to eliminate them through a natural physical field.

LITERATURE REVIEW

With advanced treatment of cancer with chemotherapy or radiotherapy, although survival rates for solid tumors have improved, the risk of secondary cancer arising from treatment (a long-term side effect of chemotherapy) has also increased [9]. Various studies show that excessive chemotherapy increases the risk of developing a second cancer after you have been cancer-free for some time. A study by the National Cancer Institute closely analyzed data on more than 700,000 patients with solid carcinomas. These patients initially underwent chemotherapy from 2000 to 2013 and survived for at least 1 year after diagnosis. Their ages ranged from 1 to 20 years. The researchers found that the risk of developing myelodysplastic syndromes (tMDS) and acute myeloid leukemia (AML) "increased from 84-fold to more than 1.5-fold for 10 of the 22 solid cancers examined [10]."

URL: http://dx.doi.org/10.14738/jbemi.92.11851

Another study was recently conducted by researchers from the University of Minnesota School of Medicine on more than 20,000 childhood cancer survivors. These cancer survivors were first diagnosed when they were under 21 years of age, between 1970-1999 and were treated with chemotherapy/radiotherapy or chemotherapy along with radiotherapy. The study revealed that survivors treated with chemotherapy alone, especially those treated with higher cumulative doses of platinum and alkylating agents, had a 2.8 times increased risk of subsequent malignancy compared to the general population [11].

BREAST CANCER

Breast cancer is second only to skin cancer in terms of being the most common type of cancer among women in the world. Breast cancer can affect both men and women, but it is more common in women. Breast cancer is a disease that specifically affects women, but it may also affect men, albeit in a much smaller percentage, as doctors have recently made great achievements in the fields of early detection and treatment of breast cancer to reduce the number of deaths from the disease. Previously, detection of breast cancer meant removal of the entire breast. Today, these operations are performed only in rare cases, as there is a wide range of treatments available as shown in figure 2.

Tumor grading Cancerous

Tumors are classified on a scale of 0-4IV (four), as follows:

Grade 0

Also called non-invasive or local breast cancer, although these tumors do not have the ability to invade healthy tissue in the breast or spread to other organs in the body, it is important to eradicate and remove them, because they may turn into invasive tumors in the future.

Grades 1 - 4

They are invasive tumors that have the ability to invade healthy tissue in the breast and then spread to other organs in the body. Cancerous tumors in the first degree are small and local, and the chances of complete recovery from it are very great, but the higher the degree, the less chances of recovery.

Class 4

It is a cancerous tumor that has spread outside the breast tissue and spread to other parts of the body, such as: the lungs, bones, and liver, and although the cancer cannot be cured at this stage, there is a possibility that it will respond well to a variety of treatments that may cause shrinkage and diminishment. The tumor was kept under control for a long period of time.

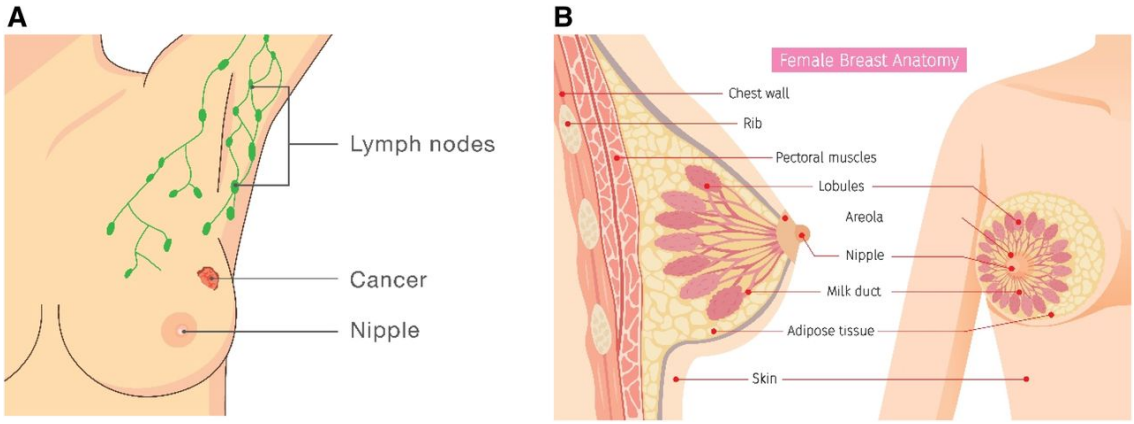

Figure 2. Illustrations of breast anatomy and lymphatic system. (A) Frontal view showing lymph nodes, cancer, and nipple. (B) Sagittal and frontal views showing additional anatomy. Critical structures when dealing with breast cancer are milk ducts, lobules, and nipple [12]

Thus, Breast cancer is a heterogeneous group of diseases, and it is known that it begins locally in the breast, and gradually spreads to the axillary lymph nodes to become invasive, and then spreads to other organs. Many factors determine the risk factors that increase the likelihood of developing breast cancer, its symptoms and signs, methods of combating it, diagnosis, staging, and treatment options.

LIVER CANCER

The liver is responsible for the continuous filtering of blood flowing in the body. It also converts nutrients and drugs that are absorbed in the digestive system into ready-to-use chemicals. The liver has other important functions, including removing toxins and other chemicals from the blood and transforming them into excretions as illustrated in figure 3. It is easy for cancer cells to reach the liver, as all the blood flowing through the body passes through it. Thus, it is possible for the liver to develop primary cancer in which it forms itself, or cancer that forms in other places in the body and then metastasizes to the liver. In most cases, liver cancer is secondary or metastasis, meaning that the source of the cancerous tumor It is found elsewhere in the body.

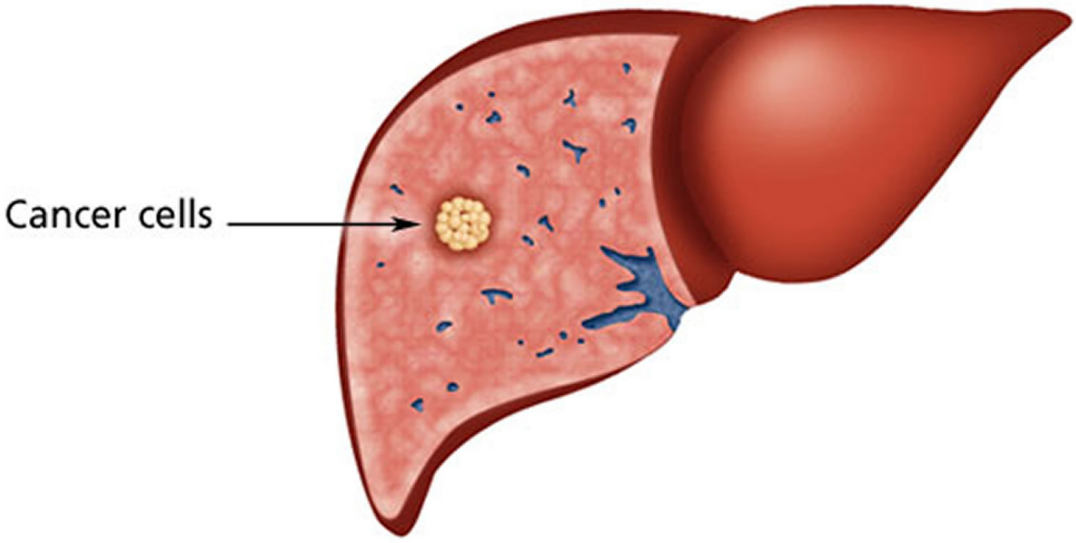

Figure 3. Liver cancer

URL: http://dx.doi.org/10.14738/jbemi.92.11851

Chemotherapy drugs can be used to temporarily shrink the tumor and prolong life, but they do not cure the cancer. Chemotherapy drugs can be injected into the main liver artery (hepatic artery), in order to deliver a large number of drugs directly to the cancer cells in the liver. Using this method reduces the exposure of the rest of the body to the drugs, so the side effects are less and less.

On the other hand, there is another type of chemotherapy to treat liver cancer known as hepatic artery thromboembolic chemotherapy, in which chemotherapy is mixed with another substance to completely block the artery. Tumor for chemotherapy directly. In the event of resorting to such a therapeutic procedure, blood continues to flow to the liver through the hepatic portal vein.

MATERIALS AND METHODS

In the context of the current research quest to verify the effectiveness of silica nanoparticles for the treatment of breast and liver cancer, the following materials and research methods have been used.

Human tumor cell lines

The human carcinoma (NCI) cell lines used in this study were obtained from the American Culture Collection (ATCC, MN, USA). Tumor cell lines were maintained at the National Cancer Institute, Cairo, Egypt, by serial subculture.

DRUG

Samples were prepared by dissolving 1:1 Stock solution and stored at -20°C in dimethylsulfoxide (DMSO). Different concentrations of the drug were used (Range of concentration used by µg/ml).

Determination of potential cytotoxicity of drug on human cancer cell line

Reagents and buffers

1. Glacial acetic acid: 1 % was used for dissolving the unbound SRB dye.
2. Sulphorhodamine-B (SRB): 0.4 % concentration was dissolved in 1 % acetic acid was used as a protein dye.
3. Trichloroacetic acid (TCA): 50 % stock solution was prepared, 10 % solution was used for protein precipitation.
4. Tris base, 10 mM, (pH 10.5) was used for SRB dye solubilization. It was prepared by dissolving 121.1 gm of tris base in 1000 ml distilled water and pH was adjusted by 2 M HCl.

Principle

The cytotoxicity was carried out using Sulphorhodamine-B (SRB) assay following the method reported by ***Skehan*., 1990**.

Sulforhodamine B colorimetric assay is used for cytotoxicity screening. Nat. Protoc. 2006:1, 1112-1116. SRB is a bright pink aminoxanthrene dye with two sulphonic groups. It is a protein stain that binds to the amino groups of intracellular proteins under mildly acidic conditions to provide a sensitive index of cellular protein content.

Procedure

1. Cells were seeded in 96-well microtiter plates at initial concentration of $4x10^3$ cell/well in a 200 µl fresh medium and left for 24 hours to attach to the plates.
2. Different concentrations (used concentrations) µg/ml of drug was added.
3. For each drug concentration, 3 wells were used. The plates were incubated for 48 hours.
4. The cells were fixed with 10 µl cold trichloroacetic acid 10% final concentration for 1 hour at 4 ^{0}C.
5. The plates were washed with distilled water using (automatic washer Tecan, Germany) and stained with 50 µl 0.2 % SRB dissolved in 1 % acetic acid for 30 minutes in dark at room temperature.
6. The plates were washed with 1 % acetic acid and air-dried.
7. The dye was solubilized with 200 µl/well of 10M tris base (pH 10.5) and optical density (O.D.) of each well was measured spectrophotometrically at 570 nm with an ELISA microplate reader (Sunrise Tecan reader, Germany). The mean background absorbance was automatically subtracted and means values of each drug concentration was calculated.

Calculation

The percentage of cell survival was calculated as follows:
Surviving fraction = O.D. (treated cells)/ O.D. (control cells).

The IC50 values (the concentrations of drug required to produce 50% inhibition of cell growth) were also calculated using prism version 5 [13].

RESULTS AND DISCUSSION

We are now reviewing the results of the experiment through the results of the central laboratories at the National Cancer Institute in the Arab Republic of Egypt.

Breast Cancer

Two different forms of silica were used, the first in the form of a gel, and the second in the form of a solid. Moreover, the different concentration of samples gel showed sharply decrease in LC50 comparison to the other concentration of solid's samples against cancer cells lines, MCF7 and MDA-MB-231 (fig 4and 5). The best results were recorded in MCF7-1 cell line (187 µg/ml); this was appeared clearly in the value e of LC50.

URL: http://dx.doi.org/10.14738/jbemi.92.11851

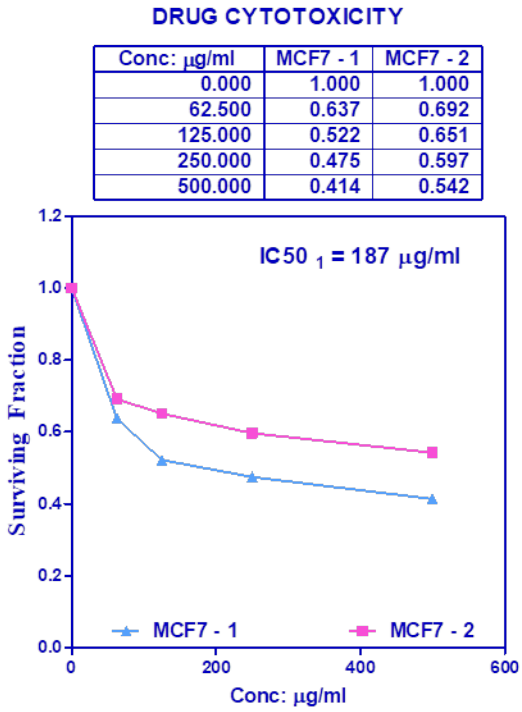

Figure 4: The effect of the difference between sodium silicate gel and sodium silicate solids on the survival of part of the breast

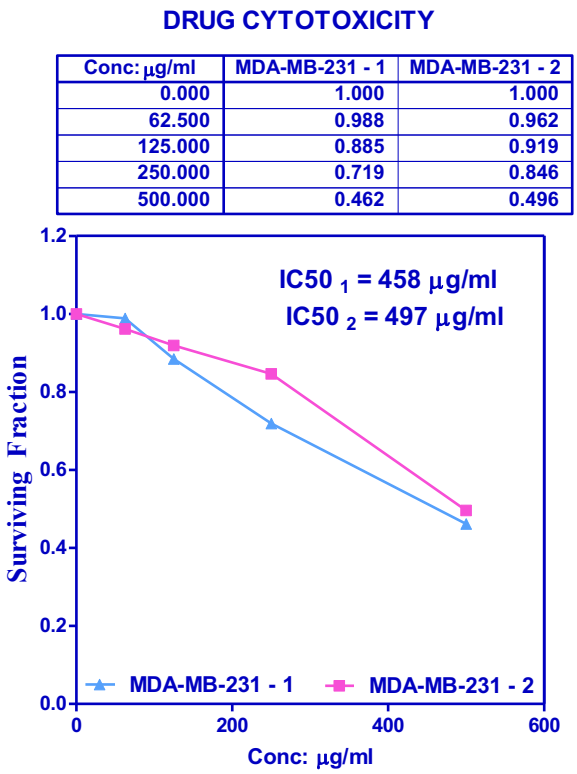

Figure 5: The effect of the difference between sodium silicate gel and sodium silicate solids on the survival of part of the breast

These results come in a related context with what a recent study - published in Cell in late October - revealed that researchers from Mount Sinai Hospital and College of Medicine in New York State, USA, were able to devise a new type of cancer immunotherapy based on training the innate immune system and helping it to Elimination of cancer cells, through the use of nanomaterials, bioengineered, and made of natural molecules combined with other therapeutic materials [14].

Liver Cancer

Moreover, this study to determine the antiproliferative effects of sodium silicate nanoparticles on hepatocellular carcinoma, HepG2, was the IC value of the gel sample towards HepG2 which scored 228 µg/ml better than the solid sample which scored 418 µg/ml.

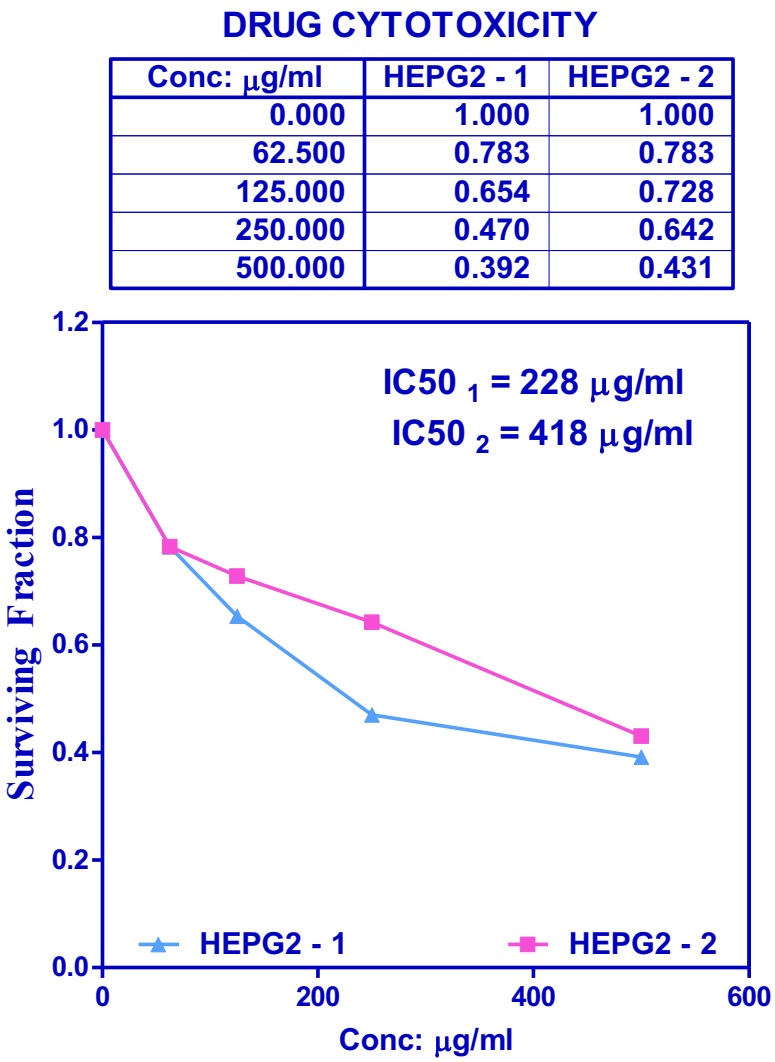

Figure: The effect of the difference between sodium silicate gel and sodium silicate solids on the survival of part of the liver.

Thus, we recommend that nanoparticles extracted from silica be relied upon for the treatment of liver circulatory system, as this type of cancer usually appears after a disease such as infection with hepatitis B and C viruses, and the presence of high amounts of iron or chronic hepatitis associated with obesity. It has increased in France. Each year, nine thousand new cases are reported, and six thousand seven hundred people die. One of the rates among cancer types is that this type of cancer is called "silent" because symptoms do not appear until at an advanced stage of the disease. Diagnosis is often delayed, and in seventy-five or even a hundred of cases, the tumor is in an advanced stage. Sometimes the sponsorship is a palliative, and the probability of surviving for 5 years remains estimated at ten, or even a hundred.

CONCLUSION

The percentage of persons who survive a given type of cancer for a specific period of time is shown in cancer survival rates, also known as survival statistics. The five-year survival rate is used in cancer statistics. In most cases, survival rates are expressed as percentages. Breast and

URL: http://dx.doi.org/10.14738/jbemi.92.11851

liver cancer, for example, have a five-year survival rate of 77 percent. This means that 77 out of 100 persons diagnosed with breast or liver cancer live for five years after their diagnosis. In comparison, 23 out of every 100 persons diagnosed with breast or liver cancer die within five years. Despite advancements in diagnosis and therapeutic methods, chemotherapy has a significant meaning and a low cure rate. The goal of this study is to determine the effectiveness of heat-treated silica nanoparticles with titanium dioxide added on breast and liver cancer cells. The tests were conducted at the National Cancer Institute in the Arab Republic of Egypt, and the results revealed a significant reduction in the rate of infection, with the percentage of tumours decreasing by about 71 percent, contributing significantly to the patient's treatment condition development. We believe that a combination of silica compounds could prove to be an effective new weapon against several forms of advanced cancer, and results from other combination drug trials have previously indicated similar benefits for patients with chronically ill kidney, skin, and bowel cancer.

References

Strongman, H., Gadd, S., Matthews, A., Mansfield, K. E., Stanway, S., Lyon, A. R., ... & Bhaskaran, K. (2019). Medium and long-term risks of specific cardiovascular diseases in survivors of 20 adult cancers: a population-based cohort study using multiple linked UK electronic health records databases. *The Lancet*, *394*(10203), 1041-1054.

Atashzar, M. R., Baharlou, R., Karami, J., Abdollahi, H., Rezaei, R., Pourramezan, F., & Zoljalali Moghaddam, S. H. (2020). Cancer stem cells: A review from origin to therapeutic implications. *Journal of cellular physiology*, *235*(2), 790-803.

Tennant, D. A., Durán, R. V., & Gottlieb, E. (2010). Targeting metabolic transformation for cancer therapy. *Nature reviews cancer*, *10*(4), 267-277.

Hudecek, M.; Sommermeyer, D.; Kosasih, P.L.; Silva-Benedict, A.; Liu, L.; Rader, C.; Jensen, M.C.; Riddell, S.R. The nonsignaling extracellular spacer domain of chimeric antigen receptors is decisive for in vivo antitumor activity. Cancer Immunol. Res. 2015, 3, 125–135.

Watanabe, N.; Bajgain, P.; Sukumaran, S.; Ansari, S.; Heslop, H.E.; Rooney, C.M.; Brenner, M.K.; Leen, A.M.; Vera, J.F. Fine-tuning the CAR spacer improves T-cell potency. Oncoimmunology 2016, 5, e1253656.

Crowther, M. D., & Sewell, A. K. (2021). The burgeoning role of MR1-restricted T-cells in infection, cancer and autoimmune disease. *Current Opinion in Immunology*, *69*, 10-17.

Partridge, A. H., Burstein, H. J., & Winer, E. P. (2001). Side effects of chemotherapy and combined chemohormonal therapy in women with early-stage breast cancer. *JNCI Monographs*, *2001*(30), 135-142.

Nurgali, K., Jagoe, R. T., & Abalo, R. (2018). Adverse effects of cancer chemotherapy: Anything new to improve tolerance and reduce sequelae?. *Frontiers in pharmacology*, *9*, 245.

Chin, V., Nagrial, A., Sjoquist, K., O'Connor, C. A., Chantrill, L., Biankin, A. V., ... & Yip, D. (2018). Chemotherapy and radiotherapy for advanced pancreatic cancer. *Cochrane Database of Systematic Reviews*, (3).

Morton, L. M., Dores, G. M., Schonfeld, S. J., Linet, M. S., Sigel, B. S., Lam, C. J., ... & Curtis, R. E. (2019). Association of chemotherapy for solid tumors with development of therapy-related myelodysplastic syndrome or acute myeloid leukemia in the modern era. *JAMA oncology*, *5*(3), 318-325.

Turcotte, L. M., Neglia, J. P., Reulen, R. C., Ronckers, C. M., Van Leeuwen, F. E., Morton, L. M., ... & Henderson, T. O. (2018). Risk, risk factors, and surveillance of subsequent malignant neoplasms in survivors of childhood cancer: a review. Journal of Clinical Oncology, 36(21), 2145.

Grabher, B. J. (2020). Breast cancer: evaluating tumor estrogen receptor status with molecular imaging to increase response to therapy and improve patient outcomes. *Journal of Nuclear Medicine Technology*, *48*(3), 191-201.

Skehan, P., Storeng, R., Scudiero, D., Monks, A., McMahon, J., Vistica, D., ... & Boyd, M. R. (1990). New colorimetric cytotoxicity assay for anticancer-drug screening. *JNCI: Journal of the National Cancer Institute*, *82*(13), 1107-1112.

Priem, B., van Leent, M. M., Teunissen, A. J., Sofias, A. M., Mourits, V. P., Willemsen, L., ... & Mulder, W. J. (2020). Trained immunity-promoting nanobiologic therapy suppresses tumor growth and potentiates checkpoint inhibition. *Cell*, *183*(3), 786-801.

URL: http://dx.doi.org/10.14738/jbemi.92.11851