Laser Light Scattering as a Tool in Cancer Treatment Research

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Laser light scattering has been used to characterize nanoparticles for over 50 years. This makes it a suitable technology to characterize silver nanoparticles. Silver has a long history of usage as an antibacterial agent and has recently shown promise in the treatment of cancer. Studies of these nanoparticles are on the rise with their newly discovered potential.

Background

Cancer is one of the leading causes of death worldwide and the number of cancer cases is projected to rise to 23.6 million cases per year by 2030.[1] Current cancer therapies include radio- and chemotherapy. These can be effective treatments but they are expensive and harsh on healthy cells. Some cancers even become resistant to these therapies. The location of some cancers, such as intracranial tumors, can make it nearly impossible to successfully surgically remove an entire tumor.[2] These limitations inspire researchers to discover different ways to effectively treat this disease. Ideally, finding out how to target only the cancerous cells, not healthy cells, and successfully deliver a drug would revolutionize how cancer is treated.

There are certain properties and characteristics that seem to affect the behavior of silver nanoparticles and drug delivery systems. Two of these properties are size and charge; the study of these properties allows researchers to determine proper coating of drugs, proper delivery, aggregation, and tumor growth, to name a few. With laser light scattering technology, size and zeta potential can be determined. That is why the following researchers chose Brookhaven Instruments' laser light scattering instrumentation to perform their studies and further our progress in cancer research.

[1] *Cancer Statistics* **2018**
[2] *Nanoscale* **2013**, *5*, 11829-11836

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Study 1

Jiangsu Key Laboratory for Biomaterials and Devices, Institute of Neurobiology, Jiangsu Key Laboratory of Molecular and Functional Imaging, and Tumor center of Zhongda Hospital at Southeast University, Nanjing, China[3]

Malignant gliomas are the most common primary intracranial tumors. The nature of these tumors makes it nearly impossible to completely remove them surgically. In addition, they have shown resistance to therapies such as radio- and chemotherapy. With a median overall patient survival rate of less than 15 months, the search for more effective treatments of this cancer is ongoing.

In the past, gold nanoparticles showed promise of enhancing doses of radiation, but they had little effect on glioma cells. It is theorized that their efficacy depends on their coating, and this phenomenon has been observed for other nanoparticles. Previous studies have shown that silver nanoparticles have potential for cancer treatment. As such, these researchers synthesized their own nanoparticles and used laser light scattering to help investigate how coating the silver nanoparticles affected their behavior in conjunction with radiation. First, the silver nanoparticles had to be synthesized and coated with polyvinylpyrrolidone (PVP). The Brookhaven ZetaPlus DLS instrument allowed them to measure the size and polydispersity of their particles to show that they successfully synthesized uncoated and coated nanoparticles with a monodisperse size distribution around 20 nm. This size range was important to achieve because the nanoparticles have to be small enough to permeate the tumor.

The ability to characterize the silver nanoparticles with Brookhaven Instruments' Particle Size analyzer allowed the researchers to conduct further experimentation. Using their coated and uncoated nanoparticles to treat gliomas in rats, they observed that both were equally toxic to cancer cells. This suggests that the silver nanoparticles themselves are very active in treating cancer cells, regardless of their packaging. They also observed that when they combined silver nanoparticle treatment with radiation treatment, the tumors decreased in size and survival rates increased, dramatically. This study was able to show that these nanoparticles have the clinical potential to improve the outcome of traditional glioma radiotherapy.

[3] *NanoScale*, **2013**, *5*, 11829-11836

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Study 2

City University of New York (CUNY), Department of Biochemistry, Ph.D. Dissertation[4]

The ability to deliver a variety of drugs to a tumor or source of infection without losing the drug in a different part of the body is the idea behind sol-gel based nanoparticles, or nanogels. The sol-gel process produces nanogels which could be used as drug carriers.

First, this researcher studied two different types of sol-gel synthetic processes to determine which methods had the highest yield, greatest stability, and least aggregation of the nanogels. To characterize these properties, the researcher performed DLS and Zeta Potential analyses with a Brookhaven Instruments 90Plus and a Brookhaven Instruments ZetaPlus, respectively. DLS revealed that each synthetic process produced different sized nanogels, while zeta potential analysis revealed that each synthetic process resulted in charge differences, as seen in **Table 1.**

Method	Size (nm)	Charge (mV)
Lyophilization	80 to 300, multiple populations	-30
Polylysine	300 to 500, multiple populations	-8

Table 1: Size and charge data for two synthetic methods for nanogels

Based on the size and charge data, the researcher continued to study the nanogels synthesized by the lyophilization method. First, the researcher tested whether suspending these nanogels in different concentrations of buffer solutions affected their size.

Table 2 shows slight size differences with different concentrations of the buffer. This information allowed the researcher to conclude that there was not a dramatic change in size based on the concentration of the buffer used to suspend the nanogels.

Phosphate Buffer Concentration (mM)	Effective Diameter (nm)
3	143
10	138
30	207
100	240
200	210

Table 2: Particle size of nanogels based on buffer concentration

[4] *Academic Works,* **2014**

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Next, the researcher studied whether adding molecules inside of the nanogel would change its surface charge. After loading the nanogels with PEG or a protein during the gelation step of the synthetic processes, zeta potential data were collected and showed that the addition of these molecules had no effect on the charge of the nanogels. This indicates that molecules inside of the nanogel matrix do not contribute to the nanogel colloidal properties.

Then, the researcher tried to limit aggregation by adding surfactant, PEG-400, to the suspensions after the nanogels were synthesized. The DLS results in **Table 3** show that there is a significant change in the effective diameter with the addition of PEG-400, suggesting its addition decreased aggregation.

[PEG-400] (%v/v)	Effective diameter of nanogels (nm)
0	800
1.25	380
2.5	500
3.75	450
5	390

Table 3: Particle size based on surfactant addition

The addition of surfactant also affected the zeta potential of the nanogels. **Table 4** suggests that the addition of PEG-400 increased the stability of the nanogels, which supports the decrease in aggregation due to an increase of electrostatic repulsion.

[PEG-400] (%v/v)	Zeta potential of nanogels (nm)
0	-8
0.25	-16
0.5	-13
0.75	-19
1	-27

Table 4: Zeta potential based on surfactant addition

After collecting all of this characterization information about the nanogels, the researcher was able to study how inserting silver nanoparticles into the nanogels would affect their colloidal properties.

As seen in **Table 5**, encapsulating the silver nanoparticles in the nanogels did not greatly affect the size or charge of the nanogels.

Sample	Effective Diameter (nm)	Zeta Potential (mV)
Silver nanoparticles	50	-50
Nanogels	360	-30
Silver nanoparticles encapsulated in nanogels	370	-30

Table 5: Size and charge analysis of nanogels, silver nanoparticles, and encapsulation

With the help of laser light scattering analyses, the researcher was able to show that encapsulating silver nanoparticles inside of nanogels is a promising drug delivery method. This method could provide a different way to treat diseases, such as cancer, since the nanogels themselves are nontoxic carriers and have the potential to deliver its contents only to the tumor.

Conclusion

It is clear that silver nanoparticles are positively impacting cancer research. These nanoparticles show promise in eliminating cancer cells while avoiding healthy cells, and show the potential to enhance current therapies and remove cancer cells from hard-to-operate regions of the body. Their cancer treatment potential piqued the interest of researchers to explore new ways to be able to deliver these nanoparticles safely to the target site. There is still so much to understand about what these nanoparticles are capable of and how to harness their abilities. With Brookhaven's technology and expertise, research can progress to discover novel ways to treat cancer and other persistent diseases.

Acknowledgements

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Literature

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