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CONTENT

CARBON NANOPARTICLES RESEARCH PROGRESS IN KAZAKHSTAN

Qing Yang, Ayan Nurkesh

Abstract: The research area of carbon dots (C-dots) is wildly known for variety of applications, including bioimaging, biomedical science, and sensors. Moreover, recent findings suggest the usage of carbon nanoparticles as an effective alternative for drug therapies. Synthesis of carbon dots is relatively cheap, fast, and green process. The results of C-dots treated bacteria and cancer cells, fluorescent imaging for detection of temperature and water pollutants all provides an interesting and promising approach of C-dots applications in different fields. Therefore, C-dots research has an important value for the scientific community and society. The following mini review provides a summary of relevant articles published by Kazakhstani scientists.

Keywords: carbon nanoparticles; cancer therapy; bioimaging; sensors

INTRODUCTION

Carbon-based nanomaterials including carbon dots (C-dots) have gained much attention within the areas of medicine, bioimaging, and sensors. C-dots have low cost and time of the synthesis, biocompatible, and represents a green type of the nanomaterial. The C-dots can be made different sources and different elemental doping are utilized to improve the properties of C-dots (Lim, Shen, & Gao, 2015; Zhang et al., 2018; Zheng, Ananthanarayanan, Luo, & Chen, 2015). Recently the field of carbon nanoparticles began to advance in Kazakhstan. The scientist studied the properties of synthetic or food-derived C-dots and their applications as antibacterial and cancer therapy drugs, sensors, and bioimaging tools. Here we will review the research progress of this field in Kazakhstan by providing a brief summary of some of the recent articles.

In one article date pits (*Phoenix dactylifera*) derived carbon dots (C-dots) were determined to have an anti-cancer effect on *in vitro* treatments of cancer cell lines. Carbon dots of about 1.1 nm size were synthesized using a hydrothermal method with addition to phosphoric acid. The particles observed to have strong fluorescence at 338 nm wavelength (near to blue). FT-IR transmittance spectrum demonstrated that C-dots composed of functional groups of RO–H, RN–H, C=O, and C=C. In concentration of 0.1 mg/ml the proliferation and migration of the human lung cancer A549, prostate cancer PC3, and breast cancer MCF7 cell lines significantly attenuated (61%). Interestingly, healthy kidney HEK293 cells growth treated with C-dots was inhibited only for 14% demonstrating the potential cancer selective cell growth inhibition. Moreover, the authors showed that C-dots exhibited fluorescence when incubated with cells which can be used for bioimaging (Yingqiu Xie et al., 2017). Imaging application of date pits derived C-dots was also observed in treating *Escherichia coli* (*E. coli)* bacteria on a gold surface. The fluorescence on the gold surface was increased in comparison to glass and showed bacterial staining or labeling properties of C-dots (Bukasov, Filchakova,

Gudun, & Bouhrara, 2018). Another usage of C-dots including date pits derived samples were semi-3D cell culturing on glass beads for the further cancer targeting. The nanoparticles were shown to have a positive electric charge in except for date pits derived particles. Then glass beads treated with C-dots were used for DNA extraction from *E.Coli* DH5α bacteria. Culturing of cancer and healthy cell lines (PC3 and NRK) in C-dots treated glass beads surface revealed distinct growth of cancerous cells that has potential in cancer therapy applications (Yingqiu Xie, Ayan Nurkesh, Keneskhanova, Altaikyzy, & Fan, 2018). Bacterial growth inhibition was also achieved by date-derived C-dots along with water pollution sensory material properties. The antibacterial effect tested on both gram negative and positive bacteria being an analog for common antibiotics. Further the interaction of particles with bacteria was used to develop bacterial pollution sensor-like material (Altaikyzy, Fan, & Xie, 2018). Further, the cell growth inhibition of date pits derived C-dots was determined to be via DNA damage. The cytotoxicity assay applied for NRK and PC3 cells demonstrated that C-dots kills both cell lines but affects cancer cells in a different way. This feature can be used for selective cancer treatment. The possible pathway was through inducing pH value drop in the cellular environment which was also observed in peroxidase activity inhibitory effect. The direct binding to the DNA resulted in fluorescence changes associated with nucleotide strands disruption or damage. C-dots may disrupt the DNA which resulted in the selective arrest of the cellular replication cycle process. Additionally, mutant bacterial strains treated with C-dots showed different degrees of growth inhibition. The application of anti-cancer drug along with C-dots suggested potential mechanisms of action such as via mammalian target of rapamycin (mTOR) and Pim-1 pathways. Overall nanoparticles were shown to be effective and low-cost green nanomaterial (Nurkesh et al., 2019).

The process of the carbon dots synthesis can be achieved by single step hydrothermal method (Figure 1). Common potato was used for nanoparticle production. The resulting particles had 1.5 nm size distribution as observed under the atomic force microscope (AFM) and amorphous structure X-ray diffraction (XRD) pattern. The analysis revealed the presence of NH_3, $N{-}(C)_3$, and NO_3 groups. The fluorescent emission was depended on the acidity of the environment. Application of C-dots was suggested for detection of cephalexin which is anti-infection drug. Concentrated amounts of the drug are harmful to human and C-dots provides a possible application as a fluorescent detection of the cephalexin (Wang et al., 2015).

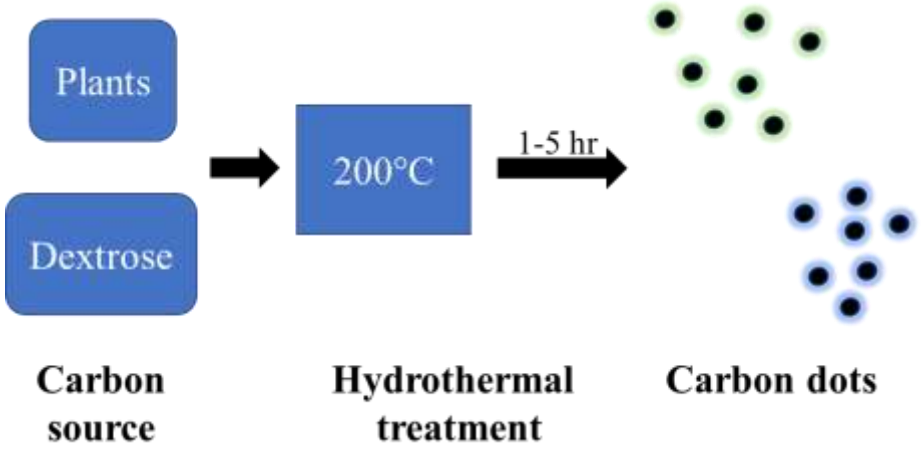

Figure 1. Carbon dots synthesis.

Similarly, beet derived carbon dots were applied for the detection of Amoxicillin (AMO) antibiotics. The beet derived C-dots were placed with different concentrations of the AMO and the fluorescence increased proportionally to the antibiotic concentration. Thus, the beet C-dots exhibited AMO sensory potential (Wang et al., 2018). The application of carbon nanoparticles was effective for the detection of ferric ions in water and showed the "thermometer-like" properties. Specifically, fluorescent nitrogen and phosphorus doped C-dots synthesized from dextrose as a carbon source. The synthesis required only about 1 hour of hydrothermal treatment at 200°C (Figure 1). The nitrogen and phosphorus doped C-dots with approximately 31-36 nm size used to detect the presence of the ferric ions in the water. C-dot probe had distinct fluorescent emissions in response to ferric ion concentrations in water. Thus, the reports demonstrated the alternative cheap method of water pollutant detection (Molkenova, Amangeldinova, Aben, Sayatova, & Atabaev, 2019; Molkenova & Atabaev, 2019). Moreover, the nitrogen doped C-dots were shown to be useful in optical temperature sensing applications. During measuring the emission of the C-dots in 25-95°C liquid solutions, the temperature increase resulted in changes of the fluorescence. The fluorescence decreased with the rise of the liquid temperature, demonstrating temperature sensing feature of the C-dots and possibility for usage in thermometry (Atabaev, Sayatova, Molkenova, & Taniguchi, 2019).

The combinatorial effect of black tea derived C-dots with rapamycin enhanced the cancer cell growth inhibition. ARF/β-catenin/YAP signaling pathway discovered in the article is important as a cancer therapy target. YAP is yes-associated protein 1 involved in cancer progression in nuclear form. The inhibition of the associated mTOR protein is one of the approaches to treat cancer. In the article, authors determined the interaction of alternative reading frame protein (ARF) with YAP and identified that C-dots accelerated the activity of ARF. Thus, the addition of C-dots may have a therapeutic advantage as a combinatorial drug to effectively treat cancers (Y. Xie et al.,

2017). One more study of the prostate cancer treatment via soybean derived C-dots was related to nuclear mesenchymal epithelial transition factor (nMET) and ARF proteins interactions. The paper identified the critical role of ARF for nMET in prostate cancer development through *in vivo* studies. The experiments confirmed the colocalization of ARF and nMET in cancer cells and decreasing the activity of either of the proteins significantly arrest cancer growth. The experimental findings also demonstrated that C-dots inhibited nMET, thus showing clinical significance in cancer therapy (Yingqiu Xie et al., 2019).

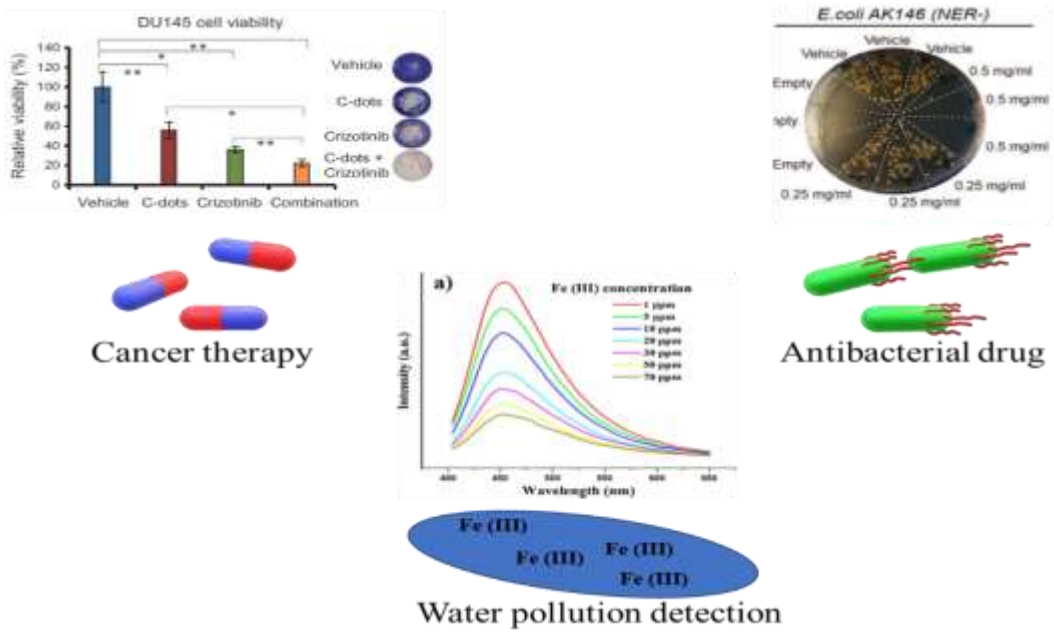

Figure 2. Applications of carbon dots.

Overall, the publications from Kazakhstani scientists about carbon dots shows quick methods for C-dots synthesis and provides numerous examples of their applications (Figure 2). The research progress in this field is important for broad scientific community and society.

Abbreviations

C-dots	Carbon dots
E.coli	*Escherichia coli*
AFM	Atomic force microscope
XRD	X-ray diffraction
mTOR	Mammalian target of rapamycin
YAP	Yes-associated protein 1
ARF	Alternative reading frame protein
AMO	Amoxicillin
nMET	Nuclear mesenchymal epithelial transition factor

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ПРОЦЕСС ИССЛЕДОВАНИЯ УГЛЕРОДНЫХ НАНОЧАСТИЦ В КАЗАХСТАНЕ

Цин Ян, Аян Нуркеш

Аннотация: Область исследований углеродных точек (С-точек) широко известна благодаря разнообразным применениям, включая биоизображение, биомедицинскую науку и датчики. Более того, последние данные свидетельствуют об использовании углеродных наночастиц в качестве эффективной альтернативы лекарственной терапии. Синтез углеродных точек является относительно дешевым, быстрым и экологически чистым процессом. Результаты обработки С-точками бактерий и раковых клеток, флуоресцентная визуализация для определения температуры и загрязнителей воды обеспечивают интересный и многообещающий подход к применению С-точек в различных областях. Поэтому исследование C-dots имеет важное значение для научного сообщества и общества. Следующий мини обзор содержит краткое изложение соответствующих статей, опубликованных казахстанскими учеными.

Ключевые слова: углеродные наночастицы; лечение рака; биоимиджинг; датчиков

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