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Bio-Based Material for Drug Delivery and Iron Chelation to Fight Cancer through Antimicrobial Activity

Chaired by **Dr. Alfredo Berzal-Herranz** and **Prof. Dr. Maria Emília Sousa**

pharmaceuticals MDPI

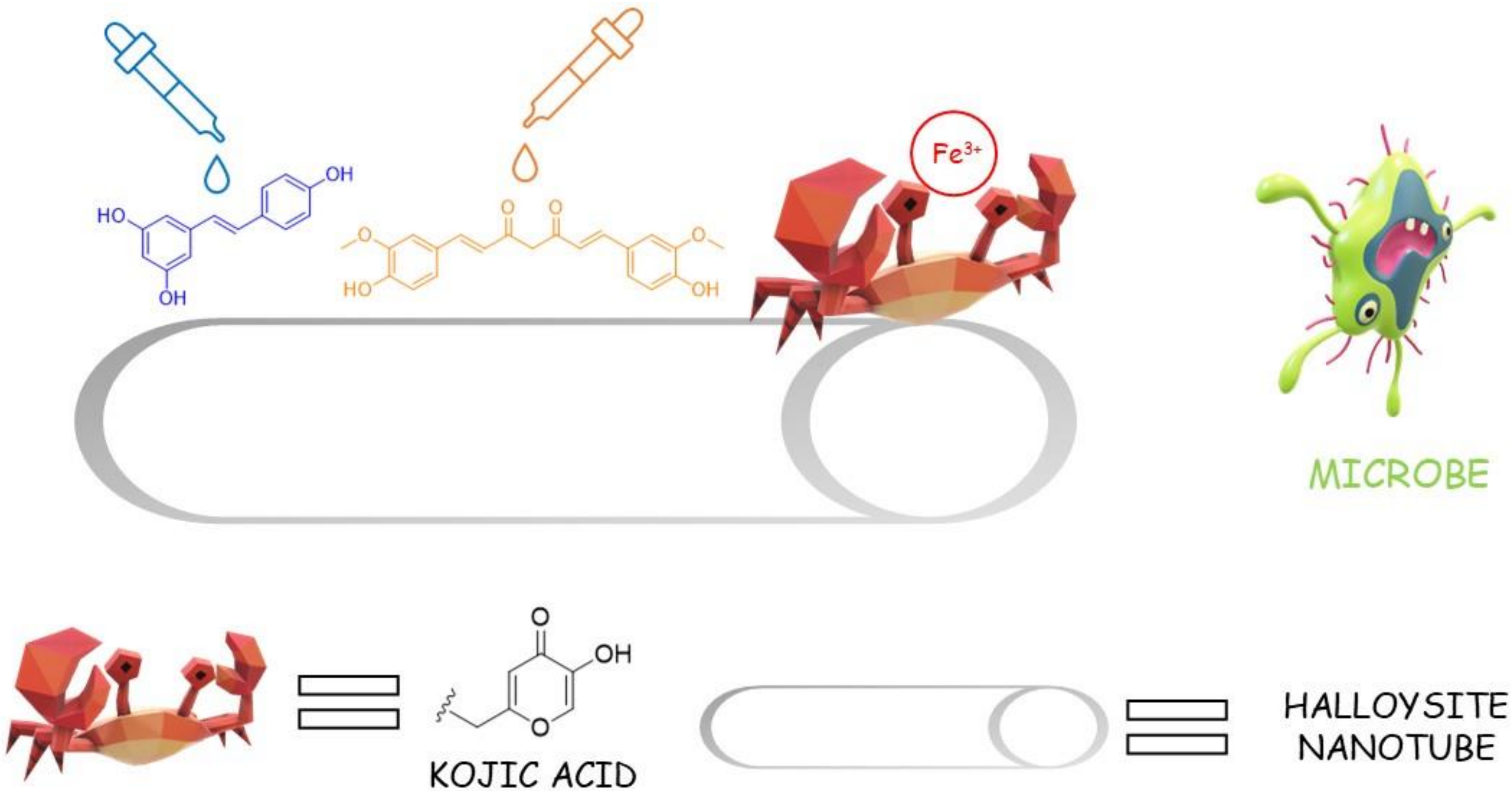
Erika Saccullo[1], Monia Camarda[1], Vincenzo Patamia[1], Chiara Zagni[1], Roberto Fiorenza[2], Virginia Fuochi[3,4], Sandro Dattilo[5], Pio Maria Furneri[3,4], Antonio Rescifina[1], Giuseppe Floresta[1,*]

[1] Department of Drug and Health Sciences, University of Catania, Viale A. Doria 6, 95125 Catania, Italy
[2] Department of Chemical Sciences, University of Catania, Viale A. Doria 6, 95125 Catania, Italy
[3] Department of Biomedical and Biotechnological Sciences (Biometec), University of Catania, 95125 Catania, Italy
[4] Center of Excellence for the Acceleration of Harm Reduction (Coehar), University of Catania, 95125 Catania, Italy
[5] Institute for Polymers, Composites, and Biomaterials, IPCB-CNR, Via Paolo Gaifami 18, 95126 Catania, Italy

***** Corresponding author: giuseppe.floresta@unict.it

Università di Catania

Bio-Based Material for Drug Delivery and Iron Chelation to Fight Cancer through Antimicrobial Activity



Abstract:
The impending growth of antimicrobial resistance has pushed research to explore alternative antibacterial strategies, including metal-chelating agents, since they can reduce the availability of essential metals and inhibit the biological function of metal-dependent proteins. Recently, the focus has shifted to nanomaterials to improve the efficacy of medication delivery. An example is the halloysite, natural clay nanotubes consisting of close layers of alumina and silica, which has shown several advantages: the production process is not dangerous, it is less costly than other nanotubes, and it has advantageous features for drug delivery carrier applications. In this communication, we report the modification of halloysite nanotubes (HNTs) to produce a dual-acting material for drug delivery and iron chelation properties with antimicrobial activity. The structure of HNTs was modified with a derivative of Kojic acid. Various methods were used to characterize HNTs-kojic acid, including IR, ICP/MS, SEM, and EDX. Drug-loading UV tests using curcumin and resveratrol were used to demonstrate the potential drug-delivery properties of the compound. Investigations evaluating the drug load capacity and encapsulation efficiency have demonstrated that curcumin had slower kinetics than resveratrol. This is likely due to the distinct solubility of the two medicines. In addition, it has been demonstrated by the antibacterial evaluation of antibacterial properties at low doses against both Gram-positive and Gram-negative bacteria. This implies that the iron chelation activity of nanotubes is incredibly effective. These findings pave the way for further research and material design application in treating infection-related disorders, including cancer.

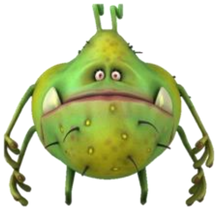
Keywords: halloysite nanotubes; kojic acid; iron chelation; antibacterial.

Introduction

The role of bacteria in the development of cancer is increasingly recognized. This has led to the development of new cutting-edge strategies to interfere with crucial biological functions in microbial cells:

Chelating Agents: may interfere with the ability of the micro-organism to metabolize essential metals involved in crucial processes. They can also make conventional antibacterial drugs more powerful.

Nanomaterials: because they can be surface modified to let them to concentrate at tumor areas and be functionalized to actively target cancer cells or tumor tissues.



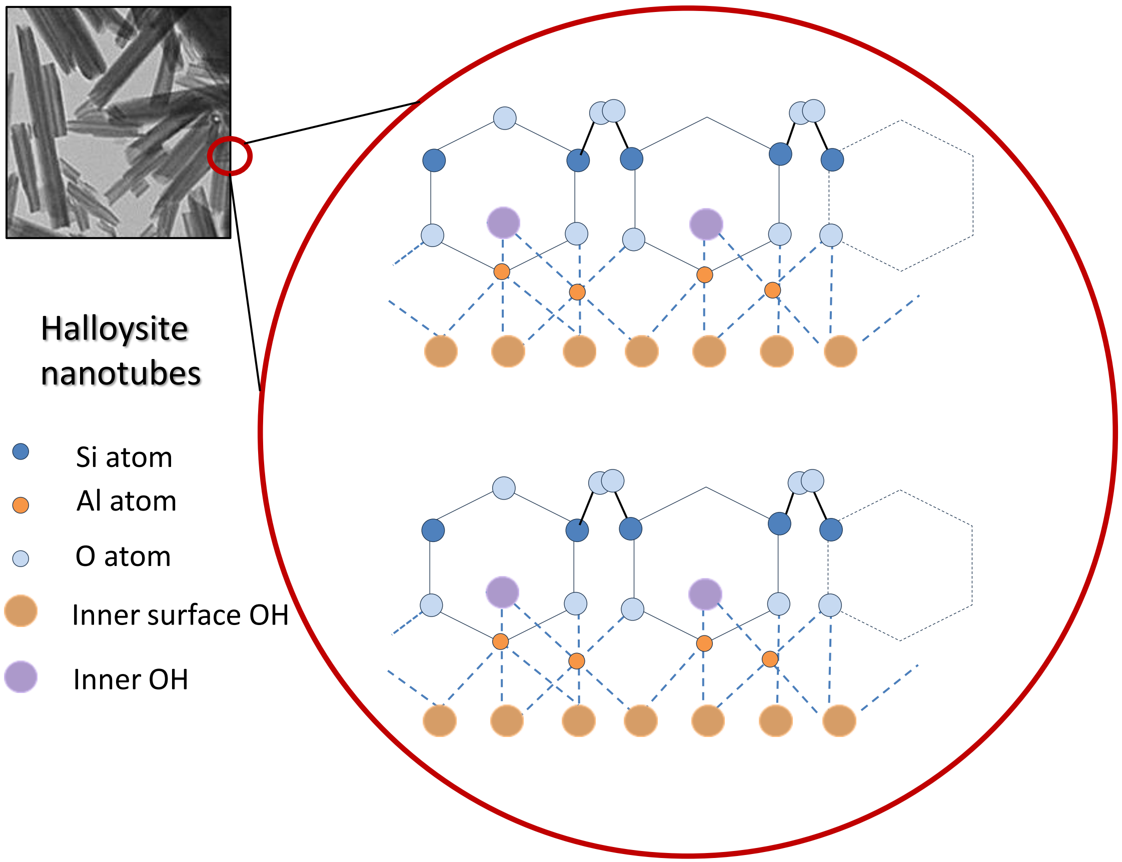
Why nanomaterials?

- ✓ Improved retention and penetration properties of nanoscale particles allow them to target tumor sites passively.

- ✓ It is possible to modify the size or form of nanomaterials for better tumor retention and to add cationic components to their surfaces to increase their capacity to penetrate tumors.

- ✓ It is feasible to load different medications in relatively high quantities, enhancing their solubility and preventing deterioration because of their hydrophobic and hydrophilic designs.

Halloysite



Alumina and silica are arranged in close layers to form natural clay nanotubes.

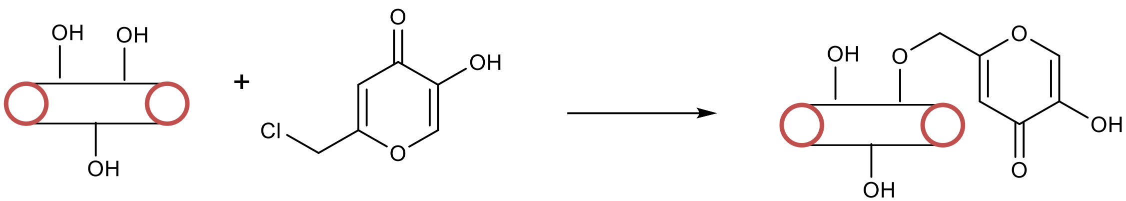
A cheap and useful nanoscale encapsulation container for physiologically active substances.

Advantages of Halloysite

- ✓ Since the production process proceeds naturally, it is not risky.
- ✓ Less expensive than other nanotubes.
- ✓ Large particle size.
- ✓ Many hydroxyl groups useful for functionalization.
- ✓ Excellent stability in physiological fluids suitable for drug delivery carrier applications.

Discussion and results

A new nanomaterial was synthesized by modifying HNTs with a derivative of kojic acid.

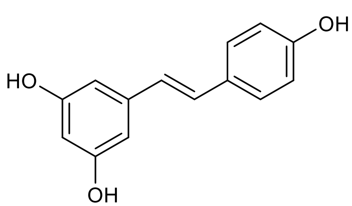


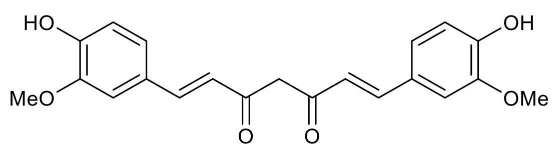
HNTs

HNTs-kojic

NEW NANOMATERIAL

Then HNTs-Kojic was encapsulated with resveratrol and curcumin.





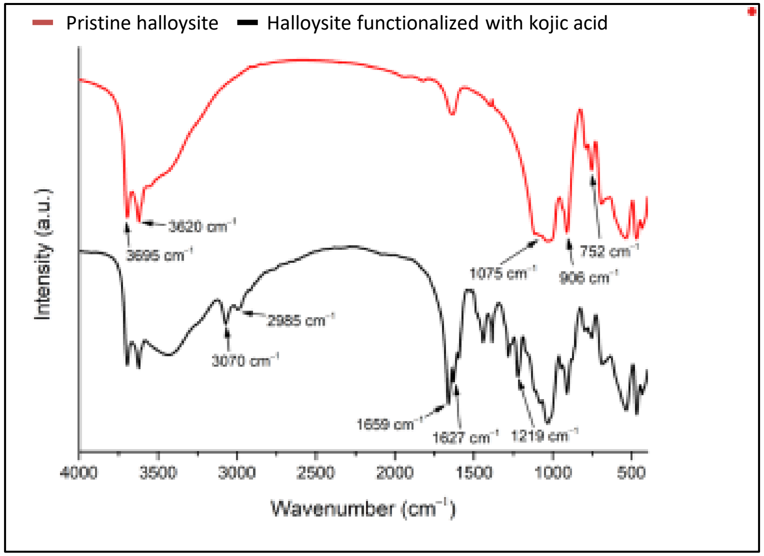
Natural phenolic substances with antiviral, neuroprotective, anti-oxidant, and anticancer activities.

Resveratrol

Curcumin

Characterization of new nanomaterial

IR



The effective functionalization of the halloysite nanotubes with kojic acid is demonstrated by comparing IR spectra of HNTs and HNTs-kojic acid.

ICP/MS

To confirm that the substance could remove iron(III) from the environment, ICP-MS spectra were taken. The results showed that iron is chelated by HNTs-kojic acid.

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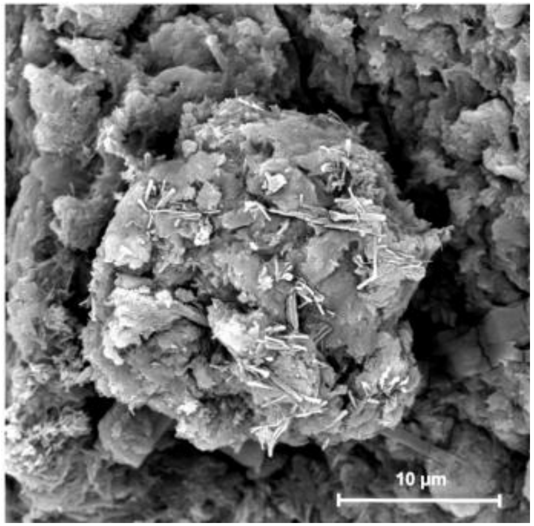
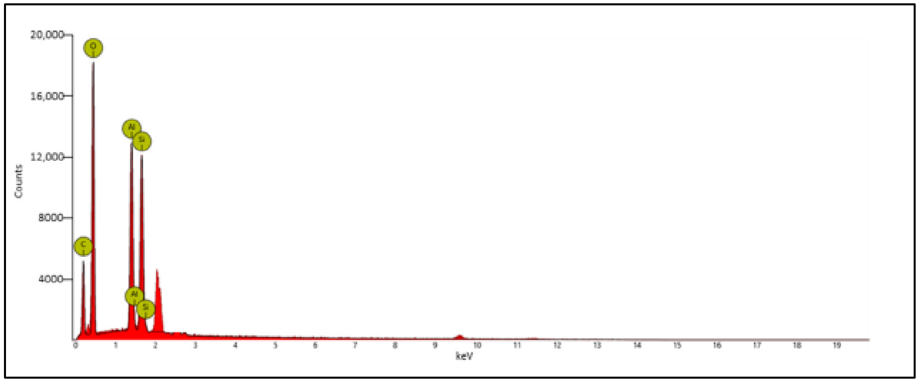
MDPI

SEM



SEM scans revealed the existence of pure and functionalized HNTs in the form of cylindrical tubes, with an average particle size of 400 nm.

EDX

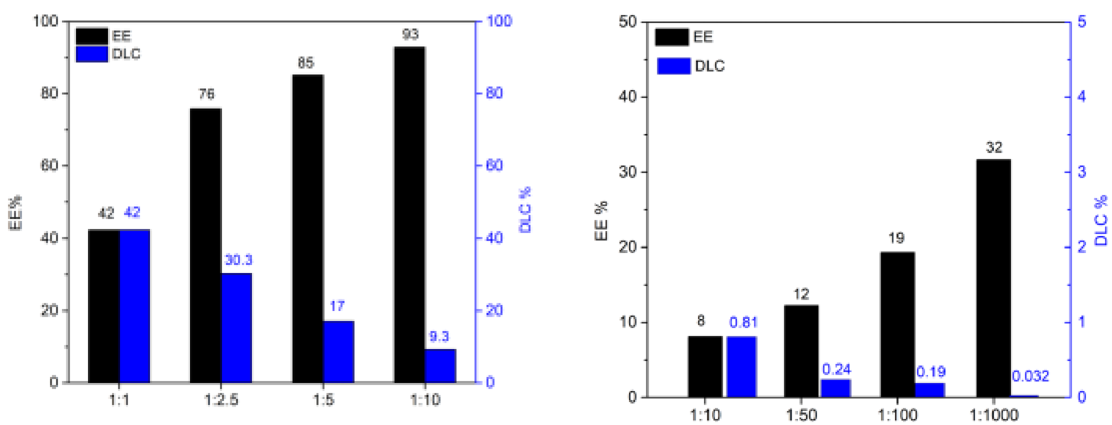


Oxygen, aluminum, and silicon were found as the major constituents of HNTs by SEM-EDX elemental mapping, while the HNTs-kojic acid shows the presence of carbon, oxygen, silicon, and aluminum.

Drug Loading and Release

Drug-loading capacity (DLC) = loaded drug amount/total HNTs-kojic amount

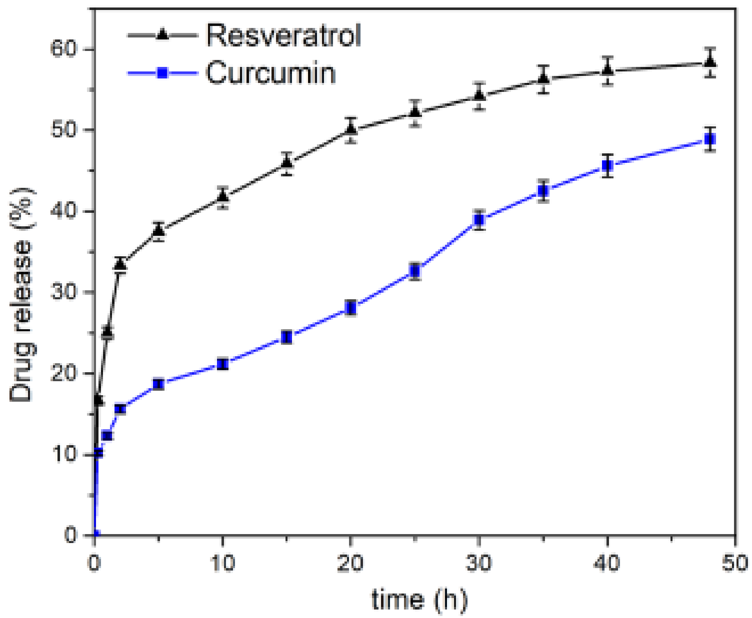
Encapsulation efficiency (EE) = loaded drug amount/total drug amount



Drug-loading capacity (DLC) and Encapsulation efficiency (EE) of resveratrol (left) and curcumin (right) on the HNTs-kojic acid.

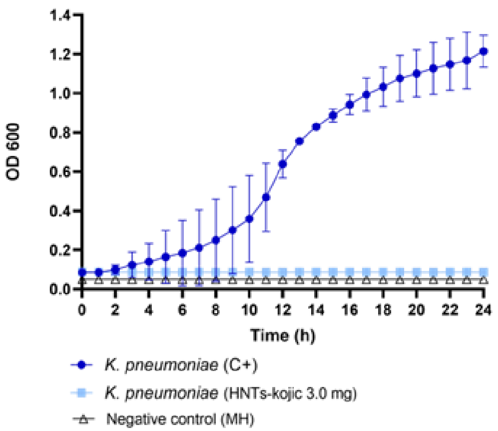
The highest EE can be obtained with the highest amount of material. As reported in the literature, the distinct solubility of the two drugs (resveratrol is weakly soluble in water, while curcumin is soluble in ethanol) can be a reasonable explanation for the distinction in the load capacities of resveratrol and curcumin with the HNTs-kojic acid system. The unique nanotubular form of the HNTs-kojic acid sample and the strong interaction of drugs with it, however, bodes well for the potential use of this material as a drug carrier.

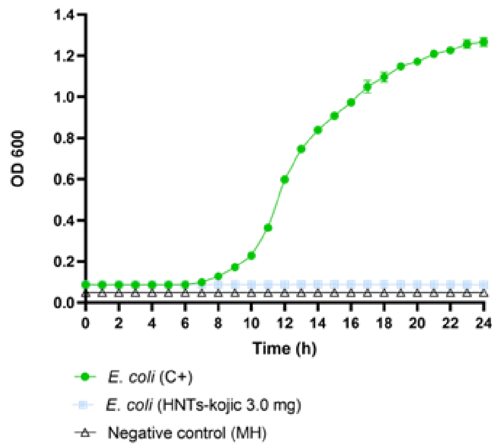
Release kinetics



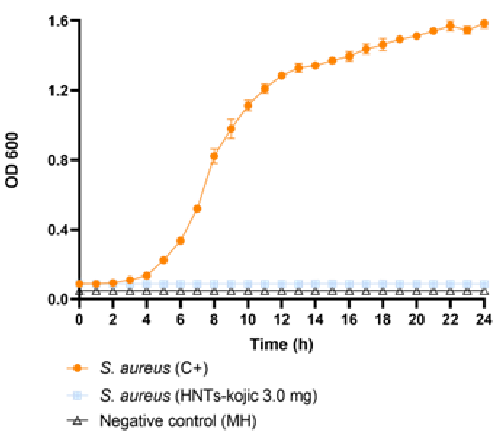
Resveratrol and curcumin had relatively fast release kinetics of up to 10 hours (about 40% and 20%, respectively). Subsequently, the release of resveratrol and curcumin is slowed; in 20 hours, 50% and 30% are released, respectively, to reach 60% and 45% in 40 hours. Unlike resveratrol, the latter drug had slower kinetics. Additional drug molecules were gradually released from the sample surface, and this delivery was similarly affected by the diffusion phenomenon. The rapid release of drugs in the first hours of the experiments was caused by drugs adsorbed in halloysite nanotubes that rapidly fade.

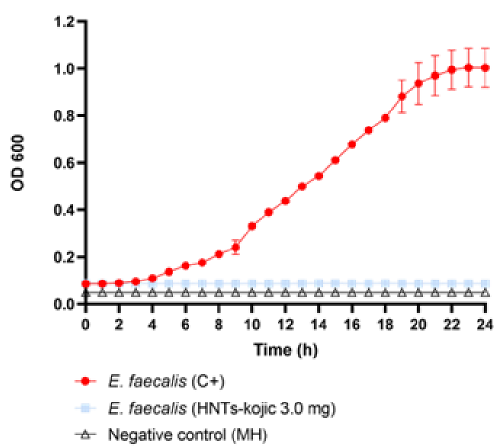
Microbiological Assays





With a MIC value of 3.0 mg, HNTs–kojic acid demonstrated strong antibacterial activity against every pathogen tested. The novel material showed exceptional antibacterial efficacy against both Gram-positive and Gram-negative strains, as evidenced by the bacterial growth curves.





The iron chelation action of the nanotubes is exceptionally efficient.

Conclusions

Since the advent of nanomedicine, the use of antibiotics in cancer treatment has advanced significantly. Overall, anti-bacterial nanosystems have significantly improved cancer treatment; however, additional research must be done before they can be applied safely and effectively. HNTs have been attracting much attention lately in the biomedical field due to their excellent biocompatibility and on-demand drug delivery.

HNTs-kojic

↓

A novel material with combined effects from the medicine and the iron-chelating properties.

These results provide opportunities for more investigation and use of the produced material in the treatment of cancer and other infections-related diseases.

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