Egyptian Journal of Chemistry

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Synthesis of Bionanomaterials (silver loaded gold) in colorectal cancer therapy

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Abstract

Silver nanoparticles (AgNPs) and gold nanosheets (Au nanosheets) have outstanding properties that make them suitable for use in multiple fields including the biomedical field. In the current study, silver nanoparticles (AgNPs) and gold nanosheets (Au nanosheets) were fabricated by chemical method and their mixtures using deposition technique, which is one of the most popular methods. The production of these materials is simple because they produce molecules with high bioavailability and low toxicity. Nanostructures (Au, Ag, and Au+Ag nanosheets) have been used to treat a variety of cancers, including colorectal cancer, due to their biocompatibility, large surface area, and high dispersibility. Several analysis methods (X-ray diffraction, optical properties, scanning electron microscopy, transmission electron microscopy, etc.) have been used to study the characterization of the synthesized nanomaterials. Moreover, these nanomaterials have been used in cancer treatment and antibacterial activities against various bacteria. We present here a technological platform for engineering Au nanotopographies by templated electrodeposition on antibacterial surfaces. Three different types of nanostructures were fabricated: nanoparticles, nanorods and nanosheets. The nanoparticles are the basic structures and are 50 nm in diameter and 100 nm in height. Particular arrangement of the nanoparticles in various geometries formed nanorods and nanosheets. Flat surfaces, rough substrate surfaces, and various nanostructured surfaces were compared for their abilities to attach and kill bacterial cells. Methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli* and Kiebsiella Sp. a Gram-positive and a Gram-negative bacterial strain responsible for many infections in health care system, was used as the model bacterial strain. It was found that all the Au nanostructures, regardless their shapes, exhibited similar excellent antibacterial properties. A comparison of live cells attached to nanotopographic surfaces showed that the number of live *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli* and Kiebsiella Sp. cells was <1% of that from flat and rough reference surfaces. Our micro/nanofabrication process is a scalable approach based on cost-efficient self-organization and provides potential for further developing functional surfaces to study the behavior of microbes on nanoscale topographies. According to the study, these nanoparticles kill more than 80% of cancer cell lines. A comparison was made between the goods.

***Keywords*:** Gold nanosheets, silver nanoparticles, Chemical synthesis, Colorectal cancer, Anti-cancer, Antibacterial.

1. Introduction

Nanotechnology is an evolving field that combines biology, physics, and chemistry to create nano-sized particles (1–100 nm) with specialized functions and applications in physics, medicine, pharmacology, food technology, and materials science[1, 2]. Metallic nanosheets made of metals such as gold (Au) are among the most researched nanomaterials. Gold nanosheets are one of the most studied metallic nanoparticles due to their unique properties, which include chemical stability, biocompatibility, ease of preparation and modification, plasmonic that make them suitable for a wide range of therapeutic applications, such as delivery systems[3, 4]. Medicines in diseases such as cancer, cardiovascular disease, diabetes and the development of biosensors and environmental applications[2, 5]. Both chemical and physical methods can be used to create composite sheet. However, since conventional cancer drugs are often expensive and contain toxic by-products, recently Au nanosheets have been tested in order to search for alternative conventional cancer therapies[6]. Colorectal cancer, also known as colon cancer, is one of the most common cancer types individuals and governments large amounts of money on treatment[7, 8]. Although the causes of colorectal

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Receive Date: 30 April 2022, Revise Date: 25 May 2022, Accept Date: 28 May 2022

DOI: 10.21608/EJCHEM.2022.136666.6017

cancer are not identified yet, some risk factors, such as nutrition, cigarette smoke and excessive alcohol consumption, are closely related to the causes of this disease. People with certain genetic syndromes or who have a family history of colorectal cancer are also more likely to develop the disease[9, 10]. The most common starting point is polyps, which are small, noncancerous (benign) groups of cells that grow inside the colon, over time; some of these polyps may develop into colon cancer[11-13]. The novelty of this research is to simplicity production materials with high bioavailability and low toxicity. Nano papers (Au, Ag, and Au+Ag nanosheets) have been used to treat a variety of cancers, including colorectal cancer, due to their biocompatibility, large surface area, and high dispersibility.

2. Materials and methods:

2.1. Synthesis of sliver nanoparticles by chemical method:

Silver nanoparticles were prepared by chemical method, in which 0.5gm silver nitrate ($AgNO_3$) was dissolved in 50 ml hydrochloric acid (HCL). And when the silver nitrate salts were dissolved in acid, they were distilled by burette on 50 ml of ethanol, and the result was a suspension of silver nanoparticles in the liquid particles. At the end, the liquid was dried to obtain the nanoparticles in the form of powder so that physical tests such as (XRD, SEM, EDX and TEM) could be carried out to know the properties of the nanomaterial, as well as biological tests were conducted to determine the extent of synthesized nanoparticles'effect on some types of bacteria and the effect of these particles on colorectal cancer. **As in Fig 1**.

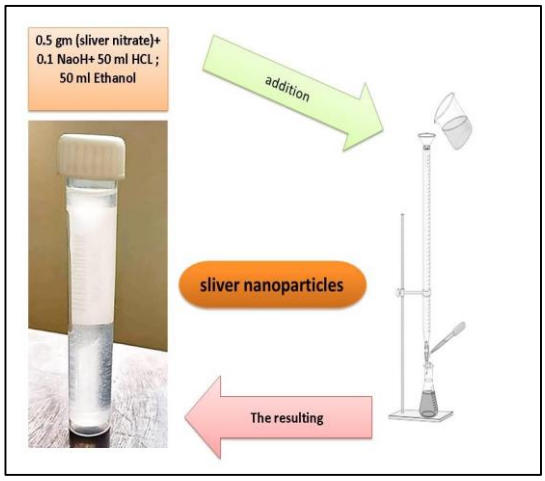


Figure 1: Synthesis of silver nanoparticles by chemical method.

2.2. Synthesis of gold nanosheets by using electrochemical method:

Gold nanosheets were prepared by the electrochemical method, where 0.5 g of gold chloride salts were dissolved in 50 ml of hydrochloric acid, and after the salts were completely dissolved in acid, the solution was placed in the electrochemical cell, where the cell was connected to the electric circuit as shown in the **fig. 2**, for half an hour at a voltage of 30 volts. Then gold sheets suspended in the solution were obtained. **As shown in Fig. 2**.

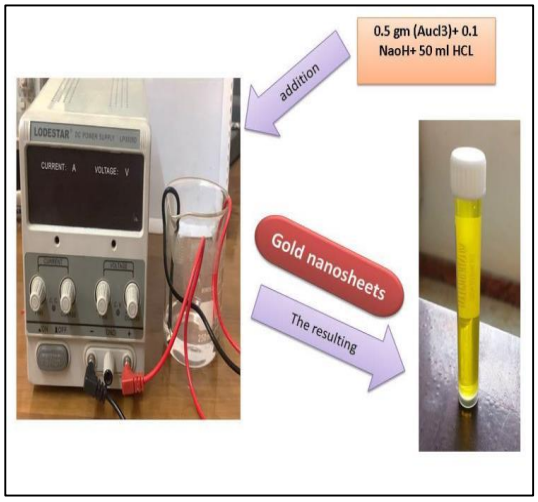


Figure 2: Synthesis of gold nanosheets by electrochemical method.

2.3. Antimicrobial activity of Au Nanoparticles

The antimicrobial activity of AuNPs determined using disc diffusion method. The antibacterial activities of gold nanoparticles were studied against the gram-negative and gram-positive bacterial strains. The bacterial strains were grown in nutrient broth at 37◦C with continuous shaking at 200 rpm for 24h. The nanoparticles were sub-cultured on Muller Hinton agar medium (MHA) using standard method and incubation was kept for a period 48 h at 50°C and stored in 5°C in refrigerator to maintain stock culture. The serial dilutions were conducted with different level of concentrations 100 µL, 200 µL, and 300 µL of gold nanoparticles. The zone growth of the plate incubation was observed after 48 h using a negative bacterium as a standard positive control. Growth kinetics was determined by measuring optical density at 560 nm at every 1 h interval from the time of incubation.

2.4. Cell culture

The human colon cancer cell lines HT-29 expressing GFP and HCT-116 expressing red fluorescent protein (RFP) were maintained in DMEM

(Irvine Scientific, Irvine, California) supplemented with heat-inactivated 10% fetal bovine serum (Gemini Biologic Products, Calabasas, California), 2 mM glutamine, 100 U/mL penicillin, 100 µg/mL streptomycin, and 0.25 µg/mL amphotericin B (Life Technologies, Inc., Grand Island, New York). The cells were incubated at 37°C in 5% CO_2. OBP-401 was used to label colon cancer with GFP in vivo.

3. Results and Discussion:

3.1. X-ray diffraction:

In order to explain the structural properties, the nature and the crystal growth of nanoparticles, X-ray diffraction measurement was carried out done according to the ASTM (American Society of Testing Materials) cards, using (Philips pw 1050 X-ray diffractometer of 1.54 Å from Cu-kα, Japan). Cu radiation source, at a scanning speed of 2 min^{-1}, 40 kV tube voltage, and 30 mA tube current.

The crystallinity of synthesized material, the average particle (green) size (Dg) of NPs has mostly calculated by using the Debye–Scherrer's equation after the successful synthesis [28, 29]. The Scherrer's equation is considered as the most fundamental and widely used equation to calculate the particle size by the combination of 2θ and FWMH values from the XRD data.

$$D = K\lambda\ \beta\cos\theta \quad (1)$$

In this equation, D represents the Particle size (Diameter), K is Scherrer's constant (0.9), λ = 0.15406 nm (Wavelength of X-ray source), β represents Full width at Half-maximum intensity (FWHM) in radians and q is used to denote the Peak positions in (Radians), and θ is the Bragg's diffraction angle of the respective XRD peak.

X-ray diffraction (XRD) investigation confirmed the crystalline character of (Au nanosheets), as shown in **Fig.3(A)**. were found at (2Ɵ) 38.5, 44.493, 64.75 and 77.533, corresponding to (111), (200), (220), and (311), which also corresponds to the FCC crystal structure of (Au nanosheets) (JCPDS file: 04-0784). **Fig. 3(b)** shows the X-ray diffraction (XRD) pattern of the as-prepared silver nanoparticles (AgNPs) that were synthesized using the chemical reduction method. A number of Bragg reflections corresponding to groups (111), (200), (220), (311) and (222) levels of the retina are observed. These peaks correspond to the silver cubic (FCC) structure (JCPDS file number 04-0783).

While the X-ray diffraction of gold: silver nanosheets (Au:Ag nanosheets) and nanosheets were mixed into a mixture and characteristic the peaks of (Au:Ag nanosheets) were also found at (2Ɵ) corresponding to (111), (200) and (220), which also corresponds to the crystal structure of FCC for (Au:Ag nanosheets) (JCPDS data number 04–0783 and 4–0784 cards) as shown in. **Fig. 3(C).**

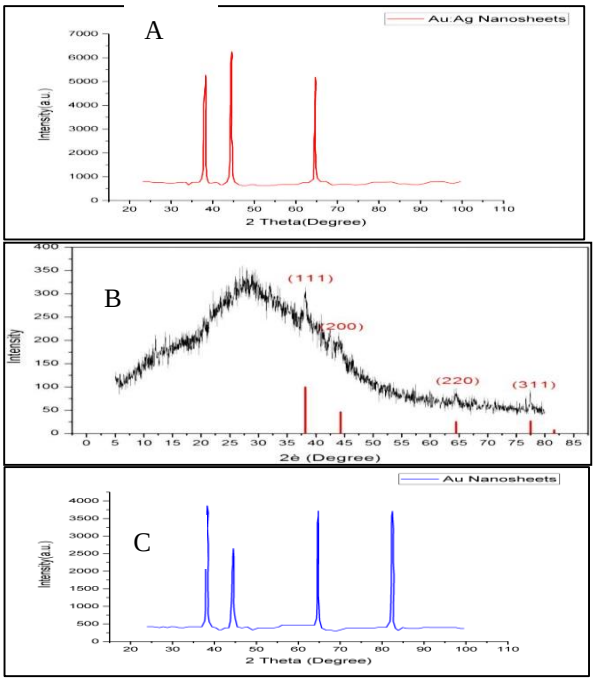
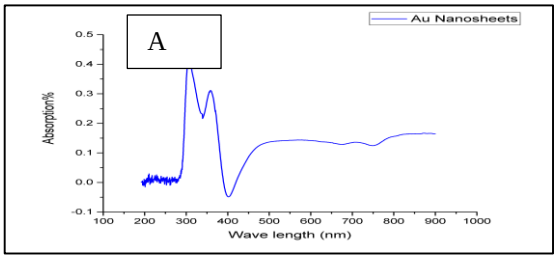


Figure 3: XRD Patterns of gold nanosheets, silver nanoparticle, and mixed gold: sliver nanosheets.

3.2. UV-absorbance:

Figure 4A shows the UV absorption spectra of the suspension-produced gold nanosheets (Au nanosheets), which present a similar and broadband of ~200 nm. This means that the presence of spherical gold nanosheets (Au nanosheets) with minimal size dispersion, which correlates with gold sheets at the nanoscale[14].

Fig. 4B shows that UV-visible spectroscopy is an important technique to confirm the formation and stability of AgNPs in chemical solution [10]. AgNPs are known to exhibit dark brown colours, depending on the density and size of the nanoparticles; Colours appear due to surface plasmon resonance (SPR) excitation of AgNPs. The absorbance and permeability of gold: silver nanosheets in mixture are shown in **fig .4C**



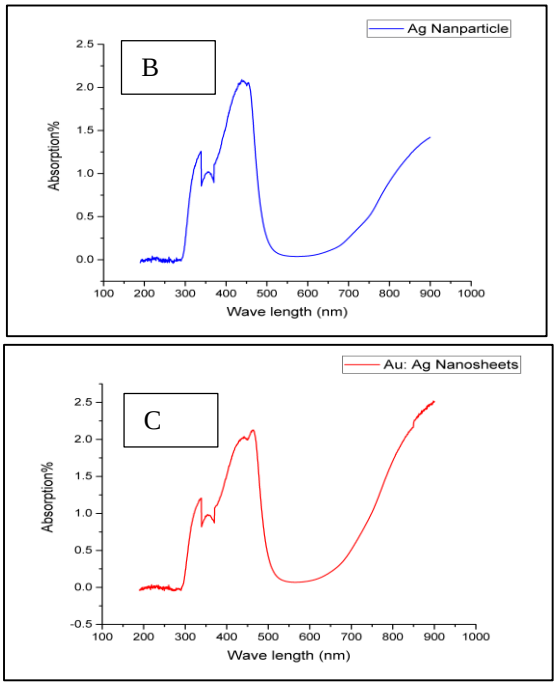


Figure 4: Absorbance of gold nanosheets, sliver nanoparticle, and mixed gold: sliver nanosheet

3.3. Fourier transformation infrared spectroscopy (FTIR):

A typical infrared spectrometer (Au nanosheets) was acquired using a Perkin Spectrum One ATR (Japan). The spectrum was evaluated, with all peaks recognized using the NIST FT-IR database. Fourier Infrared Spectroscopy (FTIR) is an essential tool for detection functional groups. It was used in this work to characterize the diverse functional groups involved in reducing the stability of the prepared Au+Ag nanosheet sample. The FTIR spectrum of the synthesized Au+Ag nanosheets, shown in Fig. (5), reveals clear peaks throughout the full range (400 to 4000 cm^{-1}) of the observation. The O-H expansion can be attributed to the observed band at 3658 cm^{-1}. The visible range at 2905 cm^{-1} is attributed to the C–H (alkane) curvature. N - H (amine) stretching peaks at 1509 cm^{-1}. The bending of C-H (alkanes) and the expansion of C-O (alcohol/ether) are represented by the weakest band at 1357 cm^{-1}, respectively. Also, the two weaker bands observed at 864 cm^{-1} can be traced back to the C-H curvature of the Alkyne may be due to the chemical reaction.

3.4. Transmission Electron Microscopy (TEM):

TEM images (A, B, and C) of nanocrystal formation of Au, AgNPS, and Au + Ag nanosheets, respectively. The average nanomaterial size is less than 50 nm. Figure (6) shows TEM micrographs of (A, B, and C), which clearly revealed a spherical shape, sheet shape and narrow particle size distribution. This dispersible material was observed under TEM analyzes even at high magnification; crystallization was impossible to identify. With a low level of aggregation, some nanoparticles and nanosheets took an uneven shape.

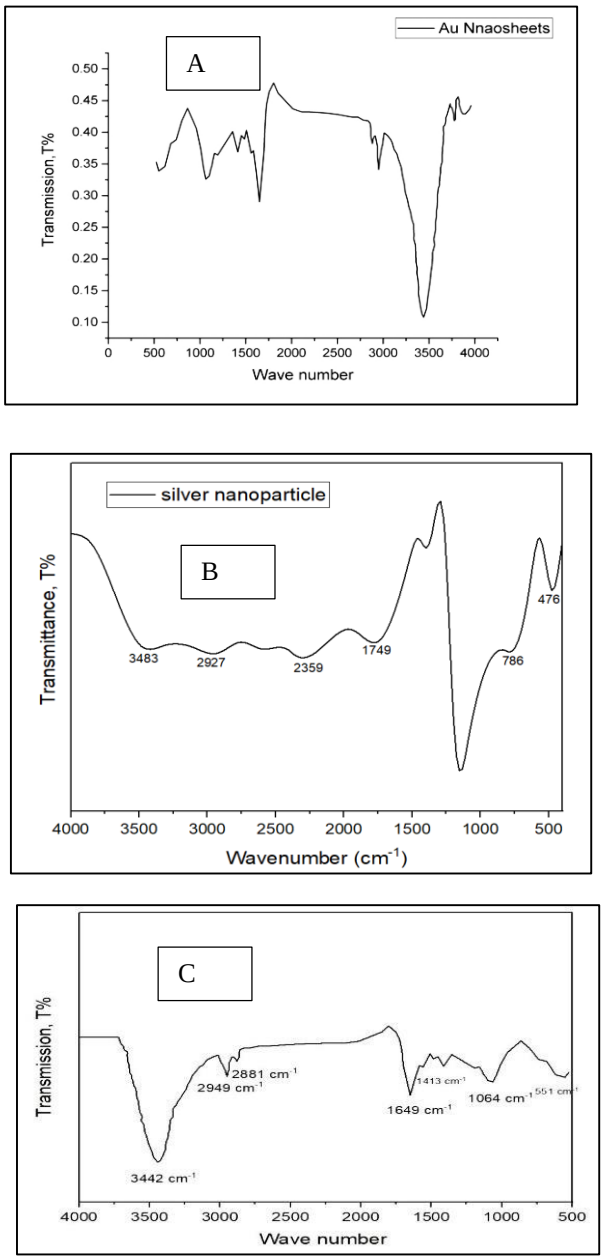


Figure 5: FTIR of gold nanosheets, silver nanoparticle, and mixed gold: sliver nanosheets.

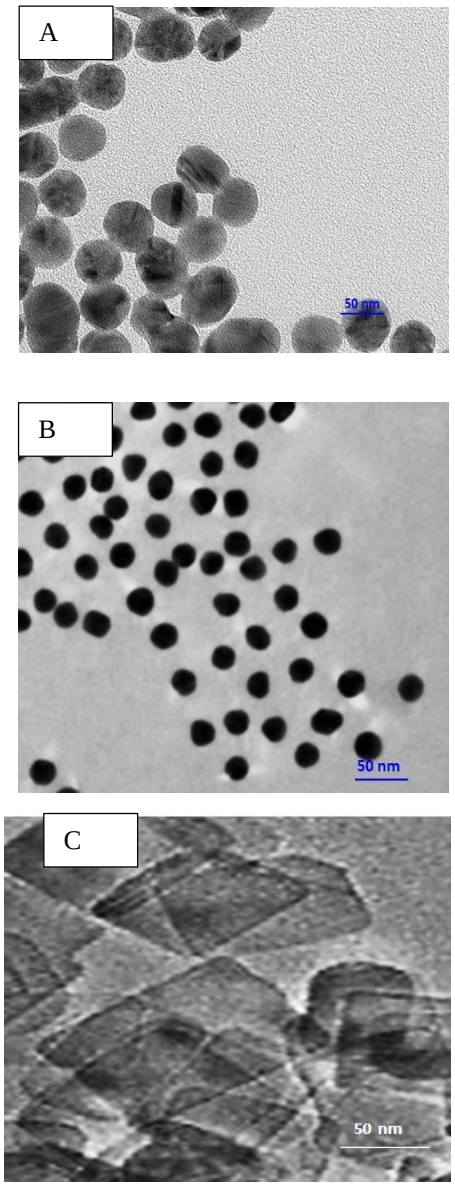


Figure 6: TEM images (A, B and C) of gold nanosheets (Au nanosheets), sliver nanoparticle (AgNPs) and mix gold: sliver nanosheets (Au+Ag nanosheets), 50 nm.

3.5. Scanning Electron Microscope (SEM):

Scanning Electron Microscopy (SEM) images (A, B and C) of Au nanosheets, AgNPS and Au + Ag nanosheets respectively are shown in **Fig (7)**. The SEM images indicated the particle size of the Au, AgNPS, and Au + Ag nanosheets in the 50 nm range. The morphological structure of the Au, AgNPS, and Au + Ag nanosheets. The nanoparticle products are determined by SEM analysis. **Fig. (7)** (A, B, and C) prepared by the chemical method deposited on a glass substrate at different magnifications. The morphology of the Au, AgNPS and Au + Ag nanosheets shows that their distribution is relatively uniform and homogeneous. Also, these nanomaterials assemble into an array of sheet spheroids with different diameters due to the stability of mass distribution and colloid formation. Particle sizes estimated from SEM images range from (10–50 nm), which are larger than the sizes obtained from XRD analysis and TEM images using Scherer's formula. This can be attributed to the large agglomerates deposited on the surface of the film due to the general structure consisting of small grains on the glass substrate during drying.

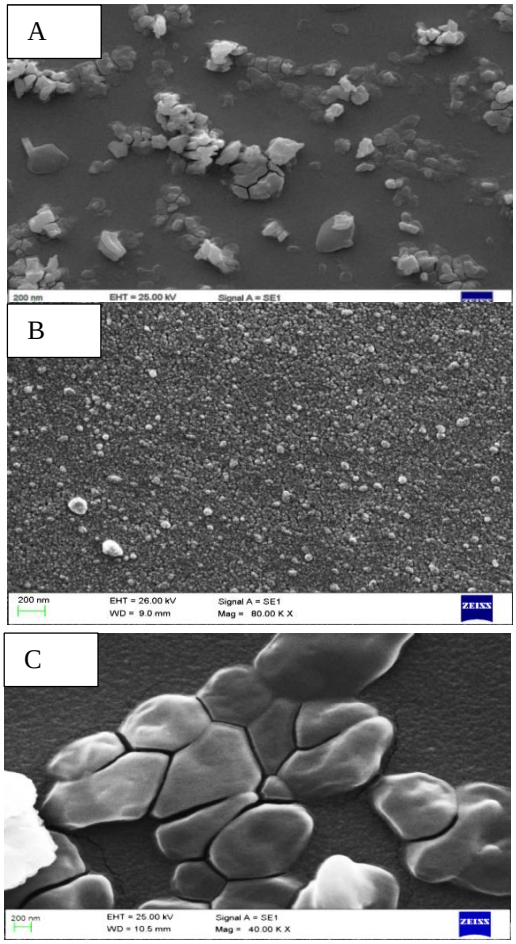


Figure 7: The Scanning Electron Microscope (SEM) images for Au nanosheets, AgNPS, and Au + Ag nanosheets, 200 nm.

3.6. Antibacterial activity of Au nanosheets, AgNPs and Au: Ag nanosheets:

Au nanosheets are attracting a great deal of interest in their use in various biomedical applications (eg viruses and bacteria) because their size is comparable to that of biological molecules (eg

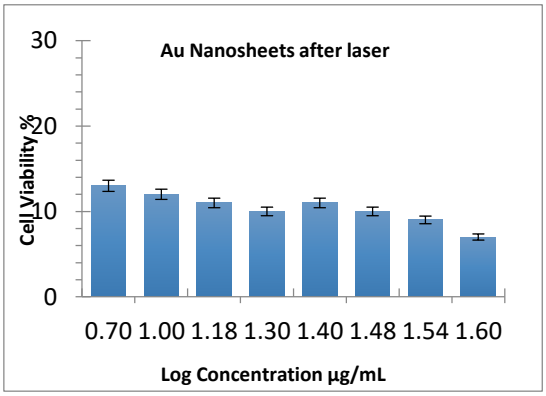
proteins and DNA),[15-17]. Studies of the action of various drugs and antibacterial formulations in the form of nanosheets have yielded promising results. Gold is an inorganic, non-toxic and harmless antibacterial agent that has been used for ages and is capable of destroying about 650 types of pathogenic microbes[18-20]. Since the 1880s, silver nanoparticles (AgNPs) have been used as antipathogens, because it has a broad antibacterial effect against a large variety of microbes. Due to its exceptional properties such as chemical stability, catalytic activity, excellent conductivity and, most importantly, antimicrobial and antifungal activity against fungal species, silver nano particles have received a lot of attention[20]. The antimicrobial properties of noble metals, such as gold nanosheets, silver nanoparticles and their compounds, allow them to be used in treatment. The greater biological performance of gold nanosheets may be due to the increased surface area to volume ratio when compared to their bulkier counterparts[21]. The antibacterial activity of Au+Ag nanosheets was evaluated using a chemical approach, and these particles showed outstanding inhibitory efficacy against a variety of bacteria as shown in **table** 1. This result is consistent with the research[22, 23].

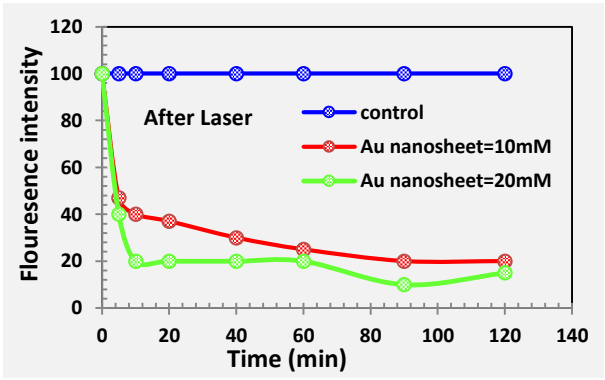
Table 1. Antibacterial activity of Au nanosheets, AgNPs and Au: Ag nanosheets

No	Name of bacteria	Inhibition(mm)		
		Au nanosheets	AgNPs	Au+Ag nanosheets
1	*Staphylococcus aureus*	26	18	26
2	*Staphylococcus epidermidis*	25	23	30
3	*Escherichia Coli*	27	17	25
4	*Kiebsiella Sp.*	23	15	21

3.7. Anticancer activity of Au nanosheets and Au: Ag nanosheets:

The use of gold nanosheet technology in cancer treatment has shown promising results. The features of gold nanosheets, such as their small size, non-toxicity, shape and immunodeficiency, make them suitable candidates for targeted drug delivery systems[24, 25]. The ability to bypass the body's natural barriers becomes more plausible as tumor-targeted delivery routes decrease[26]. Tumor-specific ligands can be grafted onto particles using chemotherapy drug particles to allow these particles to circulate throughout the tumor without being redistributed in the body, increasing specificity and drug delivery potential[27]. The cell line screening method, the anti-tumor capacity, of Au and Au + Ag nanosheets was investigated in a colorectal cancer cell line. At varied doses (70-160 µg/ml), Au and Au + Ag nanosheets showed significant cytotoxicity against colorectal cancer cell line[28]. Au and Au + Ag nanosheets induced tumor cell death at a specific concentration of 160 µg/ml. With the increase in the amount of gold nanosheets, the percentage of cell viability decreases in colorectal cancer cell line (Fig. 8) and (Fig. 9), this result agrees with[29]. A flow cytometer was used to examine the cellular uptake of Au nanosheets in a cancer cell line to better understand the factors that contribute to toxicity. The difference in incubation time was 0-120 min, Au and Au + Ag nanoplates were suspended in medium at two concentrations of 10 mM and 20 mM plus control cells and doses[30]. Western blot technique was performed here to access the effects of Au and Au + Ag nanosheets from tumor cells as shown in the figure. (8) and (9) (c), protein levels decreased after treatments of Au nanosheets and Au + Ag nanosheets.





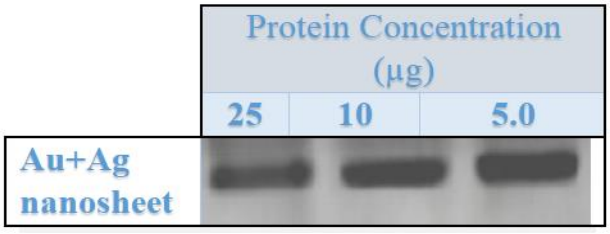
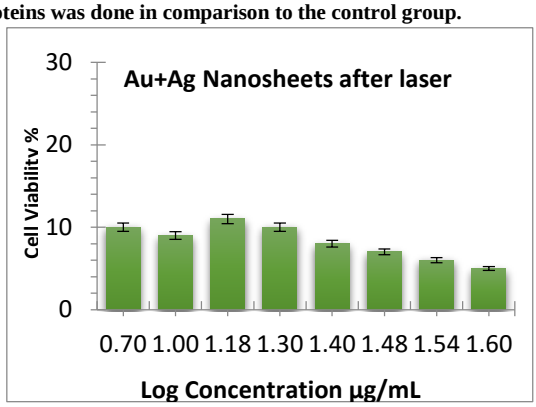
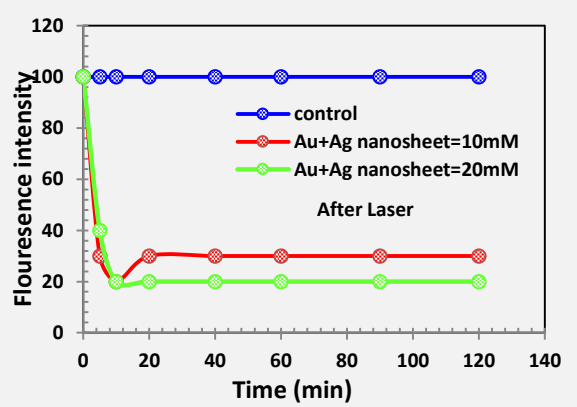


Figure 8: (a) Anticancer activity of Gold nanosheets (Au nanosheets) in Colorectal cancer, (b) Fluorescence intensity analysis of the three cells (control un dosed cells, cells were incubated several times with 10 mM of Au nanosheets and 20mM of Au nanosheets) and (c) Western blot analysis -related proteins was done in comparison to the control group.





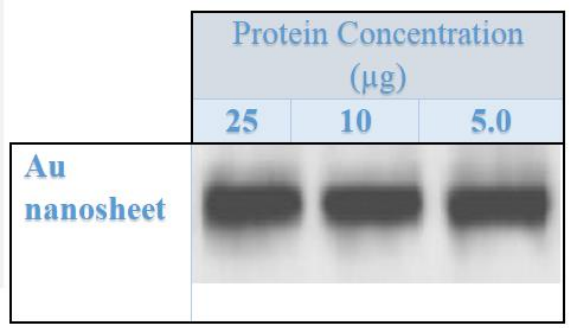


Figure 9: (a) Anticancer activity of Gold nanosheets with silver (Au+Ag nanosheets) in Colorectal cancer, (b) Fluorescence intensity analysis of the three cells (control un dosed cells, cells were incubated several times with 10 mM of Au+Ag nanosheet and 20mM of nanosheets) and (c) Western blot analysis -related proteins was done in comparison to the control group.

4. Conclusion:

In conclusion, the gold nanosheets and the gold and silver particles together were chemically produced using an affordable, fast and safe chemical procedure that does not need to use any harmful chemicals. The nanomaterial has good shapes and structure, according to TEM and SEM device imaging. Furthermore, the UV absorption showed that the surface of the nanoparticles exhibits a visible UV pattern for the absorption and transmission of the gold nanosheets. In addition to the FTIR permeability assay of gold nanoparticles, colorectal cancer cell death has been demonstrated by the nanomaterial. Moreover, these substances were biologically active, destroying microorganisms.

5. Conflicts of interest

"There are no conflicts to declare".

6. Acknowledgments

I would like to extend my sincere thanks to the Physics Department at the College of Science - Al-Mustansiriya University, as well as to everyone who helped me in completing this research paper.

7. References

[1] R. C. Sanfelice *et al.*, "Hybrid composite material based on polythiophene derivative nanofibers modified with gold nanoparticles for optoelectronics applications," *Journal of Materials Science*, vol. 52, no. 4, pp. 1919-1929, 2017.

[2] C. C. Wang *et al*" ,.Optical and electrical effects of gold nanoparticles in the active layer of polymer solar cells," *Journal of Materials Chemistry*, vol. 22, no. 3, pp. 1206-1211, 2012.

[3] H. R. M. Jhong *et al.*, "Gold Nanoparticles on Polymer-Wrapped Carbon Nanotubes :An Efficient and Selective Catalyst for the Electroreduction of CO2," *ChemPhysChem*, vol. 18, no. 22, pp. 3274-3279, 2017.

[4] T. D. Tran, M. T. Nguyen, H. V. Le, D. N. Nguyen, Q. D. Truong, and P. D. Tran, "Gold nanoparticles as an outstanding catalyst for the hydrogen evolution reaction," *Chemical Communications*, vol. 54, no. 27, pp. 3363-3366, 2018.

[5] B. Li *et al.*, "Colorimetric sensor array based on gold nanoparticles with diverse surface charges for microorganisms identification," *Analytical chemistry*, vol. 89, no. 20, pp. 10639-10643, 2017.

[6] M.-M. Chen *et al.*, "Spatiotemporal imaging of electrocatalytic activity on single 2D gold nanoplates via electrogenerated

chemiluminescence microscopy," *Chemical science*, vol. 10, no. 15, pp. 4141-4147, 2019.
[7] A. Plan Sangnier *et al.*, "Photothermal Therapy: Endosomal Confinement of Gold Nanospheres, Nanorods, and Nanoraspberries Governs Their Photothermal Identity and Is Beneficial for Cancer Cell Therapy (Adv. Biosys. 4/2020)," *Advanced Biosystems*, vol ,4 .no. 4, p. 2070042, 2020.
[8] E. Roduner, "Size matters: why nanomaterials are different," *Chemical Society Reviews*, vol. 35, no. 7, pp. 583-592, 2006.
[9] H.-L. Liu *et al.*, "Size-controllable gold nanopores with high SERS activity," *Analytical chemistry*, vol. 89, no. 19, pp. 10407-10413, 2017.
[10] I. H. El-Sayed, X. Huang, and M. A. El-Sayed, "Surface plasmon resonance scattering and absorption of anti-EGFR antibody conjugated gold nanoparticles in cancer diagnostics: applications in oral cancer," *Nano letters*, vol. 5, no. 5, pp. 829-834, 2005.
[11] O. Veiseh *et al.*, "Optical and MRI multifunctional nanoprobe for targeting gliomas," *Nano letters*, vol. 5, no. 6, pp. 1003-1008, 2005.
[12] W. C. Chan and S. Nie, "Quantum dot bioconjugates for ultrasensitive nonisotopic detection," *Science*, vol. 281, no. 5385, pp. 2016-2018, 1998.
[13] S. Al-Musawi, S. Albukhaty, H. Al-Karagoly, and F. Almalki, "Design and Synthesis of multi-functional superparamagnetic core-gold shell nanoparticles coated with chitosan and folate for targeted antitumor therapy," *Nanomaterials*, vol. 11, no. 1, p. 32, 2020.
[14] S. Safat, F. Buazar, S. Albukhaty, and S. Matroodi, "Enhanced sunlight photocatalytic activity and biosafety of marine-driven synthesized cerium oxide nanoparticles," *Scientific Reports*, vol. 11, no. 1, pp. 1-11, 2021.
[15] N. Kohler, C. Sun, J. Wang, and M. Zhang, "Methotrexate-modified superparamagnetic nanoparticles and their intracellular uptake into human cancer cells," *Langmuir*, vol. 21, no. 19, pp. 8858-8864.2005 ,
[16] M. Raffi, F. Hussain, T. Bhatti, J. Akhter, A. Hameed, and M. Hasan, "Antibacterial characterization of silver nanoparticles against E. coli ATCC-15224," *Journal of materials science and technology*, vol. 24, no. 2, pp. 192-196, 2008.
[17] S .R. Banoon and A. Ghasemian, "The characters of graphene oxide nanoparticles and doxorubicin against HCT-116 colorectal cancer cells in vitro," *Journal of Gastrointestinal Cancer*, pp. 1-5, 2021.
[18] A. S. Al-Ragehey, O. A. A. Dakhil, H. Saadoun, A. H. Mohammed, and M. Hassan, "Employment of DC Sputtering for Synthesizing Nano Cadmium Oxide for Sevoflurane Anesthetic Gas Sensor," in *Materials Science Forum*, 2021, vol. 1039: Trans Tech Publ, pp. 406-415 .
[19] L. Al-Hadedee, H. Saadoun, and W. Al-Mashhadani" ,Preparation of nanogold and binding of nisin to increase its effectiveness in inhibiting the positive and negative bacteria," *Iranian Journal of Ichthyology*, vol. 8, pp. 290-299, 2021.
[20] B. Brar *et al.*, "Nanotechnology in Colorectal Cancer for Precision Diagnosis and Therapy," *Frontiers in Nanotechnology*, vol. 3, p. 699266, 2021.
[21] N. H. Aldujaili and S. R. Banoon, "Antibacterial characterization of titanium nanoparticles nano synthesized by Streptococcus thermophilus," *Periodico Tche Quimica (Online)*, vol. 17, no. 34, pp. 311-320, 2020.
[22] C. Su, K. Huang, H.-H. Li, Y.-G. Lu, and D.-L. Zheng, "Antibacterial properties of functionalized gold nanoparticles and their application in oral biology," *Journal of Nanomaterials*, vol. 2020, 2020.
[23] B .M. Elmowafy, A. Abdelghany, R. M. Ramadan, R. Ghazy, and T. Meaz, "Synthesis, structural characterization, and antibacterial studies of new borate 13-93B3 bioglasses with low copper dopant," *Egyptian Journal of Chemistry*, 2022.
[24] M. Abbas and M. S. Alqahtani, "The Potential Role of Nanoparticles as an Anticancer Therapy in the Treatment of Rectal Cancer," *Processes*, vol. 9, no. 12, p. 2172, 2021.
[25] S. Albukhaty *et al.*, "Investigation of dextran-coated superparamagnetic nanoparticles for targeted vinblastine controlled release, delivery, apoptosis induction, and gene expression in pancreatic cancer cells," *Molecules*, vol. 25, no. 20, p. 4721, 2020.
[26] G. Funston, G. Abel, E. J. Crosbie, W. Hamilton, and F. M. Walter, "Could Ovarian Cancer Prediction Models Improve the Triage of Symptomatic Women in Primary Care? A Modelling Study Using Routinely Collected Data," *Cancers*, vol. 13, no. 12, p. 2886, 2021.
[27] A. S. C. De-Souza and T. A. Costa-Casagrande, "Animal models for colorectal cancer," *ABCD .Arquivos Brasileiros de Cirurgia Digestiva (São Paulo)*, vol. 31, 2018.
[28] K. M. Soto, S. Mendoza, J. M. López-Romero, J. R. Gasca-Tirado, and A. Manzano-Ramírez, "Gold nanoparticles: synthesis, application in colon cancer therapy and new approaches-review," *Green Chemistry Letters and Reviews*, vol. 14, no. 4, pp. 665-678, 2021.
[29] D. N. Păduraru *et al.*, "Recent Developments in Metallic Nanomaterials for

Cancer Therapy, Diagnosing and Imaging Applications," *Pharmaceutics,* vol. 14, no. 2, p. 435, 2022.

[30] H. Rashdan, A. Ahmed, H. Okasha, T. Yousef, and M. Krisha, "Synthesis and In-vitro Biological Analyses of New quinazolin-2, 4-dione Derivatives," *Egyptian Journal of Chemistry,* 2022.