Cadmium Sulfide Nanoparticles: Preparation, Characterization, and Biomedical Applications

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Abstract

Background: Colorectal Cancer is the third most commonly diagnosed cancer in males and the second in females in world with continuously increased incidence and mortality. The main treatment for Colorectal Cancer is surgery, generally associated with chemotherapy, and radiation therapy.

Objectives: A prospective study was conducted to primarily investigate the anticancer properties of synthesized cadmium sulfide nanoparticles with three different complex agents on Caco-2 epithelial colon adenocarcinoma. The study also involved comparing the efficacy of nanoparticles versus radiation therapy.

Materials and Methods: Nanoparticles were produced using a wet chemical process and characterized for their physical and chemical properties using X-ray diffraction, scanning electron microscopy, transmission electron microscopy, Fourier-transform infrared spectroscopy, and optical property analysis. The research involved exposing cancerous colon Caco-2 cells to different concentrations of CdS1-NPs, CdS2-NPs, and CdS3-NPs, and combining the nanoparticles with radiation therapy. The cells were treated with three doses over a span of three days, each dose consisting of 80 CGy delivered using an Elekta Precise Linear Accelerator with photons energy at 6 mega volts.

Results: The cadmium sulfide (three different complex agents) are crystallite size (9 -12.59) nm, and energy gap (3.31- 3.86) eV. When used nanoparticles alone CdS1-NPs, CdS2-NPs, and CdS3-NPs killed about 75%, 71%, 79% of cells respectively. But when used nanoparticles and radiation. {Radiotherapy alone, ((CdS1 – NPs, CdS2- NPs, and CdS3-NPs) with radiotherapy)} the death rate of cells is (27.15 %, 90.35%, 69.1%, 58.82%) respectively, as after the third dose.

Conclusion: The current investigation demonstrated that combining nanoparticles with radiotherapy resulted in a more significant effect compared to radiotherapy alone.

Keywords: Colorectal Cancer; Nanoparticles; Cadmium sulfide; Complex agents; Radiation.

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Introduction

Cancer is the leading cause of death, where incidence and mortality are rapidly growing worldwide, and a major public health problem in 2020 **(Siegel et al., 2023; Oh et al., 2020).**

Cancer resulting from genetic mutation because it is a complex disease , in Europe it is the most common cause of death and in the USA it is second leading cause of death, following the cardiovascular diseases **Xie et al. (2021).**

The most common cancer treatments are restricted to chemotherapy; radiation and surgery **Igarashi et al. (2020).**

Colorectal cancer (CRC) is the third most prevalent type of cancer worldwide. It is also the second most common cause of cancer-associated mortality; it accounted for about 9.2% of all cancer deaths in 2018**(Li et al., 2021; Bray et al., 2018**).

CRC has been the prevalence dramatically growing at an alarming rate globally in recent years. Where CRC accounts for 10% of global cancer incidence and 9.4% of cancer deaths, in 2020, the main treatment for CRC is surgery, generally associated with chemotherapy, radiation therapy and combination therapy **Xi et al. (2021)**.

CRC is starts in the colon or the rectum. Colon Cancer depends of where they start. Most colon cancer start as growth on the inner of the colon is called polyps. Some polyps can change with time becomes cancer (adenocarcinoma), this depend on types of polyps. Colon cancer is one of the most frequent types of cancer, with a higher incidence in the developed countries **Sawicki et al. (2021).**

The most important treatments used in CRC cancer are surgery, chemotherapy, radiation therapy, biologic therapy, immunotherapy, and it can be used treatment surgery alone ,or surgery and radiotherapy or chemotherapy with surgical. In radiation therapy X-rays or other radiation methods are used to exterminate carcinogenic cells. **(Biller et al., 2021; Marley et al., 2016; Millan et al., 2015; Wolpin et al., 2007).**

Radiation therapy is used in the treatment of cancer, but it has side effects as it affects cancer cells as well as healthy cells. In recent years, nanotechnology is the promise of cancer treatment. Nanotechnology is a fast growing field of science rapidly entering into medical science. Nanotechnology is defined as the application science, engineering, and technology conducted at the nano scale using materials of size ranging from 1 to100nm. At the nano scale, materials can possess characteristics that differ from their bulk state, expanding the use of such materials for various biomedical applications. Such applications include drug delivery; bio imaging and phototherapy, in addition to various other clinical, diagnostic and therapeutic applications **(Ansari et al., 2022; Nikazar et al., 2020)**.

Cancer cells could be targeted by nanoparticles as they are very small, where they could penetrate endothelial wall of the blood vessels into the tumor tissue. Thus, the toxicity of the nanoparticles is concentrated in cancer cells without healthy cells **Das et al. (2023).**

Cadmium is renowned for its exceptional electrical conductivity and corrosion resistance. Within the semiconductor group II-VI, CdS-NPs exhibit extraordinary optical and fluorescent properties, along with a wide band gap. These distinctive attributes render CdS-NPs highly suitable for a range of applications, encompassing optical and electrical devices, cancer therapy, diagnosis, biosensors, bio-imaging, nano-

medicines, molecular pathology, drug delivery, and photovoltaic cells **Rose et al (2021), Munyai et al (2021).**

Extensive studies have been conducted on the potential biological uses of cadmium sulfate nanomaterials (CdS NPs). These remarkable nanoparticles have demonstrated promising applications in various fields such as imaging, drug delivery, diagnosis, treatment, sensors, and antibacterial devices. One notable area where CdS NPs have shown potential is in anti-cancer research. Several studies, including those by **Ghasempour et al (2023), and Akhtar et al (2020)**, have observed that cell death might be attributed to the generation of reactive oxygen species (ROS) or the release of internal cadmium ions (Cd+2) from CdS NPs into the cellular environment.

Cadmium sulfide (CdS) nanomaterials have demonstrated their potential in various bioimaging applications. In a study conducted by **Harish et al. (2020),** cadmium coated with Chitosan was used, and it was found that chitosan-coated CdS NPs reduced the toxicity of cadmium sulfide nanoparticles while retaining their fluorescent properties in Human Jurkat and erythrocyte cell lines.

Another research by **Nasrin et al. (2022)** involved the synthesis of CdS nanoparticles (CdS NPs) and their application in lung cancer cells (A549). The study revealed that CdS NPs induced cell death in lung cancer cells, highlighting their potential in combating this type of cancer.

Furthermore,**Shivashankarappa et al. (2020)** investigated the cytotoxic effects of CdS nanoparticles on Mus musculus skin melanoma (B16F10) and human epidermoid carcinoma (A431) cell lines. The results demonstrated that CdS nanoparticles exhibited superior cytotoxic activity against the cells compared to an anticancer drug.

In another study by **Alsaggaf et al. (2020)**, CdS NPs synthesized using green synthesis were employed for cancer treatment in breast cancer (MCF7), lung cancer (A549), and prostatic carcinoma (PC3). The observed cell death could be attributed to the generation of reactive oxygen species (ROS) or the release of internal cadmium ions (Cd+2) from CdS NPs into the cell medium.

Bioimaging Application, Fluorescence imaging is a highly effective modality for obtaining high-contrast and high-resolution images. Among the extensively studied fluorescent materials, CdS NPs have gained significant attention. These nanoparticles possess the ability to readily enter cells through pinocytosis and endocytosis. However, their use in vivo is limited due to their high toxicity, as highlighted by studies conducted by **Naranthatta et al (2021**), **Stavitskaya et al (2018)**.

Órdenes-Aenishanslins et al. (2020) employed CdSAg NPs synthesized through green synthesis using E. coli. With CdS NPs measuring 5.49 nm and CdSAg NPs measuring 7.20 nm in size, they successfully utilized these nanoparticles for fluorescence imaging on HeLa cells.

Antimicrobial Activity**,** CdS nanoparticles have demonstrated antimicrobial properties, particularly against microorganisms that exhibit resistance. **León-Buitimea et al (2020)** conducted research highlighting the antimicrobial activities of CdS nanoparticles. In a study by **Calvo-Olvera et al (2021)**, CdS quantum dots (QDs) were synthesized using both chemical and green methods (Fusarium oxysporum f. sp. lycopersici). The biogenic CdS QDs had a spherical shape with a size of 4.08 ± 0.07 nm, while the chemical

CdS QDs measured 3.2 ± 0.20 nm. Employing the well-diffusion method against E. coli bacterial cells, the researchers found that biogenic CdS QDs exhibited a lower lethality compared to chemical CdS QDs. The concentration of nanoparticles inversely correlated with cell viability, indicating their potential antimicrobial effect.

The objective of this study is threefold. Firstly, it aims to prepare nanoparticles using cadmium sulfide (CdS) through three different methods involving complex agents. Secondly, the properties of these nanoparticles will be investigated, specifically focusing on the differences in size, shape, surface characteristics, and energy gap. Lastly, the study seeks to examine the impact of these nanoparticles on colon cancer Caco-2 cells, evaluating their toxicity towards the cells. Additionally, the study will utilize a linear accelerator to investigate the effects of radiation on Caco-2 cells. Furthermore, it aims to explore the combined effects of nanoparticles and radiation on the behavior of Caco-2 cells.

Materials and Methods

Materials

To prepare the different CdS nanoparticles we used: Thiourea (CH_4N_2S) 99% (Sigma) as a source of Sulfate. Cadmium Acetate dehydrate $Cd(CH_3COO)_2.2H_2O$ (Baker) as a source of Cadmium. Ammonium hydroxide (NH_4OH), and Sodium hydroxide pellets (NaOH) (Panreac) as a source of complex agent.

Preparation of nanoparticles: Nanoparticles of CdS-NPs were prepared as described by **(Pandian et al., 2021; Lin et al., 2017).** The preparation process involved several steps. Firstly, we prepared the Cadmium Acetate Solution by dissolving 6.66324g of Cadmium Acetate in 50ml of distilled water. Next, the Thiourea Solution was prepared by dissolving 1.903g of Thiourea in 50ml of distilled water. Additionally, we prepared the complex agents using the following methods:

1. NaOH solid: 2g of NaOH was added to 100ml of distilled water.
2. NaOH solid + NH_4OH solution: 2g of NaOH was added to 100ml of NH_4OH solution and 100ml of distilled water.
3. NH_4OH solution: 100ml of NH_4OH was used.

To create three different types of CdS nanoparticles (CdS-NPs), the following mixtures were prepared:

1. CdS1-NPs: Cadmium Acetate Solution + Thiourea Solution + complex agent NaOH were combined and thoroughly mixed.
2. CdS2-NPs: Cadmium Acetate Solution + Thiourea Solution + complex agents NaOH + NH_4OH were mixed together.
3. CdS3-NPs: Cadmium Acetate Solution + Thiourea Solution + complex agent NH_4OH were mixed.

The mixed solutions were then subjected to magnetic stirring until a yellow color appeared, indicating the formation of nanoparticles (CdS1-NPs, CdS2-NPs, and CdS3-NPs).

The reaction mixture was cooled down to room temperature, then centrifuged for 15 min and washed with of high purity acetone for effective removal of impurities. The final product was dried at 50°C-70°C until completely dry show in (**Fig .1).**

Characterization of synthesized Nanoparticles: Precisely characterizing of the nanoparticlesin terms of their size, shape, composition, surface area, and disparity is very important .This is done through Different analytical and spectroscopic techniques (**Zamani Kouhpanji et al., 2020; Komaraiah et al., 2019**).

Where the crystal structure of the **CdS NPs** was analyzed with X-ray diffraction, the size and surface morphology was characterized by scanning electron microscopy and transmissions electron microscopy (SEM, TEM), the functional group analysis was done by fourier transforms infrared (FTIR), and the absorption spectra were recorded by a UV–Vis spectrophotometer **(Chandraker et al., 2021; Dawadi et al., 2021; Alsaggaf et al., 2020).**

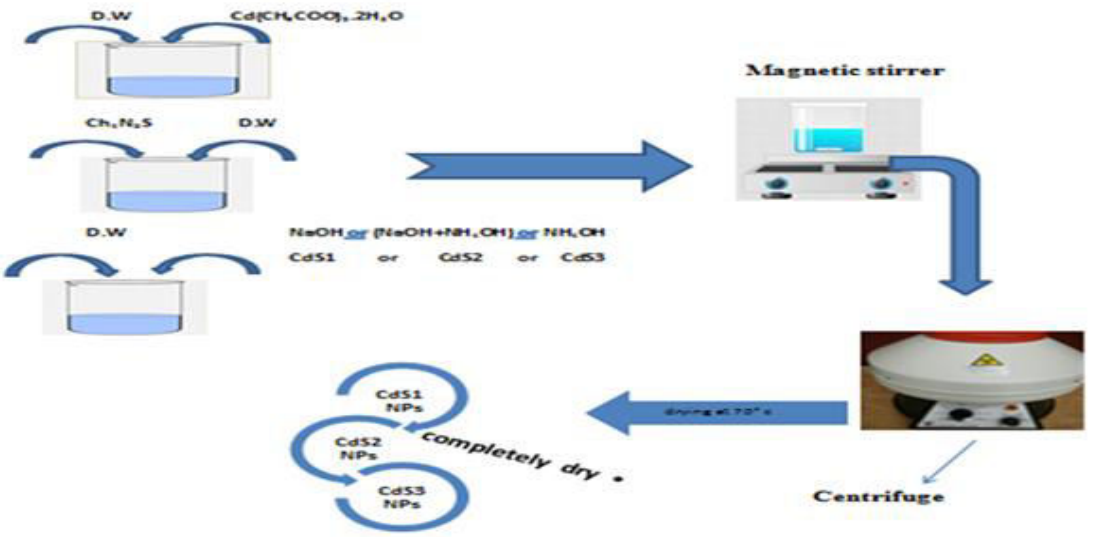


Fig. 1. Preparation procedure of different CdS-NPs.

Cell Culture

Caco-2 epithelial human colon adeno carcinoma from the serum and vaccine lab in Cairo, media (Dulbecco's Modified Eagle Medium) (MDEM), sodium bicarbonate, Trypsin-EDTA(1X) 0.25% (gibco, UK) , Fetal Bovine Serum(FBS), Phosphate Buffered Saline (PBS), Trypan Blue0.5% solution (biowest), Ethanol 70%, nanoparticles.

In Vitro

1- Effect of CdS nanoparticles alone with Caco-2 cells using Trypan Blue Study:

To investigate the in vitro nanoparticles effects of CdS nanoparticles **(CdS1-NPs, CdS2-NPs, and CdS3-NPs**), Caco-2 cells were cultured (1×10^5 cells/ml) in a 48-well plate with 1 ml of DMEM media for 24 h at 37°C. For the experimental study, the experiment was divided into 2 groups:

- **The first group** contained the Caco-2 culture medium only (control group).
- **The second group** contained various concentrations of **CdS1-NPs, CdS2-NPs, CdS3-NPs** (10, 15, 20, 25, and 30 µg/ mL) in Caco-2.

The control and the experimental groups, cells were incubated for 24 h.

2- Effect nanomaterials and radiation therapy with Caco-2 cell-line using Trypan Blue Study: To investigate the *in vitro* radiation therapy and nanoparticles effects of CdS1-NPs, CdS2-NPs, CdS3-NPs, we used radiation therapy (three doses over three days, each dose 80 CGy), at room temperature with a linear accelerator using (photons) energy = 6

Mega Volte a dose rate of 80 CGy and time/muontry unit = 90 Mu with used water solid 5 cm SSD (The distance between the source and plate) = 100cm, Caco-2 cells were cultured (1×10^5 cells/ml) in a 48- 24 well plate with 1 ml of DMEM media for 24 h at 37°C after doses three days each dose after 24 h.

For the experimental study, the experiment was divided into 3 groups:

The first group contained the Caco-2 culture medium with **Radiation therapy** (dose 80 CGy, 3 days of dose) only (control group).

The second group contained various concentrations of **CdS1 NPs** (10µg/ mL) with radiation therapy (dose 80 CGy, 3 days of dose) in Caco-2.

The third group contained various concentrations of **CdS2-NPs, CdS3-NPs** (25 µg/ mL) with radiation therapy (dose 80 CGy, 3 days of dose) in Caco-2.

The control and the experimental groups, cells were incubated for 24 h after each dose.

After 24 hours from incubation of all treatment, in **Fig 3 (c) Fig 4 (b)** show the cell viability was calculated by using the following equation:

Cell Viability= (total viable cells)/ (total cells (viable + dead) x100

Statistical analysis

Data was collected, coded, revised, and entered into the Statistical Package for Social Science (IBM SPSS) version 27. The data were presented as mean, and standard deviations, for the numerical variables. **One-way ANOVA** compares more than two groups with quantitative data and parametric distribution, followed by post hoc test using Bonferroni correction for pairwise comparison.

The allowable margin of error was set at 5%, while the confidence interval was set at 95%. Consequently, the p-value was deemed significant as follows:

- P > 0.05: Non-significant (NS)
- P < 0.05: Significant (S)
- P < 0.01: Highly significant (HS)

Results

(Tables 1 and 2) show a statistically significant difference between nanoparticles concerning cell viability at concentrations of 10 µM, 15 µM, and 20 µM (p-values = 0.032, 0.026, and 0.014, respectively). So, the post hoc test with Bonferroni correction was done to determine the nature of the difference between the three types of nanoparticles. Cancer cell viability at 10 µM was significantly lower with CdS 1 than with CdS 3 (72.06 ± 1.28 vs. 87.083 ± 0.58, respectively, p-value = 0.043). Cancer cell viability was significantly lower with CdS 2 than with CdS 3 (64.583 ± 2.94 vs. 76.38 ± 1.96, respectively, p-value = 0.034). Cancer cell viability with CdS 1 was significantly higher than with CdS 2 and CdS 3 (55.736 ± 1.44 vs. 41.319 ± 3.43 and 40.064 ± 2.26, respectively, p-values = 0.032 and 0.025).

Table 1. Cell viability at different concentrations of nanoparticles

Cell viability (%)	Nanoparticles			P value
	Mean ± Standard deviation			
	CdS 1	CdS 2	CdS 3	
At 10 µM	72.06 ± 1.28	81.56 ± 4.86	87.083 ± 0.58	**0.032***
At 15 µM	69.439 ± 0.97	64.583 ± 2.94	76.38 ± 1.96	**0.026***

At 20 µM	55.736 ± 1.44	41.319 ± 3.43	40.064 ± 2.26	**0.014***
At 25 µM	44.58 ± 5.93	30.465 ± 5.86	36.94 ± 2.74	**0.147**
At 30 µM	28.37 ± 4.17	30.0 ± 4.71	21.206 ± 1.7	**0.187**

*One-way ANOVA, CdS: cadmium sulfide

Table 2. Pairwise comparison of cell viability at different concentrations of nanoparticles

Group pairs	Mean difference	P value
At 10 µM		
CdS 1 vs. CdS 3	-15.019923	0.043*
CdS 1 vs. CdS 2	-9.49909	0.143
CdS 2 vs. CdS 3	-5.520833	0.466
At 15 µM		
CdS 1 vs. CdS 3	-6.9489538	0.140
CdS 1 vs. CdS 2	4.8566017	0.318
CdS 2 vs. CdS 3	-11.80555	0.034*
At 20 µM		
CdS 1 vs. CdS 3	15.672766	0.025*
CdS 1 vs. CdS 2	14.4174245	0.032*
CdS 2 vs. CdS 3	1.2553418	1.00

*Post-hoc test

(Tables 3 and 4) show a statistically significant difference between radiotherapy and nanoparticles concerning cell viability after 1st, 2nd, and 3rd doses (P values = 0.002, 0.003, and < 0.001, respectively). So, the post hoc test with Bonferroni correction was done to determine the nature of the difference between radiotherapy and different types of nanoparticles. Cancer cell viability after the 1st dose was significantly lower with CdS 3 compared to CdS 1, CdS 2, and radiotherapy (50.516 ± 1.88 vs. 75.35 ± 4.97, 80.61 ± 2.88, and 90.4025 ± 3.77, respectively, p values = 0.013, 0.006, and 0.002, respectively). Cancer cell viability after the 2nd dose was significantly lower with CdS 3 compared to CdS 2 and radiotherapy (42.665 ± 1.03 vs. 68.96 ± 8.01 and 77.1186 ± 1.198, respectively, p values = 0.020 and 0.007). Cancer cell viability after the 3rd dose was significantly lower with CdS 1 compared to CdS 2, CdS 3, and radiotherapy (9.658 ± 3.31 vs. 30.94 ± 1.97, 41.83 ± 2.37, and 73.4301 ± 1.07, respectively, p values = 0.005, <0.001, and <0.001, respectively).

Table 3. Impact of radiotherapy and nanoparticles on cancer cell viability

Cell viability (%)	Nanoparticles and radiotherapy				P value
	Mean ± standard deviation				
	Radiotherapy	CdS 1	CdS 2	CdS 3	
After 1st dose	90.4025 ± 3.77	75.35 ± 4.97	80.61 ± 2.88	50.516 ± 1.88	0.002*
After 2nd dose	77.1186 ± 1.198	47.46 ± 1.85	68.96 ± 8.01	42.665 ± 1.03	0.003*
After 3rd dose	73.4301 ± 1.07	9.658 ± 3.31	30.94 ± 1.97	41.83 ± 2.37	< 0.001*

*one-way ANOVA

Table 4. Pairwise comparison of cell viability among radiotherapy and nanoparticles

Group pairs	Mean difference	P value
After the first dose		
Radiotherapy vs. CdS 1	15.05046531	0.081
Radiotherapy vs. CdS 2	9.79033310	0.310
Radiotherapy vs. CdS 3	39.88648814	0.002*
CdS 1 vs. CdS 2	-5.26013221	1.00
CdS 1 vs. CdS 3	24.83602282	0.013*
CdS 2 vs. CdS 3	30.09615504	0.006*
After the second dose		
Radiotherapy vs. CdS 1	29.65147709	0.013*
Radiotherapy vs. CdS 2	8.15383508	0.739
Radiotherapy vs. CdS 3	34.45278892	0.007*
CdS 1 vs. CdS 2	-21.49764201	0.041*
CdS 1 vs. CdS 3	4.80131183	1.00
CdS 2 vs. CdS 3	26.29895384	0.020*
After the third dose		
Radiotherapy vs. CdS 1	63.77157094	<0.001*
Radiotherapy vs. CdS 2	42.48971559	<0.001*
Radiotherapy vs. CdS 3	31.59210812	0.001*
CdS 1 vs. CdS 2	-21.28185536	0.005*
CdS 1 vs. CdS 3	-32.17946283	<0.001*
CdS 2 vs. CdS 3	-10.89760747	0.057*

*Post-hoc test

Fig.2(a) shows the XRD pattern of the CdS NPs synthesized by the complex agents {**CdS1-NPs, CdS2-NPs, and CdS3NPs**}. Peaks of the XRD patterns of **CdS1-NPs** are in good agreement with the six peaks with 2θ values of 26.383°, 31.253°, 43.9°, 51.579°, 54.9° and 70.924° corresponding to the (111), (200), (220), (311), (222) and (331). But **CdS2-NPs** shows six peaks with 2θ values of 26.87º, 31.79º, 44.27º, 51.7º, 55.52º, and 65.72º, corresponding to the (1 1 1), (2 0 0), (2 2 0), (3 1 1), (2 2 2), and (4 0 0). The results showed that fine, intense peaks can be indexed as the cubic phase of CdS1-NPs and CdS2-NPs, and the diffraction data were in good agreement with No. (01-080-0019) **Singh et al. (2009).**

But **CdS3-NPs** shows five peaks with 2θ values of 26.9°, 31.9°, 44.54°, 51.926°, and 55.474° corresponding to the (1 1 1), (0 0 2), (0 2 2), (1 1 3) and (2 2 2) crystal planes of CdS3-NPs, respectively (JCPDS card No. 01-001-0647) **Devi et al. (2022).**

The broadening of the peaks indicates that the nanocrystalline nature of the material, and the crystallite sizes are 9–12.59 nm from XRD analysis.

Fig .2 (b) shows the TEM images of CdS NPs. According to the obtained TEM, irregular spherical CdS-NPs with a highly crystalline structure were observed in samples synthesized by using different complex agents and found to be different in size with different complex agents.

Fig. 2(c) shows the SEM analysis for the morphology of CdS-NPs for different complex agents observed under the SEM that is presented. The effect of the different complex agents on the surface of the materials was found; **CdS1-NPs** indicates the formation of nanoclusters and is

mostly triangle-shaped **Shivashankarappa et al. (2015).**

But **CdS2-NPs** and **CdS3-NPs** spherical particles also have a uniform semispherical morphology and size **(Alani et al., 2022; Khan et al., 2019).**

Fig. 2(d) shows the FT-IR spectrum observed for the **CdS1-NPs** with broad bands at 3421.1, 2358.51, 2155.06, 1539.88, 1455.99, 1004.73, 858.16, and 651.82 cm^{-1}. **CdS2-NPs** have broad bands at 3360.35, 2363.33, 2134.81, 1663.3, 1557.23, 1410.67, 1049.08, 1018.23, 937.23, 850.45, and 652.78 cm, however, but **CdS3-NPs** have broad bands at 3432.67, 2942.84, 2145.41, 1999.82, 1624.73, 1398.13, 1167.68, 859.13, and 652.78 cm^{-1}.

(**Table. 5**) shows the effect of particle size on the Energy gap (Eg) at different complex agents for CdS-NPs. Eg depends on particle size; a decrease in particle size leads to an increase in Eg.

The anticancer activity of the synthesized nanoparticles against the Caco-2 epithelial human colon adenocarcinoma cell line indicates that after 24 hours of treatment with different formulations of CdS1-NPs, CdS2-NPs, and CdS3-NPs, these materials were effective and could act as anticancer agents.

Fig 3(a) shows the viable cells with concentrations of nanoparticles (0µM, 10µM, 15µM, 20µM, 25µM, 30µM). control is 0µM (cells which are non-nanoparticles), In this study, it was found that CdS1-NPs had killed about 71.65% of cells at a concentration of 30 µM, which is the highest concentration, CdS2-NPs had a cell death rate of 70% while CdS3-NPs had a cell death rate of 78.7% .

Fig. 3(b) shows the cell with highest concentration (30µM) of nanoparticles. The higher the concentration of nanoparticles, the less living cells. It was found that CdS3-NPs have more effect on cells than other nanoparticles.

Fig. 3 (C) shows the concentration of nanoparticles in cells; increasing the concentration of nanoparticles leads to increased cell death. The different sizes and energy gaps of CdS1-NPs, CdS2-NPs, and CdS3-NPs led to a difference in the rates of viable cells by 1:25. When using nanoparticles at concentrations of 10, 15, 20, 25, and 30 µM on Caco-2 cells, it was found that the higher the concentration of nanoparticles, the higher the death rate of cells **Liu et al. (2017).**

Table 5. The effect of particle size on the Eg at different complex agents for CdS-NPs.

samples	Particle size	Eg (ev)
CdS1-NPs	9.83 nm	3.86
CdS2-NPs	12.127 nm	3.31
CdS3-NPs	12.59 nm	3.34

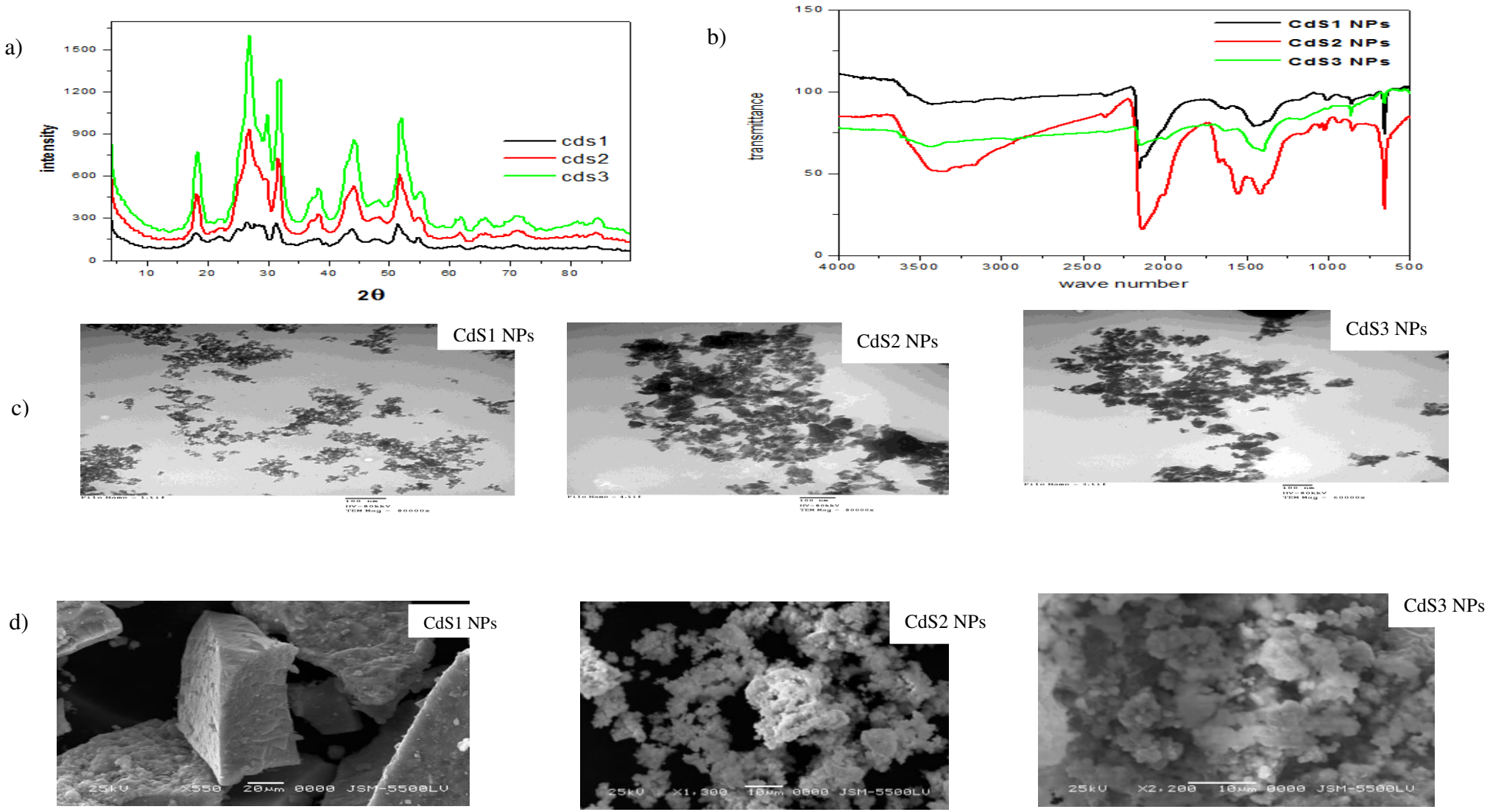


Fig 2. **(a)** XRD for CdS-NPs **(b)** FT-IR spectra for different complex agents CdS-NPs **(c)** TEM images of synthesized CdS-NPs **(d)** SEM for CdS- NPs

On the other hand, when nanoparticles used with radiation, it was found it had a greater effect than radiotherapy alone.

Fig 4(a) shows viable cells with nanoparticles **CdS1-NPs** at a concentration of approximately 10µM, while **CdS2-NPs** and **CdS3-NPs** at a concentration of approximately 25µM.
In this study, after the third dose of radiotherapy(when used alone), the death rate of cells was 26.57%, which is a very small percentage compared to nanoparticles and radiation therapy together as follow;
-after the third dose of radiotherapy when used with **CdS1-NPs**, death rate of cells was about 90.35%, although its concentration was only 10 µM.
-While when used with CdS2-NPs and CdS3-NPs at a concentration of 25 µM; the death rate of cells was about 69.1% and 58.16% respectively.

Fig 4 (b) shows the concentration of a different nanoparticles used with radiation doses for treatment Caco-2 (colon adenocarcinoma)and percentage of viable cells after each dose **(CdS1-NPs** concentration of 10 µM)**, (CdS2-NPs and CdS3-NPs** concentration of 25 µM) . It was found that **CdS1-NPs** after the third radiation dose had more toxicity on cancer cells than **CdS2-NPs** and **CdS3-NPs** .

Discussion

CdS-NPs were prepared using three different complex agent CdS1-NPs (complex agent NaOH), CdS2-NPs (complex agent NaOH+NH_4OH), and CdS3-NPs (complex agent NH_4OH).

X-ray diffraction measurements were performed to examine the crystalline structure of CdS1- NPs, CdS2- NPs, and CdS3- NPs.

The Broadening of the peaks indicates the nanocrystalline nature of the material and the crystallite sizes are 9 - 12.59 nm from XRD analysis **Dumbrava et al. (2010)**.

The agglomerations of the contiguous crystals help restrict the particle size to nanoscale range. As a result, the XRD peak intensity decreases and the width of the peak increases with decreasing crystallite size **Ramrakhiani et al. (2013).**

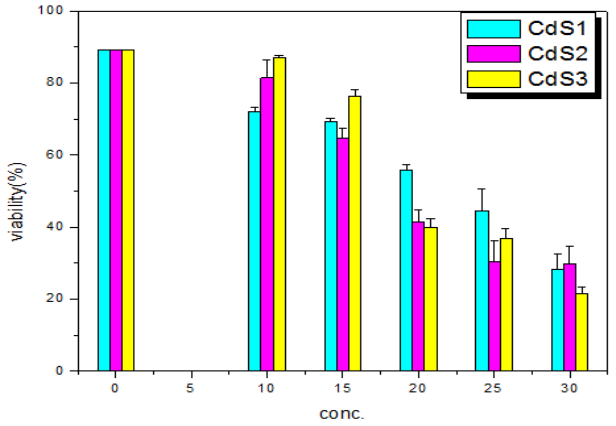
And the results showed fine intense peaks can be indexed as the cubic phase of **CdS1-** NPs, CdS2-NPs and the diffraction data were in good agreement with No.(01-080-0019) **Singh et al. (2009)**, and CdS3-NPs and the diffraction data were in good agreement with No. (00-001-0647) **Devi et al. (2022)**.

CdS1-NPs, CdS2-NPs and CdS3-NPs can be observed that these peaks correspond to the (111), (200), (220), (311) crystal planes of the CdS of the cubic sphalerite structure like search **Khalid et al. (2021).**
One peak (0 0 2) in the hexagonal phase, possibility to be **CdS-NPs** at this position shows the formation of cubic and hexagonal phase **Tangsiri et al. (2020); Riaz et al. (2020)**.

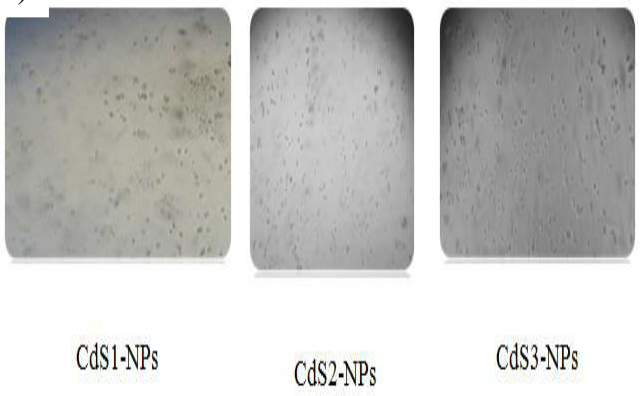
However, the XRD results overestimated the size of the nanoparticles, this disagreement in the results from two different techniques is justifiable because the XRD line broadening does not take into account other factors such as lattice defects and strain **Rao et al. (2017)**.

Since TEM is the best way to investigate nanoparticles size and shape, it was employed to obtain direct information about the size of the produced CdS-NPs different complex agent.

a)



b)

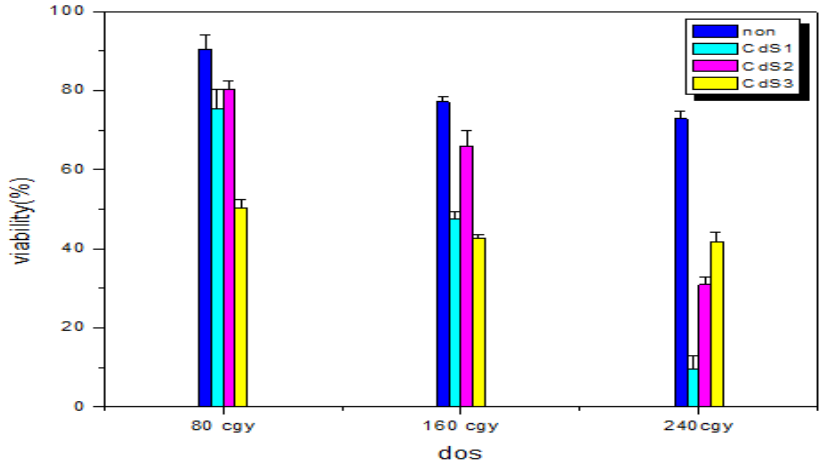


c)

Conc.	10µM	15 µM	20 µM	25 µM	30 µM
CdS1-NPs	72.02%	69.37%	55.7%	44.59%	28.35%
CdS2-NPs	81.5%	64.6%	41.35%	30.45%	30%
CdS3-NPs	87.08%	76.38%	40.06%	36.9%	21.21%

Fig. 3. (a).The viable cells with concentration of nanoparticles (0µM, 10µM, 15µM, 20µM, 25µM, 30µM), 0µM control (cells non nanoparticales). (b) The cells with high concentration (30µM) of nanoparticles, and (c)Table show The viable cells with concentration of nanoparticles (10µM, 15µM, 20µM, 25µM, 30µM)

a)



b)

Conc.	80CGy one day	80CGy second day	80CGy third day
non	90.4	77.12	73.43
CdS1-NPs	75.3%	47.47%	9.65%
CdS2-NPs	80.6%	68.96%	30.9%
CdS3-NPs	50.51%	42.66%	41.84%

Fig .4. (a). The viable cells with nanoparticles CdS1-NPs with conc.10µM, but CdS2-NPs, CdS3-NPs, conc.25µM and doses. And (b) Table show the viable cells with nanoparticles CdS1-NPs with conc.10µM, but CdS2-NPs, CdS3-NPs, conc.25µM and doses.

According to the obtained TEM irregular spheric CdS -NPs with the highly crystalline structure was observed in samples synthesized by using different complex agent, and TEM found different in size with CdS-NPs different complex agent. Similar results were also obtained by **Shivashankarappa et al. (2015).**

The SEM analysis conducted on CdS1-NPs, CdS2-NPs, and CdS3-NPs revealed distinct morphologies of CdS-NPs influenced by the complex agents used. Specifically, the SEM images of CdS1-NPs indicated the formation of nanoclusters, predominantly appearing in a triangular shape. These findings align with a study conducted by **Shivashankarappa A et al. (2015),** which focused on SEM analysis of CdS nanoparticles with varying ratios of cadmium chloride and sodium sulfide (1:1, 2:1, 3:1, and 4:1).

The SEM analysis of CdS2-NPs and CdS3-NPs revealed the presence of spherical particles with a uniform semispherical morphology and size. These observations are consistent with the findings reported by **Alani et al (2022), Khan et al (2019), and Sabah et al (2010)** in their respective studies. **Alani Ret al. (2022)** investigated CdS nanoparticles synthesized from cadmium chloride and sulfur S, while **Khan A et al (2019)** examined Gd-doped CdS nanoparticles. **Sabah et al. (2010)** focused on SEM analysis of CdS nanoparticles prepared from cadmium sulfate and thioacetamide. The agreement between the observed morphologies in our study and the findings of these previous works supports the consistency and reliability of the results.

The FT-IR spectra were used to identify the possible functional biomolecules responsible for CdS1-NPs, CdS2- NPs, and CdS3 -NPs.

According to the obtained FT-IR data, curves of CdS-NPs are nearly similar. The strong band at 3432.67 – 2942.84 cm^{-1} in all samples related to (-OH) groups stretching. While 2363.33 - 2358.51cm^{-1} were due to the stretching of a -CH (alkane) group. But Bands at 1663.3 – 1539.88 cm-1 appeared due to C=C stretching. The bands at 1167.68 – 1004.73 were due to the responsible for C-O-C stretching of acetyl group present or can be assigned to the C- N stretching vibrations of the aromatic and aliphatic amines, while the band at 652.78-651.82 cm^{-1} is due to CdS bond. The findings presented in this study align with the research conducted by **Liu et al., (2023)**, which examined the impact of UV-irradiated CdS nanoparticles (NPs) derived from a cadmium thiosulfate complex on the photocatalytic degradation of dyes. Similarly, the results are consistent with the work of **Sheng et al., (2023)**, where CdS nanoparticles were synthesized through precipitation and subsequently subjected to thermal treatment at 320 °C. The pH response was also investigated in their study.

UV-Vis spectrometry was employed to characterize the photocatalytic property for nanoparticles **(Rao et al., 2017; Liu et al., 2012).**

According to the obtained data, the optical absorption is found to decrease with increasing wavelength for all samples. The optical band gap was found to be 3.86, 3.31 and 3.34 eV for CdS1-NPs, CdS2-NPs and CdS3-NPs respectively. The band gaps value of CdS1-NPs higher other nanoparticles.

During the research conducted by **Varmazyari et al. (2020),** CdS-NPs were found to have an average size ranging from 8 to 25 nm, with an energy gap of 2.02 eV. However, in a separate study conducted by **Ullah et al. (2021),** the size range of CdS nanoparticles synthesized using an extract of the plant Dicliptera Roxburghiana was reported to be between 2.5 and 8 nm. Additionally, the band gap of these nanoparticles was measured to be 3.31 eV. These findings highlight the variability in size and energy gap values depending on the synthesis method and

materials used, as evidenced by the different research studies.

The size and morphology of CdS nanoparticles were examined by SEM analysis. The images were analyzed for all samples which showed the presence of nanoparticles **(Shivashankarappa et al., 2015; Rajeshkumar et al., 2014).**

The agglomerations of the contiguous crystals help restrict the particle size to nanoscale range. As a result, the XRD peak intensity decreases and the width of the peak increases with decreasing crystallite size **Salem et al. (2017).**

The optical band gap energy increase when decrease size particle **(Salam et al., 2018; Zhang et al., 2020).**

Zhang et al. (2020) corroborated the understanding that the energy gap (Eg) of CdS nanoparticles falls within the range of 2.7 to 5.5 eV when synthesized using alternative methods. This finding aligns with other studies that have also reported similar energy gap values for CdS nanoparticles utilizing different synthesis techniques.

The results indicate that the size and properties of cadmium sulfide (CdS) nanoparticles vary depending on the complex agent used. Specifically, the size of CdS1-NPs synthesized with the complex agent NaOH is smaller compared to CdS2-NPs synthesized with the combination of NaOH and NH4OH as the complex agent. Additionally, CdS3-NPs synthesized with the complex agent NH4OH exhibit their own distinct size characteristics. These findings highlight the influence of different complex agents on the size variations observed in CdS nanoparticles.

The size range typically associated with quantum dots is 1-10 nm. Hence, the CdS1-NPs synthesized with the complex agent NaOH can be classified as quantum dots due to their size. In this case, the size of CdS1-NPs is specifically measured as 9.83 nm, and the energy gap is determined to be 3.86 eV. This finding is in agreement with the research conducted by **Kumar et al (2020)** on CdS nanoparticles capped with glucose, where similar size and energy gap values were reported.

TEM analysis of CdS1-NPs revealed a smooth and spherical morphology, which was consistent with the sizes measured. The average particle size was estimated to be between 5 and 10 nm, indicating that they can be classified as quantum dots. These findings align with the research conducted by **Gopi et al (2021),** who performed TEM analysis on CdS quantum dots (QDs) and reported similar size ranges and morphological characteristics.

The investigation focused on CdS nanoparticles synthesized using three different complex agents aimed to understand how a simple change in the synthesis process could impact the properties of CdS-NPs. The results demonstrated that altering the complex agent used in the synthesis of Cadmium sulfide led to significant variations in the properties of CdS nanomaterials, including changes in size, shape, and energy gap. This finding highlights the sensitivity of CdS nanoparticles to the choice of complex agent, emphasizing the importance of careful selection in tailoring their desired properties.

One of the important applications of nanoparticles used in cancer treatment; we will use (CaCo2) colon cell line with nanoparticles and also radiation therapy as well as both.

Regarding treatment Caco-2 (colon adenocarcinoma) with nanomaterials, when using nanomaterials at concentrations of (10, 15, 20, 25, 30 µM) on Caco-2 cells, it was found that the higher the concentration of nanomaterials, which leads to the death of more and more cells. This is evidence that there is toxicity of the nanomaterials used (CdS1-NPs, CdS2-NPs, and CdS3-NPs) on Caco-2 cells, but in varying degrees. With the highest concentration of (30Mm), When using nanoparticles at concentrations of (10, 15,20,25,30 µM) on Caco-2 cells, it

was found that the higher the concentration of nanoparticles, which leads to the death of more and more cells. In studies conducted by **Ziental et al (2020)** and **Talarska et al. (2021)**, the use of nanoparticles at various concentrations (10, 15, 20, 25, 30 µM) on Caco-2 cells, EMT6 and HeLa cells, and human hepatocellular carcinoma cells (HepG2) respectively, revealed a concentration-dependent increase in cell death, indicating the toxic effects of the nanoparticles (CdS1-NPs, CdS2-NPs, CdS3-NPs, MCZnPc-TiO2, and silver nanoparticles) on the respective cell lines. Additionally, a decrease in cell viability and an increase in apoptosis were observed with higher nanoparticle concentrations.

Furthermore, in a study by **Martins (2022),** silver nanoparticles (Au NPs and BBN-Au NPs) were utilized at different concentrations (50, 200, 400 µM) in combination with radiation at doses of 2 and 10 Gy on the BxPC-3 pancreas cell line. After 24 and 72 hours, it was observed that the nanoparticles enhanced cell death by 20 to 30% at concentrations of 50 and 200 µM, with a radiation dose of 2 Gy. These findings suggest a potential benefit of combined treatment involving nanoparticles and radiation.

This is evidence that there is toxicity of the nanoparticles used (CdS1-NPs, CdS2-NPs, and CdS3-NPs) on Caco-2 cells, but in varying degrees. With the highest concentration of (30Mm). Thus, cell death depends on the size and type of nanoparticles and cell type **Saberi et al. (2017).**

Also physicochemical characteristics (such as size, shape, surface area, and surface features), production method, studied biological target, coated materials play key roles in the nanoparticles-induced toxicities **(Mortezaee et al., 2021; Murugadoss et al., 2017).**

When used CdS1-NPs with complex agent (NaOH) found it killed about 71.65% of cells at a concentration of 30, While CdS2-NPs complex agent (NaOH + NH_4OH) had a cell death rate of 70%, and also CdS3-NPs complex agent (NH_4OH) had killed about 78.79% of cells, which is the highest concentration. And found highest kills from cells CdS3-NPs, and smallest kills from cells CdS2-NPs, but CdS1-NPs smallest size in the middle.

Olawale et al. (2022) used Green-Synthesized for CdS QDs, the results Showed greater cytotoxicity in lung cancer (A549) cells and breast cancer cells (MCF-7), with good biocompatibility in normal cells.

In more researches **(Paesano et al., 2023; Marmiroli et al., 2023; Olawale et al., 2022).** The effect of CdS -NPs from treated cancer cells has been mainly linked to cellular oxidative stress, with different mechanisms. When Cd^{2+} is released and combines with molecular oxygen. The high concentration of oxidizing species results in oxidative stress that causes damage to DNA and other intracellular proteins and leads to death of cells.

Rodríguez-Fragoso et al. (2012) investigated the Effect of CdS-MD nanoparticles on cell viability on CaCo-2 cells. When Cells were exposed in cultured medium with different concentrations (1.64, 3.28, 4.92, 6.56, 8.20 nM) for 24 h. Intestinal cells (CaCo-2) effect was observed at Concentrations 8.20 nM of CdS-MD nanoparticles increased the number of viable cells; however, this effect decreased with the increase in concentration (60 to 20%).

Aleissa et al. (2019) examined different concentration(1,3,15,45 µg/ml) of capsebon CdS nanoparticles with CaCo-2, results showed CdS NPs activity was increased time and dose dependent manner.

Gholami et al. (2020)found effects of CdS QD size 2-10 nm on MCF-7 cell line by concentration (25,50,100mg/ml)in concentration 100 found cells viability less than 50%, and cells viability decrease with concentrations increase.

Many previous studies indicated that the CdS nanoparticles produce reactive

oxygen species (ROS) by destroying the intracellular antioxidant system by direct interaction of CdS nanoparticles or by elevating the ROS molecules by the release of Cd^{2+} ions,or by either forming electron hole pairs to transfer electron to oxygen , and CdS nanoparticles produce ROS molecules both in presence or absence of light **(Alsaggaf et al ., 2020; Shivashankarappa et al., 2020; Rodríguez-Fragoso et al.,2012; Dailianis et al., 2005).**

There are some other nanoparticles that also have toxicity on caco2 cells, such as carbon NP, gold NP and silver NP **(Martínez-Esquivias et al., 2022; Lu et al., 2022; Garriga et al., 2020; Zein R et al., 2020).**

Nanoparticles quantum dots QDs (such CdS, CdSe QDs) are considered the best biomaterials for colon cancer diagnosis and treatment **Khan et al. (2022).**

The application of nanoscale particles in radiation therapy has aimed to improve outcomes in radiation therapy by increasing toxicity in tumors and reducing it in normal tissues **Fernandes et al. (2020).**

When using radiation (photons) at a dose of 80 CGy per day for three consecutive days alone and also with nanoparticles (CdS1-NPs, CdS2-NPs, and CdS3-NPs) using only one concentration, it was found that the ratio of living cells after the third dose of radiation alone 73.43%, while after the third dose with nanoparticles was different where it occurred significant increase in dead cells, and the least affect was (CdS3- NPs) by 41.84% living cells.

After only the third dose of radiotherapy, the death rate of cells is 26.57 %, which is a very small percentage compared to nanoparticles and radiation therapy together, as after the third dose.

CdS1–NPs death is about 90.35%, although its concentration is only 10 µM, as CdS1- NPs is the size of a quantum dot. but nanoparticles other a concentration of 25 µM, while CdS2- NPs had killed about 69.1% of cells, so CdS3-NPs had a cell death rate of 58.16%. A highest effective death cell with radiation is CdS1-NPs > CdS2-NPs > CdS3-NPs.

Another study **Fernandes et al. (2020).** Delivery of gold followed by ionizing radiation. Gold and silica nanocore shells 12–15 nm to treat of human colorectal cancer and given dose a 10 Gy X-ray dose were given 20–24 h.

Two mechanisms were identified as contributing to the treatment's efficacy: vascular collapse in the tumor due to accumulation of nanoparticles around the blood vessels, and an increase in perfusion resulting in a decrease in tumor hypoxia.

The observations confirm that (CdS1-NPs, CdS2-NPs, and CdS3-NPs) may improve radiotherapy on cancer treatment where the dose and number can be reduced and thus less effect on healthy cells **Liu et al. (2017).**

Nanoparticles used in this search and radiotherapy can drastically decrease radiation dose required, thereby, decreasing adverse effects and sparing normal tissue like search with hyperthermia **Hainfeld et al. (2014).**

Thus, if the cells were exposed to nanomaterials and irradiation, there is a significant increase in cell death compared to those exposed to radiation alone **(Saberi et al., 2017; Wang et al., 2013; Geng et al., 2011).**

In more research Interest in combining nanoparticles with radiotherapy has increased due to the promising therapeutic advantages. So, change in concentration of NPs, and dosimeter sensitivity, are important to produce observable impact **Sisin et al. (2022)**

Effect of radiation is dose and time-dependent, and one of the main critical targets of ionizing radiation is nuclear DNA, cells Caco2 is radio resistant when only exposed to radiation more than exposed to radiation and nanoparticles **Guardamagna et al. (2021).**

Found Radiation therapy is widely used in cancer treatment by acting on cancer cells through high-energy radiation, causing DNA damage and resulting in cell damage and death. However, radiation therapy not the therapeutic effective high. Even if radiation therapy is started at the earliest stage of cancer, it is still difficult to cure cancer by low-dose alone without damaging normal tissue, so good used nanoparticles with radiation therapy, Where the dose used can be reduced of radiation therapy such research **Xie et al. (2022) .**

Nanoparticles an X-ray enhancer for radiation cancer therapy was substantiated by their drastic enhancement of the concentration of reactive oxygen species (ROS) in X-ray irradiated tumor cells **Klein et al. (2014**).

Thus, it can be said that nanoparticles have a significant and effective with radiation, and this leads to reducing the radiation dose and reducing the side effects of radiation.

The study revealed that altering the complex agents used in the synthesis of Cadmium sulfide nanoparticles (CdS-NPs) not only affected their properties but also had an impact on cancer treatment. These findings suggest that the choice of complex agent can potentially influence the behavior and effectiveness of CdS-NPs in the context of cancer treatment. Further research and investigation are necessary to fully understand and harness the potential of CdS-NPs with different complex agents for improved cancer therapeutic applications.

Conclusions

Quantum dots and CdS NPs are superior to other metal NPs because of their amazing optical and electrical qualities, which make them useful in a variety of applications including drug administration, molecular pathology, biosensing, nanomedicines, and bioimaging methods. At low concentrations, cadmium sulfide (1-2-3) nanoparticles affect Caco-2 colon cancer cells, causing cell death. Only in this way may dosages be lowered while still increasing the death of cancer cells, negating any negative effects on healthy cells or overall health in humans.

This study recommends doing more studies to find out the toxicity of nanometer particles on healthy cells and how to get rid of them from the body in order to have real feasibility and even benefit from them in the treatment of cancer.

Future prospects: - CdS-NPs can be tested in vivo and with radiation; - CdS-NPs can be coated (core/shell) with different materials to lessen their toxicity and enable them to target cancer cells exclusively, avoiding healthy cells, in order to be used clinically in the future.

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