2023

Gold Nanoparticles and Liposomal Nanocarriers for Drug Delivery in Cancers

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PHYS 197F – Lasers, Nanoparticles, and Molecular Medicine, Fall 2022

Abstract

Cancers are a complex range of diseases that are universally characterized by uncontrolled cell growth that often manifest as malignant tumors. Worldwide, they are the second leading cause of death. The most prevalent current treatments, chemotherapy and radiotherapy, indiscriminately damage both cancerous cells and healthy cells. This results in an abundance of short-term and long-term complications, which can kill the patient before killing the tumor. This illustrates the need for more targeted, effective treatments with fewer adverse effects on healthy tissue, and the use of both organic and inorganic nanoparticles is among the most promising solutions (Yang et. al., 2022). This research focuses on the use of gold nanoparticles (AuNPs) and liposomal nanocarriers in conjunction with polyphenols, specifically curcumin, for drug delivery to specific cancer types. In a recent study, ligand coated gold nanoparticles induced cell death in 73% of tumor cells compared to untreated cells after a two-day in vitro incubation period (AL-Jawad et. al., 2019). In an in vitro study utilizing curcumin carrying liposomal nanoparticles with both cancerous and healthy cells, the liposomal nanocarriers effectively induced apoptosis in the majority of cancer cells without adversely affecting healthy cells (Piwowarczyk et. al., 2022). The processes, effects, benefits, and drawbacks are compared between both AuNPs and liposomal nanocarriers as well as their next steps toward wider implementation. Though more in vivo testing has occurred with liposomal nanocarriers, stability continues to be an issue; while AuNPs have more stability but less in vivo testing. Despite the contrast in material composition, both kinds of nanoparticles have been shown to provide effective, targeted treatments.

Gold Nanoparticles (AuNPs)

Gold nanoparticles are categorized by their versatility with many variables affecting their efficacy and toxicity in both cancerous cells and healthy cells. Such factors include particle size, ranging from <5 nanometers (nm) to 100< nm, and shape, including spheres, rods, prisms, stars, and flowers. Another aspect of their versatility derives from the surface chemistry and charge of AuNPs with their many potential conjugates, with positive AuNPs found to be more toxic than negative ones (Yang et. al., 2022).

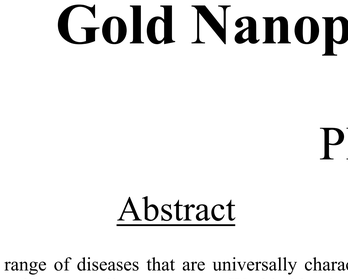

Fig 1. Representation of an AuNP with different potential conjugates. (Siddique et. al., 2020)

Liposomal Nanocarriers with Attached Polyphenols

Liposomes are spherical phospholipid bilayers that resemble cell membranes around a hydrophilic core, a common particle in research as it can carry both hydrophobic and hydrophilic substances. Liposomal nanocarriers ensure controlled targeting and delivery, reduce drug degradation and toxicity, and provide a sustained release system, while being non-toxic, biodegradable, and non-immunogenic (Olusanya et. al , 2018). Polyphenols are a group of organic compounds typically from plants. Curcumin is non-toxic to humans in large doses up to 12 grams a day while still inhibiting metastasis and angiogenesis of cancer cells. In a study, curcumin was able to kill late-stage and drug-resistant tumors in conjunction with chemotherapy (Basak et. al , 2015). In another study curcumin was administered successfully alongside photodynamic therapy, inducing apoptosis (Vetha et. al., 2020).

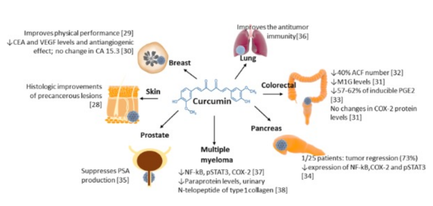

Fig 2. Curcumin Affects on Different Cancers (Araya-Sibaja et. al, 2021)

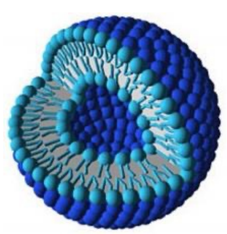

Fig 3. Liposomal Nanocarrier (Collins, 2017)

Gold Nanoparticles (AuNPs) - Results and Discussion

Four studies have focused on AuNPs with differing conjugates, but each study has produced promising results for AuNPs. One functionalizes AuNPs with folic acid (FA) and curcumin, with FA aiding in stabilization and sustained release of curcumin, a known anticancer agent for suppressing tumor growth. An 80% release of curcumin was observed at acidic pH levels consistent with breast cancer tumor sites in mice without harming normal cells (Mahalunkar et. al., 2019). Another hybridized AuNPs with an iron metal-organic framework (FeMOF) and camptothecin (CPT), which enhances the efficacy of chemotherapy through increasing the permeability and generating a greater accumulation of both AuNPs and chemotherapeutic drugs in tumor sites with a reduced systemic impact (Ding et. al., 2020). Another demonstrated that Enterococcus can be conjugated to AuNPs to inhibit growth in colon cancer cell lines (Vairavel et. al., 2020). Another compared the use of two natural ligands, Bovine Serum Albinum (BSA) and Glutathione (GSH), as coatings for AuNPs that induce cytotoxicity without damaging healthy cells (AL-Jawad et. al., 2019).

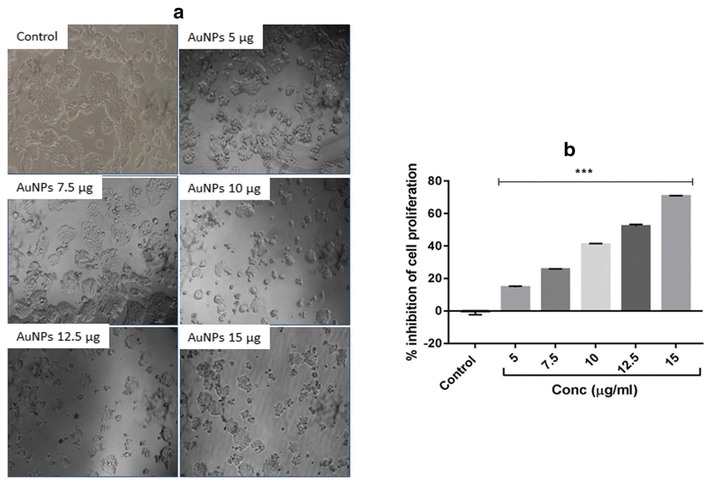

Fig 4. Inhibited growth in colorectal cancer cells induced by Enterococcus-AuNPs (Vairavel et. al., 2020)

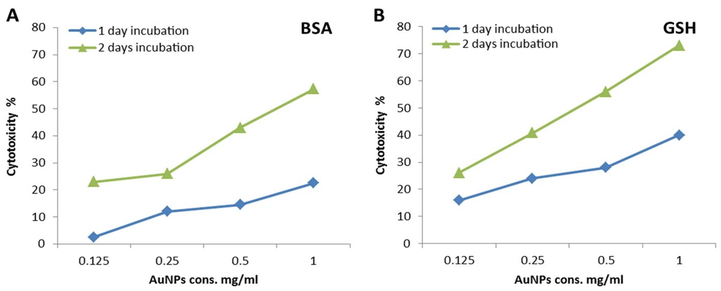

Fig 5. Cytotoxicity in cancer cell lines induced by GSH- and BSA- AuNPs (AL-Jawad et. al., 2019)

Future Directions: In-vivo testing on cancer cells

Liposomal nanocarriers with curcumin and an additional polyphenol such as p-EGCG or HPE to help with stability could be used in late-stage cancer, and as it is only harmful to cancer cells, could be simply injected into the bloodstream near the tumor and when it activates in the body will kill the tumor. More testing, both in vitro and in vivo testing for both types of liposomal nanocarriers with curcumin will be necessary. The studies on liposomal nanocarriers show that the anticancer affects and stability of curcumin can be improved with the addition of other polyphenols. Further testing on these methods is something that should be done in the future. Looking more into the cancer lines that curcumin can induce apoptosis in, to see if the affects are more pronounced with certain cancer lines, as well as more research into curcumin with both HPE and p-EGCG is also called for.

The in vivo research currently available for AuNP treatments is extremely limited, though current in vitro results suggest that AuNPs with the appropriate conjugates have the potential to effectively target and eradicate cancerous cells in the body with minimal adverse effects on the surrounding healthy cells. That said, more research is needed to explore the interactions of AuNPs with systems in the human body to ensure that any toxicity is mitigated and that the results are optimized for maximum efficacy. Research in this area is still developing, but with the proper time and testing, great strides could be made toward human trials and wider clinical implementation.

Liposomal Nanocarriers - Results and Discussion

Two studies have focused on liposomal nanocarriers with curcumin as a potential treatment for cancer, the differences in the two studies lie in the cancer types they tested the cells on and the additional polyphenol that was used as a stabilizer. One study used HPE, and the other used p-EGCG, in conjunction with curcumin in liposomal nanocarriers. Both the studies showed promising results in the use of these liposomal nanocarriers to induce apoptosis in different cancer cell lines. The combination curcumin and p-EGCG increased stability and efficiency in the anticancer effects and shows that liposomal nanoparticles carrying a mix of curcumin with another polyphenol is a viable potential cancer treatment (Piwowarczyk et. al., 2022). Both HPE and curcumin show promising ability to induce apoptosis and show increased stability and anti-cancer affects when used together (Farzaneh et. al, 2022).

Cell Line	Curcumin		pEGCG		Curcumin+pEGCG	
	24 h	48 h	24 h	48 h	24 h	48 h
5637	17.12 ± 4.09	12.27 ± 2.91	>40	>40	19.50 ± 3.23	15.33 ± 2.03
LNCaP	38.96 ± 2.90	22.06 ± 3.14	>40	>40	>40	>40
MRC-5	>40	>40	>40	>40	>40	>40

Fig 6. IC50 Values on Different Cell Lines (Piwowarczyk et. al., 2022)

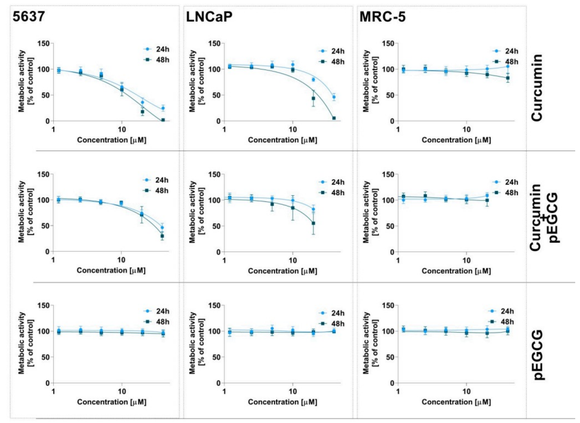

Fig 7. The Affects of Polyphenols on Different Cell Lines (Piwowarczyk et. al., 2022)

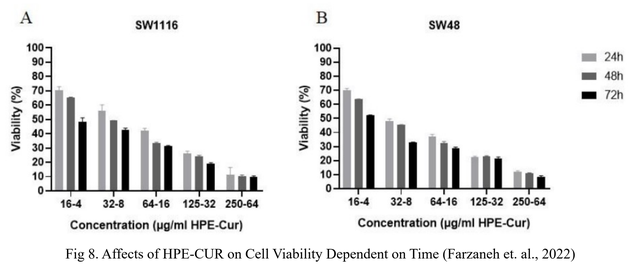

Fig 8. Affects of HPE-CUR on Cell Viability Dependent on Time (Farzaneh et. al., 2022)

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