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Chemotherapeutic Silver Nanoparticles: Input of Drug Combinations

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Cytotoxic drugs are used during cancer chemotherapy to inhibit tumor growth and metastasis. However, many chemotherapeutic drugs, such as doxorubicine (Dox), have limited cellular uptake and a strong tendency to bind to off-target macromolecules. Together these characteristics lead to low therapeutic indices. Increasing the intracellular uptake of cancer drugs could prevent these complications.

Another pitfall of chemotherapy is drug resistance. One strategy for avoiding drug resistance is drug combination. This approach can prevent side effects by allowing for reduced dosages and can improve efficacy if the chosen drugs act synergistically. For example, bisphosphonates act synergistically with many other anti-cancer agents. Alendronate (Ald), one of the most potent bisphosphonates, has been shown to increase cancer cell death *in vitro* when combined with Dox in breast cancer cells.

We present here the synthesis of a silver nanoparticle-based drug delivery system that improves the anticancer therapeutic indices of doxorubicin (Dox) using alendronate (Ald) as an adjuvent. Water, under microwave irradiation, was used as the sole reducing agent for the size-controlled, bisphosphonate-mediated preparation of silver nanoparticles (AgNPs). The AgNPs were coated with and stabilized by the bisphosphonate alendronate (Ald). The bisphosphonate group of Aldtemplated the formation of the AgNPs, and was the site of the drug's attachment to the nanoparticles. The free primary ammonium group of Ald was subsequently functionalized with either Rhodamine B (RhB) by amide linker formation or Dox through imine bond formation. The RhB-conjugated nanoparticles (RhB-Ald@AgNPs) were studied in HeLa cell cultures. Confocal fluorescence microscopy studies determined the main mechanisms of cellular uptake of the nanoparticles. The imine linker of the Dox-modified nanoparticles had significantly greater anti-cancer activity *in vitro* than either Ald or Dox alone.

Thus, the ability of Ald to promote the assembly of Ald@AgNPs in a one step reaction, and the straightforward post-modification of Ald@AgNPs, offer an easy and environmentally friendly strategy for the formation of stable nanoparticles that couple the antiproliferative properties of the AgNPs, themselves, to those of the drug mixtures they carry. This system features a high degree of functionality and potency and is of potential therapeutic benefit.

Biography:

Dr Farah Benyettou explored the chemical processes for drug delivery and the synthesis and modification of commercial anti-cancer drugs from the Bisphosphonate family. Subsequently, shee developed new and innovative anticancer superparamagnetic nanoparticles for drug delivery from the synthesis, to the characterizations and the biological evaluations. Dr Benyettou's research approach is to use complementary properties such as porosity and magnetism, and develop new multifunctional and smart nanoplatforms for simultaneously imaging and therapy.