“Silver nanoparticles / DNA/ berberine” nanosystem for X-ray induced photodynamic therapy: formation and excitation energy transfer

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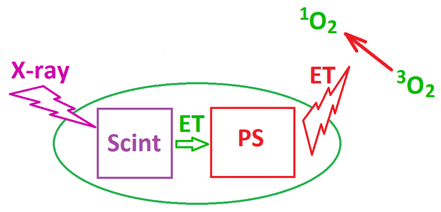
1. INTRODUCTION

Photodynamic therapy (PDT) comprises light, photosensitizer (PS), and oxygen to treat cancer and other diseases.

X-ray PDT employs X-ray irradiation to generate excited PS producing reactive oxygen species, this is suggested to overcome the main problem of PDT i.e. low depth of light penetration into biological tissues.

But PSs cannot be directly activated by X-ray due to a big mismatch between energy of X-ray photon (~keV-MeV) and that of excited electronic state of PS (~eV).

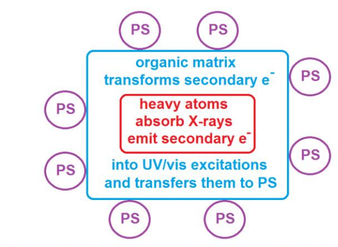
2. TRADITIONAL APPROACH



Scheme of traditional approach to construct X-ray PDT sensitizer. ***Scint*** *– scintillating NP;* ***PS*** *– photosensitizer;* ***ET*** *– excitation energy transfer.*

Conventional approach to development of sensitizers for X-ray PDT involves scintillating nanoparticles (NPs), capable of converting high energy radiation into visible light through scintillation. Scintillating materials absorb X-ray photons and generate secondary electrons, which then produce excited electronic states of the scintillator molecules or atoms. X-ray PDT nanosystems contain scintillating NPs and PS, and the electronic excitation energy of the scintillator is transferred to PS and excites it. However, as the energy of the secondary electrons remains high, their migration distance is of hundreds of nm, which strongly exceeds the NPs size, resulting in low efficiency of conversion of X-ray photons energy to that of electronic excited states of scintillator and PS and, finally, low efficiency of X-ray PDT.

4. PROPOSED APPROACH: IDEA

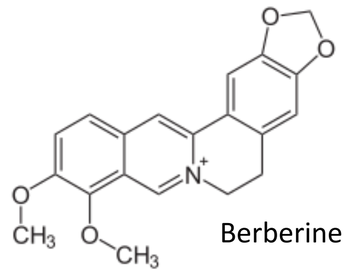


We propose using non-scintillating heavy elements to enhance the quantity of secondary electrons

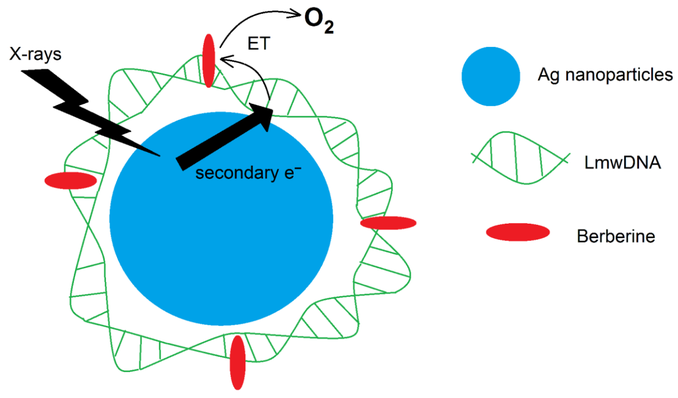
5. PROPOSED APPROACH: NANOSYSTEM

As the nanosystem to be studied, we have used the mixture of:

- Ag nanoparticles synthesized on low molecular weight DNA (LmwDNA): Ag nanoparticles to be used as heavy atoms for additional absorption of X-rays, while LmwDNA to be used as organic matrix;
- Berberine molecules to be used as photosensitizers.



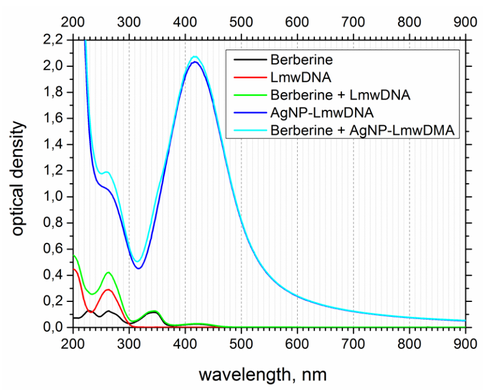
6. PROPOSED APPROACH: SCHEME



Scheme of the anticipated processes in AgNP-LmwDNA-Berberine nanosystem.

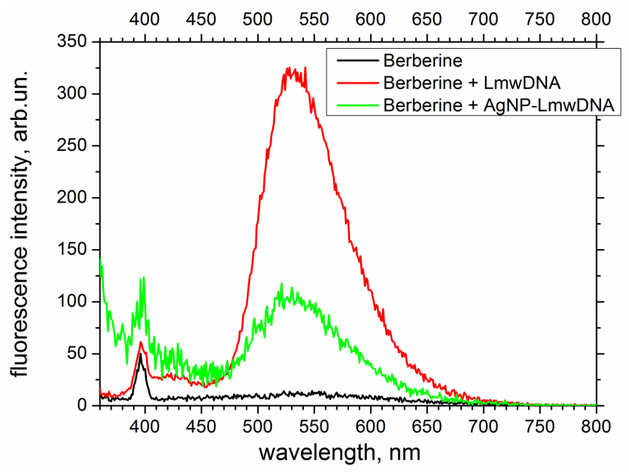
In addition to direct excitation of LmwDNA matrix by X-rays (that produces secondary electrons exciting nucleotide base chromophores), secondary electrons from the X-ray-excited AgNP also excite DNA. Excitations of nucleotide bases are further transferred to berberine *via* energy transfer (ET), and are further transferred to oxygen molecules to produce singlet oxygen.

7. RESULTS: ABSORPTION

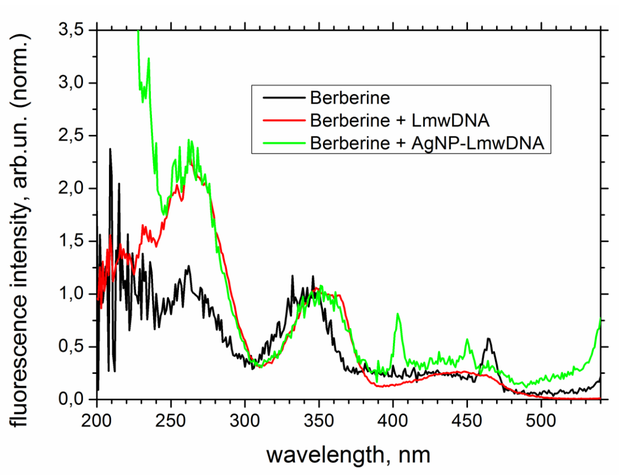


Absorption spectra of berberine (5 μM), LmwDNA (18.6 μM b.p.), AgNP-LmwDNA and berberine in the presence of LmwDNA and AgNP-LmwDNA, in H_2O.

7. RESULTS: FLUORESCENCE EMISSION AND EXCITATION



Fluorescence spectra of berberine (5 μM) free and in the presence of LmwDNA and AgNP-LmwDNA, in H_2O, excitation wavelength 350 nm. Corrected for inner filter effect and reabsorption.

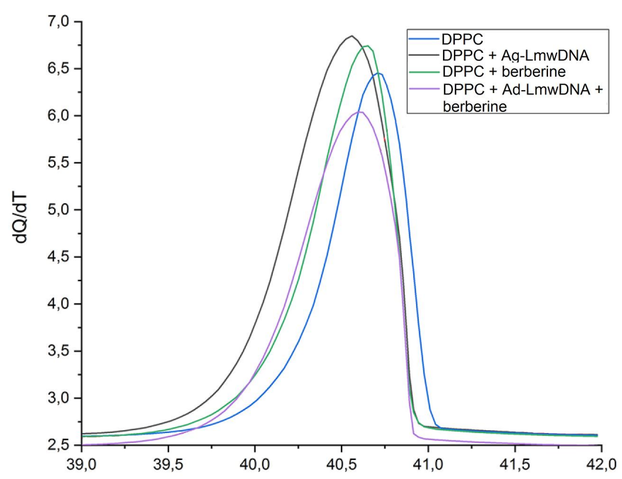


Fluorescence excitation spectra of berberine (5 μM) free and in the presence of LmwDNA and AgNP-LmwDNA, in H_2O, emission wavelength 550 nm, normalized at 350 nm.. Corrected for inner filter effect and reabsorption.

Addition of LmwDNA and AgNP-LmwDNA results in short-wavelength shift of the maximum as well as in increase in the intensity of berberine fluorescence spectrum. Thus, berberine molecules bind to AgNP-LmwDNA nanosystems (the most possibly to its DNA component) and form thus AgNP-LmwDNA-berberine nanosystem.

In the presence of LmwDNA and AgNP-LmwDNA, contribution of 260 nm band (where DNA absorption maximum is) to the spectrum increases. Thus excitation energy transfer from DNA to berberine takes place both in LmwDNA-berberine and AgNP-LmwDNA-berberine systems.

8. CALORIMETRY STUDIES



Phase transitions in model membranes of 1,2-Dipalmitoyl-sn-Glycero-3-Phosphatidylcholine (DPPC) in the presence of AgNP-LmwDNA-berberine nanosystem and its components.

Differential scanning calorimetry studies of interaction of “silver nanoparticles / DNA / berberine” nanosystem with the model phospholipid membrane was performed. Nanosystem AgNP-LmwDNA-berberine and its components shift the phase transition of the membrane.

CONCLUSIONS:

- **Formation of “silver nanparticles / LmwDNA / berberine” nanosystem was demonstrated.**
- **Electron excitation energy transfer from DNA bases to berberine in “silver nanoparticles / LmwDNA / berberine” nanosystem takes place; this transfer is an important element for this nanosystem to be appropriate as sensitizer in X-ray photodynamic therapy.**

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