Using HfO_2 nanoparticles to enhance scintillation in polystyrene for efficient X-ray photodynamic therapy

Losytskyy M.Y.[1], Vretik L.O.[1], Nikolaeva O.A.[1], Degoda V.Y.[1], Shcherbakov O.B.[2], Podust G.P.[1], Samoilov O.M.[3], Ohulchanskyy T.Y.[4], Yashchuk V.M.[1]

[1] Taras Shevchenko National University of Kyiv, Volodymyrs'ka Str., 64/13, Kyiv-01601, Ukraine.
E-mail: mlosytskyy@gmail.com
[2] Zabolotny Institute of Microbiology and Virology, NAS of Ukraine, Kyiv, Ukraine
[3] Institute for Scintillation Materials, NAS of Ukraine, Kharkiv, Ukraine
[4] College of Physics and Optoelectronic Engineering, Shenzhen University, Shenzhen 518060, P. R. China.

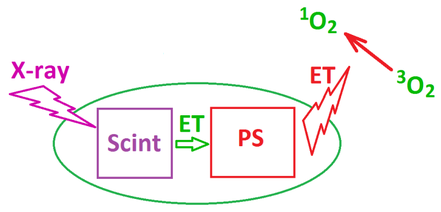
1. INTRODUCTION

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).

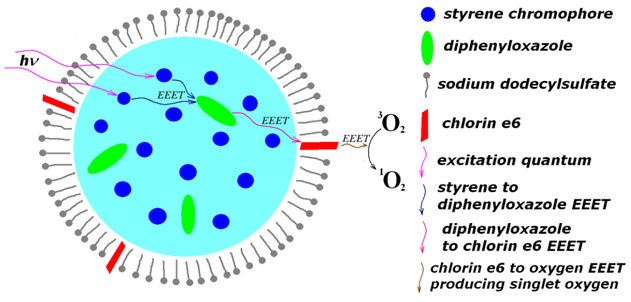
2. TRADITIONAL APPROACH



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.

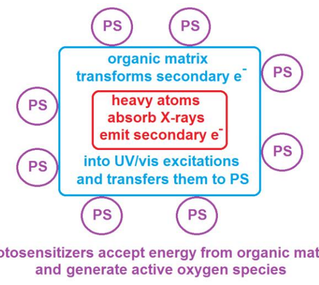
3. TRADITIONAL APPROACH BASED: EARLIER STUDIED PS-PPO NP-CHLORIN e_6 NANOSYSTEM AND PHOTOPHYSICAL PROCESSES IN IT



- excitation radiation (UV or X-ray) is absorbed by the atoms of polystyrene (pS);
- this results in electronic excitation of styrene chromophors;
- excitation energy of styrene chromophores is transferred to diphenyloxazole (PPO);
- excitation energy of PPO is transferred to chlorin e_6 bound to pS-PPO NP possibly by incorporation into the SDS shell of the NP;
- excitation energy of chlorin e_6 is transferred to molecular oxygen generating toxic singlet oxygen.

M.Yu. Losytskyy, L.O. Vretik, O.A. Nikolaeva, A.I. Marynin, N.F. Gamaleya, V.M. Yashchuk. Polystyrene-diphenyloxazole-chlorin e_6 nanosystem for PDT: energy transfer study // Molecular Crystals and Liquid Crystals. – 2016. –Vol.639, Iss.1. – P.169-176.

4. PROPOSED APPROACH: IDEA

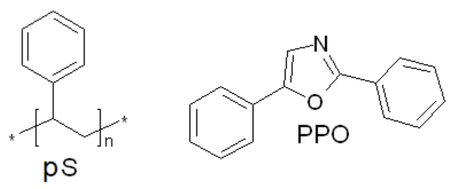


We propose using non-scintillating heavy elements to enhance the quantity of secondary electrons

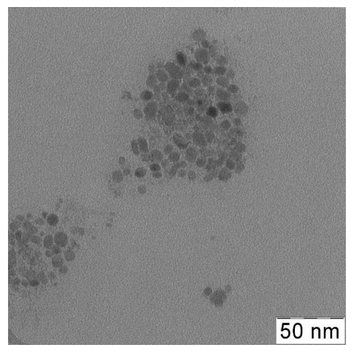
5. PROPOSED APPROACH: PROOF-OF-THE-PRINCIPLE

To prove the idea, we have used the mixture of:

- HfO_2 nanoparticles – used as heavy atoms for additional absorption of X-rays;
- Polystyrene nanoparticles with encapsulated diphenyloxazole (pS-PPO) – used as organic matrix.

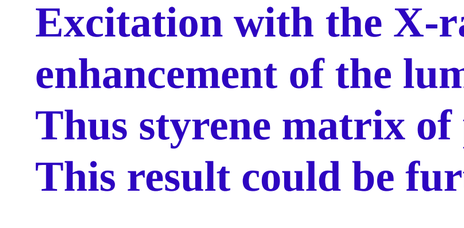


Chemical structure of the components of pS-PPO NP polystyrene (PS) and diphenyloxazole (PPO)



TEM image of HfO_2 nanoparticles

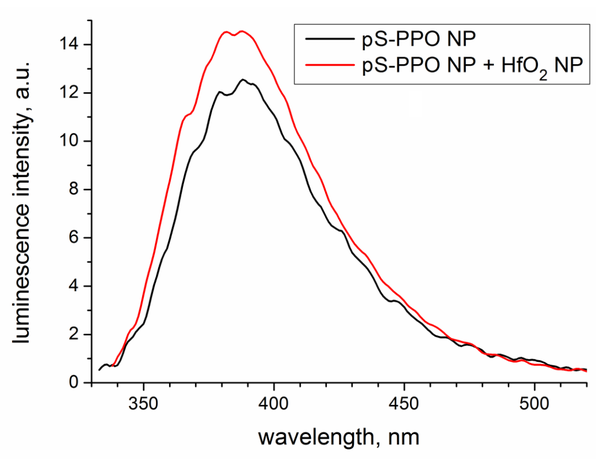
6. PROPOSED APPROACH: SCHEME



Scheme of the proof-of-the-principle experiment.
In addition to direct excitation of pS matrix of pS-PPO NP by X-rays (that produces secondary electrons exciting styrene chromophors), secondary electrons from the X-ray-excited HfO_2 NP also excite styrene. Excitations of styrene are further transferred to PPO *via* energy transfer (ET), and are registered as fluorescence emission of PPO.

7. RESULTS: X-RAY STIMULATED LUMINESCENCE

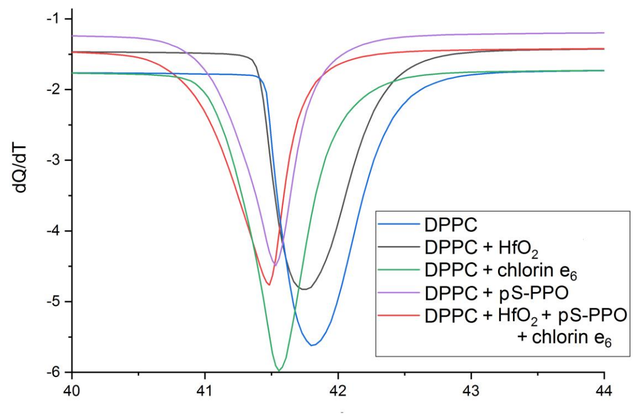
Excitation with the X-rays (energy of quanta about 15 keV) of the colloidal suspension of pS-PPO NP (about 8% by mass) in the presence of HfO_2 nanoparticles (about 1.25% by mass) resulted in the luminescence emission of PPO that was 15% more intense than the X-ray stimulated PPO emission from the analogous pS-PPO NP sample without HfO_2 nanoparticles.



X-ray luminescence spectra of pS-PPO NP and mixture of pS-PPO NP (black) and HfO_2 NP (red).

We believe that this result is attributable to the additional excitation of styrene matrix of pS-PPO NP by secondary electrons emitted after X-ray excitation of heavy Hf atoms.

8. CALORIMETRY STUDIES



Phase transitions in model membranes of 1,2-Dipalmitoyl-sn-Glycero-3-Phosphatidylcholine (DPPC) in the presence of HfO_2 / pS-PPO / chlorin e_6 nanosystem and its components.

Differential scanning calorimetry studies revealed non-additive interaction (at high concentrations) of HfO_2 NP, pS-PPO NP and chlorin e_6 with the model DPPC phospholipid membrane, pointing to a good interaction not only of the complex with the membrane, but also that of individual components of the system.

CONCLUSIONS:

- **Excitation with the X-rays of the colloidal suspension of pS-PPO NP in the presence of HfO_2 nanoparticles resulted in enhancement of the luminescence emission of PPO.**
- **Thus styrene matrix of pS-PPO NP is excited by secondary electrons emitted after X-ray excitation of heavy Hf atoms.**
- **This result could be further used in the development of sensitizing nanosystems for X-ray PDT.**

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