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A new strategy based on methylene blue and boron nitride for local photodynamic therapy

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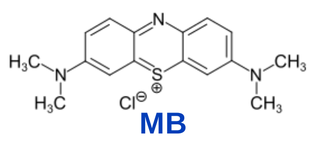
INTRODUCTION & AIM

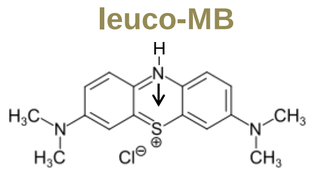
The injection use of methylene blue (MB) solutions in photodynamic therapy (PDT) is limited by their rapid transition to ineffective leuko methylene blue in the hypoxic tumor environment and the uncontrolled self-aggregation of MB molecules [1].

The concept of the presented development was the adsorption immobilization of MB on the surface of a photocatalyst support (h-BN) to create a system (h-BN/n·MB heterostructures) with consistently increased photoactivity due to the synergistic interaction of the components.

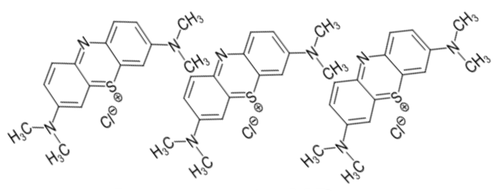


MB

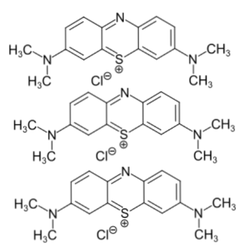
leuco-MB



low ability to produce ROS, especially singlet oxygen



J-aggregate MB



H-aggregate MB

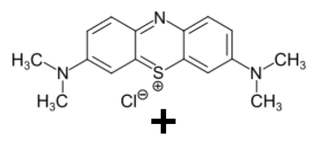
uncontrolled change in photophysical properties

METHOD

Preparation of heterostructures h-BN/n·MB

PHOTOSENSITIZER

Methylene blue (MB) in the form of hydrochloride salt (with three water molecules) "Rushim" (Moscow, Russia)



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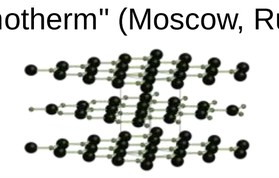
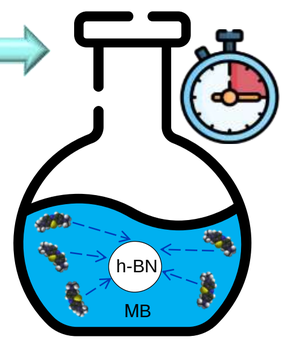
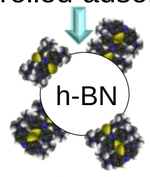
PHOTOCATALYST

Nanoparticles hexagonal boron nitride with an average size of 70 ± 5 nm (h-BN), "Plasmotherm" (Moscow, Russia)

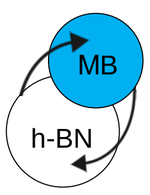




Controlled adsorption

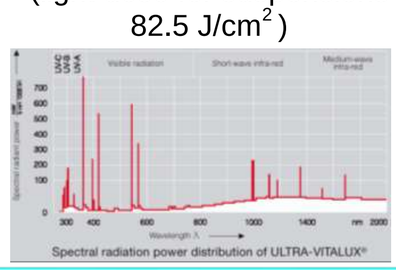


Heterostructures h-BN/n·MB with a given MB concentration



Generation of reactive oxygen species enhanced by **synergistic effect**

Exposure to sunlight (light dose for suspensions 82.5 J/cm^2)



RESULTS & DISCUSSION

Characterization of h-BN/n·MB heterostructures

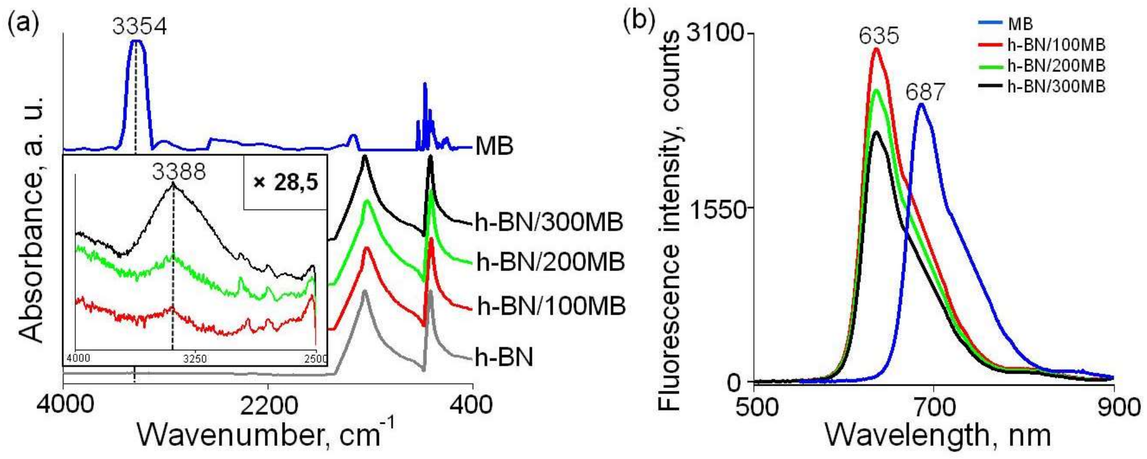


Figure 1. FTIR spectra of h-BN, dried MB solution and h-BN/n·MB heterostructures (a). Fluorescence spectra of h-BN/n·MB suspensions and MB solution (0.3 mg/mL) (b)

It was established that upon adsorption on h-BN, MB molecules form H-aggregates

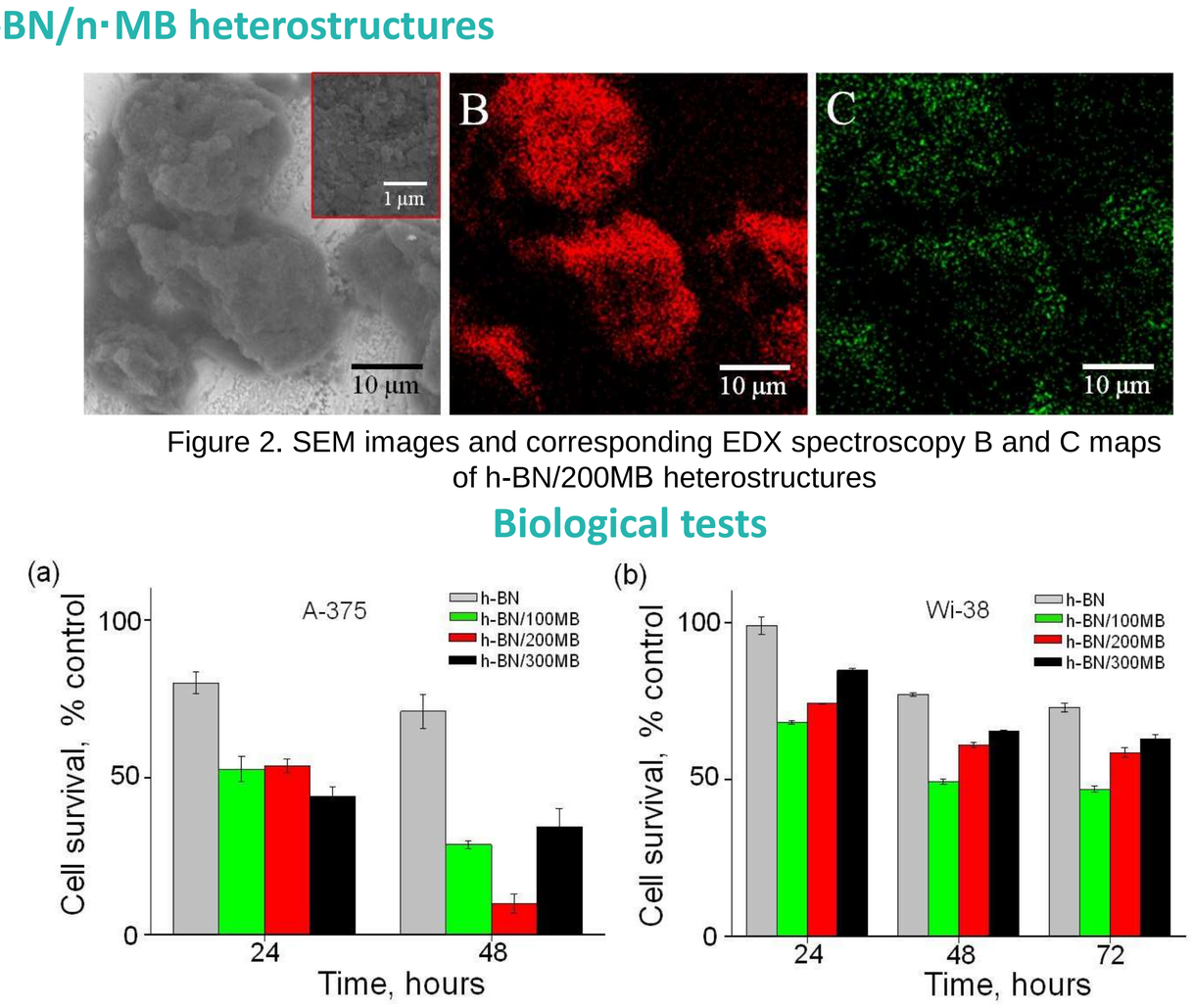


Figure 2. SEM images and corresponding EDX spectroscopy B and C maps of h-BN/200MB heterostructures

ROS formation and recombination kinetics

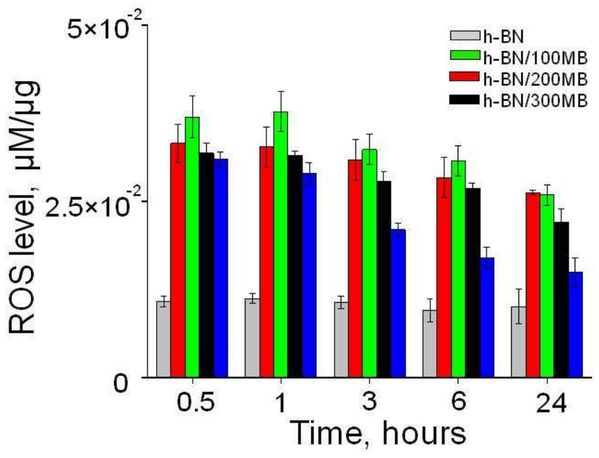


Figure 3.Changes in ROS concentration in h-BN/n·MB suspensions, h-BN NP solution, and MB solution (22.5 μg/ml) over 24 h after irradiation with sunlight for 30 min

MB adsorbed on the h-BN surface is less subject to self-oxidative photodestruction

h-BN/200MB heterostructures generated **$3.7\times10^{-2} \pm 0.2\times10^{-3}$ μM/μg** of ROS

h-BN/200MB heterostructures generated:

✓**3x** more ROS than pure h-BN

✓**1.2x** more ROS than free MB

(within the first hour after irradiation)

Biological tests

Figure 4.Viability of A-375 (a) and Wi-38 (b) cells in suspensions of h-BN NPs and h-BN/n·MB heterostructures after 24 and 48 h (a) and 24, 48, and 72 h (b) relative to control cells (without suspensions)

The **IC_{50}** of h-BN/200MB heterostructures for A-375 cells after 24 h of cultivation was total **7.5 μg**

h-BN/200MB heterostructures reduced melanoma cell survival by **89%** in 48 hours

h-BN/n·MB heterostructures **don't have** dark toxicity to fibroblasts

The density of MB **H-aggregates** affects the biocompatibility of h-BN/n·MB heterostructures

CONCLUSION

A new sunlight-activated platform for local PDT has been developed. h-BN/n·MB heterostructures demonstrate a high therapeutic potential due to their strong oxidative activity. The presented data confirm the feasibility of using heterostructures to enhance the photoefficiency of low doses of MB.

FUTURE WORK / REFERENCES

de Miranda, É. G.; Toledo, V. H.; dos Santos, C. G.; Costa, F.; Diaz-Lopez, M.; de Queiroz, T. B.; Nascimento O. R.; Nantes, I. L. Organic matrix-entrapped methylene blue as a photochemical reactor applied in chemical synthesis and nanotechnology. *Journal of Photochemistry and Photobiology A: Chemistry.* 2023, 444, 115015.