

Drug carriers – systems enabling targeted delivery of drugs to tissues – complement the drugs' physical properties, restrict their undesirable characteristics, reduce toxicity, enable targeted delivery and facilitate controlled dosage [1], [2], [3]. Chemotherapy, frequently applied in the treatment of cancer, is often effective but suffers from poor selectivity of the therapeutic agents applied. Its detrimental impact on healthy tissues has spurred a search for solutions which would improve the drugs' toxicological profile – not through reduction of dosage but by improvements in targeted delivery.

The goal of the project is to investigate the targeted drug delivery capabilities of compounds which include Congo red (CR) (Fig. 1A). These compounds form supramolecular ribbon-like aggregates (SC) (Fig. 1B) [4], [5], capable of intercalating various external molecules, including drugs. SC also selectively bind to antibody-antigen (Ab-Ag) complexes as well as to carbon nanotubes (CNT) (Fig. 1C, 1D) in sufficient quantities to disperse and recruit them for drug transport tasks. Additionally, selected SC exhibit affinity for metal ions – including Ag^+ . Earlier *in vivo* studies have shown that CR can co-accumulate with Ab-Ag complexes (e.g. local inflammation), whereupon it is gradually eliminated [8] (Fig. 3). As SC disperse hydrophobic CNT via surface interactions [9], it may be possible to greatly increase the drug transport capabilities of such compounds. A preliminary analysis of drug release from the CNT-CR system has been performed using doxorubicin (DOX) as a reference drug, supplying sufficient data for follow-up studies involving cell cultures. The ability to bind Ag^+ ions provides further support for studies aimed assessing the antibacterial properties of SC. Mixed supramolecular systems have been shown to break CNT, further extending their potential applications. The goal of our research is also to determine the mechanisms of such interactions, which is why we intend to apply microscopy (fluorescent, confocal, SEM, TEM, AFM and *in vitro* Raman microscopy), dynamic light scattering (DLS) and static light scattering (SLS) as well as field flow fractionation (Flow-FFF) and microcalorimetry (DSC). Finally, the presented interactions will be subjected to molecular modelling analysis.

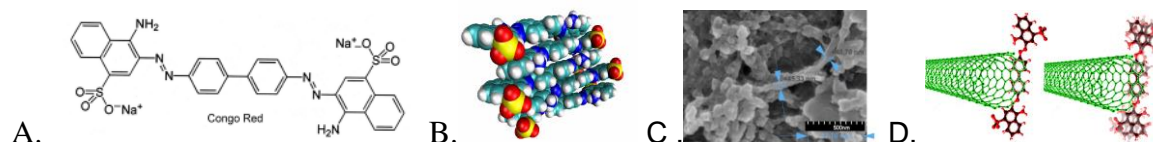


Fig. 1 A. CR – chemical composition of an individual molecule; B. association of molecules forming a supramolecular system; C. CNT-CR complex with diameter measurement points highlighted (SEM, scanning electron microscopy); D. attachment of CR to CNT surface – schematic depiction

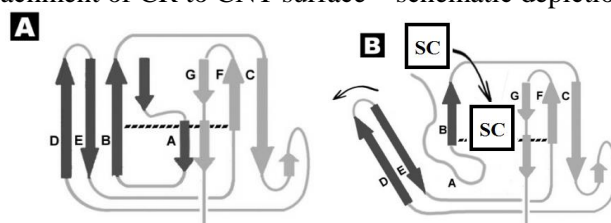


Fig. 2 Attachment of supramolecular compounds (SC) to antibody-antigen complexes – schematic depiction

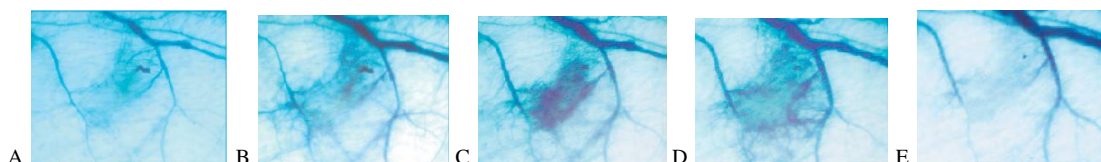


Fig. 3 Immune-targeted aggregation of supramolecular CR in an inflammation zone and its progressive removal (*in vivo* studies; ear, rabbit): A. 15 min.; B. 1h 35 min.; C. 26h 30min.; D. 74h; E. day 9

- [1] Wong B. S., Yoong S. L., Jagusiak A., Panczyk T. i wsp. *Adv. Drug Deliv. Rev.*, 65, 15 (2013) 1964-2015
- [2] Panczyk, T.; Da Ros, T.; Pastorin, G.; Jagusiak, A. i wsp. *J. Phys. Chem. C*, 118 (2014) 1353-1363
- [3] Pańczyk T., Jagusiak A., Pastorin G., Ang W. H. i wsp. *J. Phys. Chem., C*, 117, 33 (2013) 17327-17336
- [4] Skowronek M. i wsp., *Biopolymers* 46, 5 (1998) 267-281
- [5] Król M. i wsp. *J. Comput. Aided Drug Des.* 18, 1 (2004) 41-53
- [6] Piekarska B. i wsp. *Chem. Biol. Drug Des.* 68, 5 (2006) 276-283
- [7] Jagusiak A. i wsp. *Mini-Reviews in Med. Chem.* 14, 13 (2014) 1104-13
- [8] Rybarska J. i wsp. *Folia Histochem. Cytobiol.* 42, 2 (2004) 101-110
- [9] Panczyk T., Wolski P., Jagusiak A., Drach M. *RSC Adv.*, 4 (2014) 47304-47312