

DECASUBSTITUTED PILLAR[5]ARENE DERIVATIVES CONTAINING L-PHENYALANINE RESIDUES: SELF-ASSEMBLY AND INTERACTION WITH CYCLOSPORINE A

V.R. Sultanaev, L.S. Yakimova, A.A. Nazarova, I.I. Stoikov

A.M. Butlerov Chemistry Institute, Kazan Federal University, 18 Kremlevskaya Street,
420008 Kazan, Russia.

E-mail: vildan_sultanaev@mail.ru

Nanostructures and their interaction with biologically active compounds are of great interest for medicine, agriculture, industry, and rehabilitation therapy. In particular, pillar[5]arenes containing mobile amino acid fragments have potential as promising drug delivery systems due to their ability to self-associate and encapsulate substrates. The purpose of this work was synthesis and supramolecular self-assembly of pillar[5]arenes containing amino acid fragments of *L*-phenylalanine and various substituents (methyl and ethyl) at the quaternary nitrogen atom, as well as interactions with the immunosuppressive drug cyclosporine A (CsA).

The formation of different types of architectures by the synthesized pillar[5]arene derivatives was confirmed by two-dimensional ^1H - ^1H NOESY NMR and IR spectroscopy. It was shown that macrocycle with ethyl substituent is prone to a greater number of intramolecular hydrogen bonds and as evidence to the formation of nano-sized particles in water according to dynamic light scattering (DLS) method and transmitting electron microscopy (TEM) ($d=132$ nm, $\text{PDI}=0.19\div 0.01$).

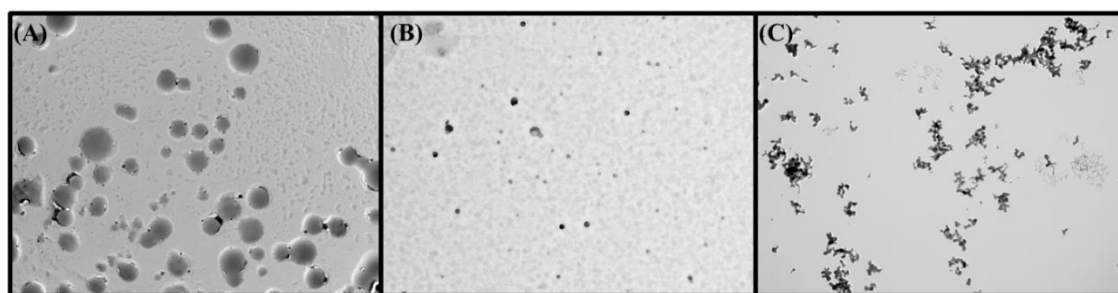


Fig. 1. TEM images of the aggregates formed by CsA (A), Cs+pillar[5]arene with methyl (B) and ethyl (C) substituent at the quaternary nitrogen atom (1×10^{-4} M).

Cyclosporin A is a cyclic undecapeptide with a strong immunosuppressive effect, it has been widely used in transplantology and significantly improved the survival rates of patients after solid organ transplantation. CsA has a number of side effects associated with high toxicity, which limits its clinical use. In this regard, we studied the encapsulating ability of the synthesized macrocycles with respect to CsA. Using DLS and TEM methods, it was shown that the macrocycle with methyl substituents forms more stable colloidal systems of particles ($\zeta=-22\pm 2$ mV) with an average hydrodynamic diameter of about 266 nm ($\text{PDI}=0.04\pm 0.03$) (Fig. 1 (B)).

These results may be useful for developing approaches to reduce toxicity or eliminate excess amounts of important therapeutic agents.

References

1. Ogoshi T., Para-Bridged Symmetrical pillar[5]arenes: Their Lewis acid catalyzed synthesis and host-guest property / T. Ogoshi, S. Kanai, S. Fujinami, T. Yamagishi, Y. Nakamoto // *J. Am. Chem. Soc.* – 2008. – Vol. 130 – P. 5022–5023.

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