New Cyclen and L-DOPA Derivatives: Solid-Phase Synthesis, Bifunctionality, Toxicity

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Macrocyclic polyamines have wide biological and medicinal applications. The new methodologies for their selective functionalization are of high interest due to their importance for a variety of diagnostic and therapeutic pharmaceuticals [1,2] and in the development of new MRI contrast agents [3]. Recently, cyclen-based bifunctional chelators have attracted much interest in cancer therapy [4]. On the other hand, L-DOPA (3,4-dihydroxyphanylalanine) derivatives play a crucial role in the therapy of Parkinson disease (PD) as they increase the BBB penetration capacity of DOPA. The DOPA peptidomimetics with amino acid kross-linked via oxygen atom were prepared and their antioxidant activities were studied [5]. Our aim was the modification of macrocyclic polyamine receptor molecules and DOPA with additional ligands (arms) to increase the capacity to interact with biomolecules moieties for a more efficient "multipoint" recognition and to increase binding sites. With this aim, new small peptide functionalized cyclen and DOPA derivatives: cyclen-HisHis, cyclen-AspHis, cyclen-GluHis, DOPA-HisHis were prepared, characterized and at first stage, their cytotoxicity was studied on mammalian cells. The cytotoxicity assay showed that cyclen- and DOPA-dipeptide hybrids are non-toxic for cell line Hep G2 - ATCC® HB-8065™ (cells are derived from human liver) and HEK-293T - ATCC®CRL-11268™ (epithelial cells derived from kidney of human fetus).

References

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