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Physicochemical characteristic of poly(amidoamine) dendrimers are their application in controlled drug delivery systems

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Poly(amidoamine) (PAMAM) dendrimers are monodisperse synthetic polymers with nanosize ranging from 1-14nm. Dendrimer synthesis can be precisely controlled in size, shape, molecular mass, composition, and reactivity [1,2]. The study's main aim was to investigate the correlation between the physicochemical properties of the carrier and the active substance and the efficiency of the PAMAM-5FU complex formation. Experimental studies show that analysis of physicochemical properties of both PAMAM dendrimers and 5-fluorouracil play a significant role in the formation of high-efficiency PAMAM-5FU complex. The ligand binding's effectiveness to the dendrimers' structure is strictly dependent on the complex formation conditions: molar ratio, ionic strength, pH, and dendrimer generation. The fact that drug molecules bind most effectively under alkaline conditions when the dendrimer is close to the isoelectric point indicates the significant influence of the ligand charge, which occurs in a deprotonated form. Studies have confirmed the system's ability to attach approximately 20 5FU molecules per dendrimer molecule for the fourth generation dendrimer and about 25 molecules for the sixth generation dendrimer. Comparing these values with the nominal number of amine groups present in the dendrimer structure, a system efficiency of 16% for G4PAMAM and 5% for G6PAMAM dendrimers was obtained.

The decrease in the zeta potential of the PAMAM-5FU systems compared to the dendrimer itself indicates a change in the carrier's surface charge by drug immobilization. In addition, it may reveal the presence of ligand molecules on the PAMAM surface. H1 NMR spectra indicate the presence of drug molecules both inside the structure and on its surface. The research confirms the possibility of immobilizing the active agent in two ways and thus indicates the unique properties of the structure of dendrimers.

We demonstrated that both G4PAMAM and G6PAMAM present no toxicity towards normal cells. Furthermore, the observed activity of 5-FU/PAMAM complexes in four cancer cell lines, resulting in decreasing of a fluorouracil IC50 dose by up to 30%. Considering that most of the traditionally administered 5-FU is decomposed to inactive metabolites before reaching its target, drug conjugation with dendrimers seems to be a promising approach that increases drug toxicity and stability, ultimately leading to overcoming of transportation-related drug resistance.

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References

1. Jachimska B. Physicochemical characterization of PAMAM dendrimer as a multifunctional nanocarriers, Nanoparticles in Pharmacotherapy. ; 2019. doi:10.1016/b978-0-12-816504-1.00003-

2. Rae JM, Jachimska B. Analysis of dendrimer-protein interactions and their implications on potential applications of dendrimers in nanomedicine. Nanoscale. 2021;13(4):2703-2713. doi:10.1039/d0nr07607d

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