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Synthesis of polymer systems containing anionic polyelectrolites and HIV-1 gag matrix protein fragments

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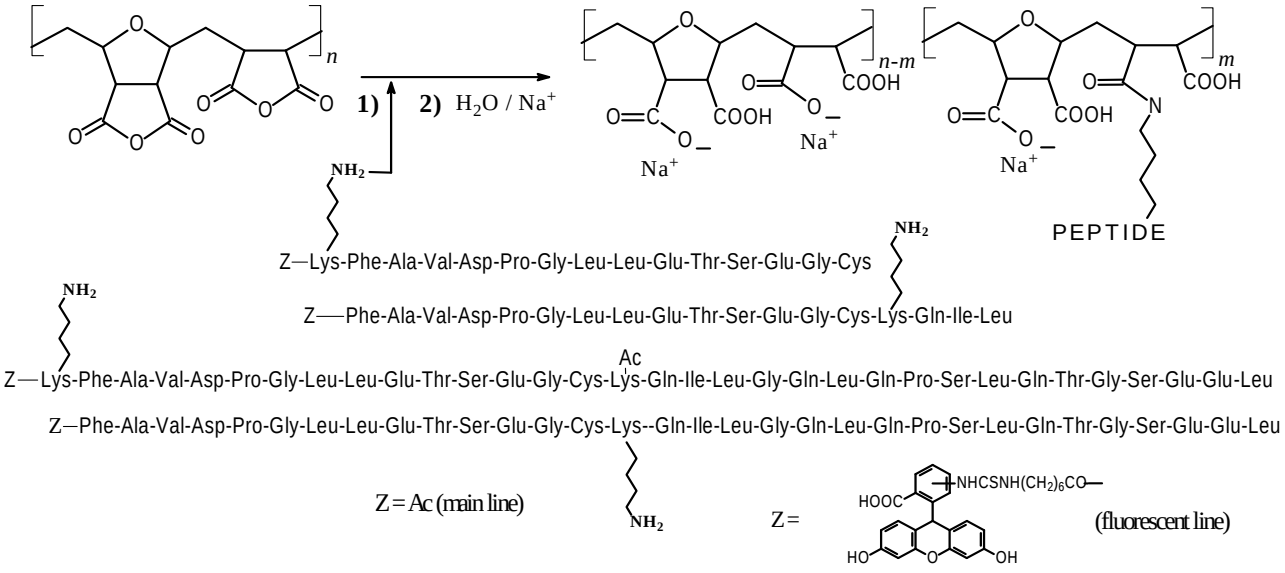
Abstract – The HIV gag matrix protein (MA) plays an essential role in the HIV life cycle at earliest (viral uncoating, RNA delivery to nuclei) and latest (RNA re-transporting toward plasma membrane, virions assembly-maturation) steps. Intervention in processes of virions assembly-maturation discovers new oppotunities to AIDS treatment. In this work fragments of HIV matrix protein p17 were synthesized and covalently conjugated with polymer. This conjugates are prepared for biological invistigations.

Synthesis of peptide fragments of HIV matrix protein p17 was carried out to develop artificial macromolecular systems for virus selective obstruction. Peptides, that model the region being responsible for autorecognition and self-assembly of coat protein, were synthesized by solide-phase synthesis according to declared technique [1]. A number of produced peptides with length from 15 to 33 amino-acid residues was produced in the form of mono-aminoreagents to conjugate with synthetic polymer. Simultaneously fluorescent-labeled products were obtained. Their purity was confirmed by HPLC and their structure was studied by MALDI-TOF spectroscopy.

Peptide conjugation with polyanhydride was realized in solution of DMF in presence of triethylamine, residual anhydride moieties were hydrolysed under mild conditions to produce water-soluble sodium salt. Final products were purified from covalently unconsolidated dirts by multi-sequencing ultrafiltration. Obtained peptide conjugates were isolated by lyophilization.

These hybrid polymers are prepared for biological invistigations as potential inhibitors of HIV-infection.



Scheme 1: Synthesis of peptide conjugates

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References

[1] Rodionov I.L., Baru M.B., Ivanov V.T. Peptide Res, 1992, v. 5 (2), P. 119-125.