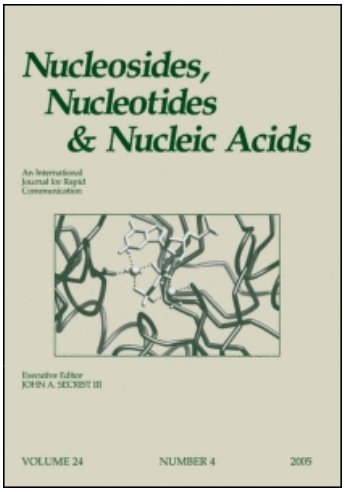

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Synthesis and Biological Properties of 2'-5' Oligodeoxyribonucleotide, an Isomer of Biologic DNA

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SYNTHESIS AND BIOLOGICAL PROPERTIES OF 2'-5' OLIGO-DEOXYRIBONUCLEOTIDE, AN ISOMER OF BIOLOGIC DNA

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ABSTRACT: Oligonucleotide having 2'-5' phosphodiester linkage has been synthesised on solid support using indigenously prepared 3'-deoxy-2'-phosphoramidites.The 2'-5' oligonucleotide showed higher half-life when subjected to 3'-exonuclease, SVPD, digestion. This oligonucleotide formed a stable duplex with complementary RNA but not with DNA. Similarly, it did not form triplex as well either with DNA or RNA duplex.

INTRODUCTION

Oligodeoxyribonucleotides (ODNs) and their modified analogues, specially with phosphodiester bond modifications, have shown promising results as therapeutic agents in antisense or antigene strategies[1,2]. So in order to explore the possibility of the uncommon and less known 2'-5' oligonucleotides, as compared to 3'-5' oligonucleotides, as probable therapeutic agents, we have synthesized such oligonucleotide and undertaken some hybridisational studies with ssDNA/RNA and dsDNA/RNA fragements.

RESULTS AND DISCUSSION

A sheer modification of the phosphodiester bond from 3'-5' to 2'-5' rendered remarkable properties to the oligonucleotides having the same base composition. The 2'-5' oligonucleotide showed much higher half-life, about 9h, when subjected to 3'-exonuclease, SVPD, digestion than normal oligonucleotides.

This 2'-5' oligonucleotide was found to form a duplex (Tm 45^0C) with complementary RNA fragment but not with complementary DNA. Similarly, it did not form a triplex either with a DNA or RNA duplex, unlike a normal DNA fragment. These observations

have been deduced from the UV thermal studies and gel shift assay. However, a small transition at 53^{0}C during triplex formation was observed (Watson-Crick duplex showed a Tm of 82.8^{0}C). Further, since the 2'-5' oligonucleotide has a long stretches of dC, it showed a behaviour like C-tetrad through i-motiff and as a result, a transition at 53^{0}C was observed during UV thermal studies on triplex formation.

EXPERIMENTAL

The modified 3'-deoxynucleosides of cytidine and thymine were synthesised via Vorbrugen glycosylation[3], using freshly distilled $SnCl_4$, between suitably protected nucleobases and 5-bz-3-deoxy-1,2-diacetoxyfuranose[4].

The 3'-deoxynucleosides were converted to 2'-phosphoramidites by reaction with chloro(2-cyanoethoxy)-N,N-diisopropylaminophosphine and a decamer, d (5'CCCCCCC TCC-2') was synthesized. Similarly, a complementary normal DNA sequence, d(GGAGGGGGGG) and an RNA sequence, (GGUGGGGGGG) and an RNA duplex, (GGGGGGGAGG) and (CCUCCCCCCC) selected from secondary structure of m-RNA of HTLV-1 were synthesized on solid support. These sequences were purified on 20% PAGE followed by ethanol precipitation. The quantification of these oligomers was done using Nearest-Neighbor method. Buffers used were Na_2HPO_4 (10mM), NaCl (100mM) and EDTA (1mM) at pH 7 for duplex and pH 6 for triplex for Tm measurement and tris-acetate (25mM), NaCl (100mM) and $MgCl_2$ (10mM) at pH 7 and pH 5 for gel retardation studies for duplex and triplex formation at 15^{0}C and 4^{0}C, respectively.

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