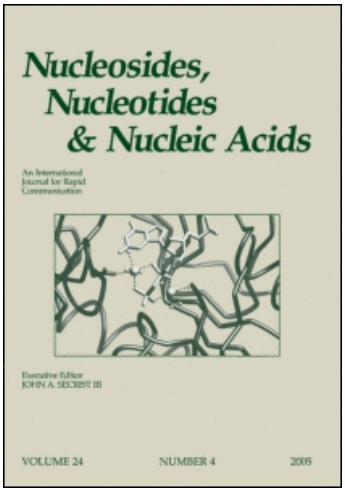

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Solid-Supported Oligonucleotide Systems for Special Biomedical Applications

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SOLID-SUPPORTED OLIGONUCLEOTIDE SYSTEMS FOR SPECIAL BIOMEDICAL APPLICATIONS

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ABSTRACT: The use of composite beads consisting of a 6 μm polystyrene core with 30 nm surface-bound silica particles to routine automatic oligodeoxynucleotide (ODN) synthesis is described.

INTRODUCTION

For routine oligonucleotide preparations macroporous supports are preferred, since they show maximum accessibility of the growing nucleotide chains to low molecular reagents and solvents. However, if there is an additional demand for the use of macromolecular reactants, e.g. enzymes, a porous matrix may cause diffusion and/or steric hindrance. Such a demand is best fulfilled by supports with an unreactive core and a functionalized outer shell[1]. As a further example, we describe here a composite bead system consisting of an unreactive 6 μm polystyrene core derivatized on the surface with silica microbeads of 30 nm average diameter[2] (Support I, Fig. 1) with respect to its application to routine ODN synthesis. These beads have also been particularly suitable for loading with an extremely small number of DNA molecules for the development of exonucleolytic sequencing[3].

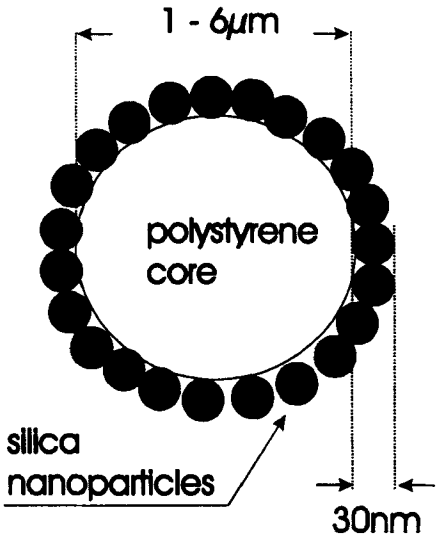

Fig. 1: Schematic drawing of a core-shell bead

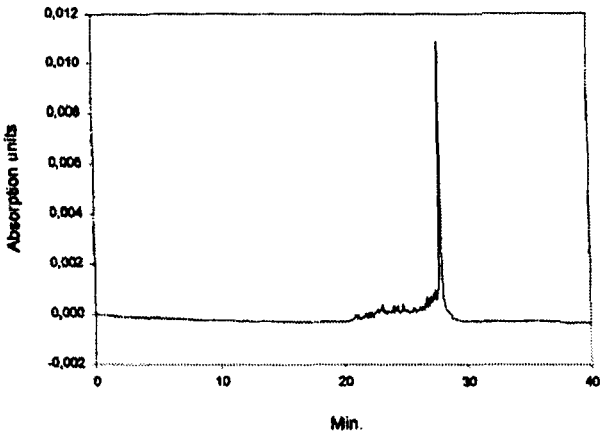

Fig. 2: CE analysis of 40mer

Table 1:

	Support	*average yield % *	*total yield %*
40 bases	I	99.1	69.4
40 bases	CPG 1000	98.0	46.1
II, 100 bases	I	99.7	76.5
II, 100 bases	CPG 1000	99.1	39.7
III, 100 bases	I	98.8	30.0
III, 100 bases	CPG 1000	98.9	34.9

EXPERIMENTS, RESULTS AND DISCUSSION

NH_2-functionalized composite beads[2] were loaded[4] with 10-27 μmol nucleoside/g. Standard ODN synthesis was done on a 0.2 μmol routine (synthesizer: Pharmacia 4-primers) with conventional workup. Composite beads with 19 μmol nucleoside/g were selected for the preparation of medium to long oligonucleotides. A 40mer sequence was synthesized in 99.1% average elongation yield. The separation of the crude solid-phase product by capillary electrophoresis is shown in Fig. 2. Two 100mers (II and III) were prepared similarly and the correct sequence verified by the Sanger technique (Table 1).

These results show, that support I, although fuctionalized only within its shell, has similar capacity and similar, if not superior, efficiency, compared to CPG.

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