HAPTEN INHIBITION STUDIES ASSESSING THE ABILITY OF A THYMINE DERIVED HAPTEN TO BIND DNA ANTIBODIES IN SERA FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Submitted to the faculty of the Graduate School
in partial fulfillment of the requirements
of the degree
Master of Sciences
in the Department of Pharmacology and Toxicology
of the Indiana University School of Medicine
May 1985

Accepted by the faculty of the Graduate School, Department of Pharmacology, Indiana University, in partial fulfillment of the requirements for the degree of Master of Science.

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ABSTRACT

A solid phase radioimmunoassay was adapted to assess the binding of a thymine derived hapten to anti-DNA antibodies (DNA Abs) present in sera from Systemic Lupus Erythematosus (SLE) patients. The synthetic thymine derivative, 4-(N_1-thyminyl)-butyric acid (TBA), had the ability to inhibit double stranded DNA (dsDNA) from binding to dsDNA coated microtitre wells although only a maximum inhibition of 50% was observed in one of three SLE sera tested. Thymidylic acid had a greater ability to inhibit dsDNA Ab binding (89.7% +/- 8.0, n=3) while uridine had less than 20% inhibition in all three sera tested.

No difference in the inhibition of single stranded DNA (ssDNA) Ab binding was seen between TBA and uridine on ssDNA coated plates where less than 45% maximum inhibition for either hapten was measured in one serum. Thymidylic acid again proved to be a better inhibitor of ssDNA Ab binding (94.4% +/- 4.6, n=3) than TBA or uridine indicating that thymidylic acid is recognized as a partial determinant for DNA Ab specificity.

As expected, DNA, being a high molecular weight species, demonstrated the strongest inhibition of antibody binding (dsDNA or ssDNA) over the three haptens. This is based on affinity values (I_{50}) attained in the range of 10^{-10}-10^{-6} M. The evaluation of hapten inhibition studies reported here suggests further use of inhibitors of a larger molecular size (at least 3-4 nucleotides in length) to probe the specificity of the

antibody combining site since haptens with a molecular weight of less than 1000 are unable to fill all available antibody binding sites. For this reason, efforts to conjugate TBA to a protein carrier are in progress for future antigen inhibition studies.

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