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**Yan et al.**

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(54) **RICIN INHIBITORS AND METHODS FOR USE THEREOF**

Szewczak et al, Proc. Nat'l. Acad. Sci. USA (1993), vol. 90(20), 9581-9585.\*

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Rutenber et al, Proteins: Structure, Function, and Genetics. (1991) vol. 10, 240-250.\*

\* cited by examiner

(\*) Notice: Under 35 U.S.C. 154(b), the term of this patent shall be extended for 0 days.

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(57) **ABSTRACT**

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Ricin A-chain is an N-glycosidase that attacks ribosomal RNA at a highly conserved adenine residue. Crystallographic studies show that not only adenine and formycin, but also pterin-based rings can bind in the ricin active site. For a better understanding of the recognition mode between ricin, and adenine-like rings, the interaction energies and geometries were calculated for a number of complexes. Shiga toxin, a compound essentially identical to the protein originally isolated from *Shigella dysenteriae*, has an active protein chain that is a homologue of the ricin active chain, and catalyzes the same depurination reaction. The present invention is drawn to identifying inhibitors of ricin and Shiga toxin, using methods molecular mechanics and ab initio methods and using the identified inhibitors as antidotes to ricin or Shiga toxin, or to facilitate immunotoxin treatment by controlling non-specific cytotoxicity.

**Related U.S. Application Data**

(63) Continuation-in-part of application No. 08/773,398, filed on Dec. 24, 1996.

(51) **Int. Cl.**<sup>7</sup> ..... **G01N 33/566**; G01N 33/53

(52) **U.S. Cl.** ..... **436/501**; 436/503; 435/DIG. 15

(58) **Field of Search** ..... 436/501, 503; 435/DIG. 15

(56) **References Cited**

**PUBLICATIONS**

Yan et al, J. Mol. Bio. (1997) vol. 266, 1043-1049.\*  
Olson, Proteins: Structure, Function, and Genetics. (1997) vol. 27(1), 80-95.\*

**6 Claims, 23 Drawing Sheets**