US005718892A

United States Patent [19]

Keefer et al.

[11] Patent Number: 5,718,892

[45] Date of Patent: *Feb. 17, 1998

[54] **POLYMER-BOUND NITRIC OXIDE/ NUCLEOPHILE ADDUCT COMPOSITIONS, PHARMACEUTICAL COMPOSITIONS INCORPORATING SAME AND METHODS OF TREATING BIOLOGICAL DISORDERS USING SAME**

[75] Inventors: **Larry K. Keefer**, Bethesda; **Joseph A. Hrabie**, Frederick, both of Md.

[73] Assignee: **The United States of America as represented by the Department of Health and Human Services**, Washington, D.C.

[*] Notice: The term of this patent shall not extend beyond the expiration date of Pat. No. 5,405,919.

[21] Appl. No.: **417,913**

[22] Filed: **Apr. 6, 1995**

Related U.S. Application Data

[62] Division of Ser. No. 935,565, Aug. 24, 1992, Pat. No. 5,405,919.

[51] **Int. Cl.**[6] **C08K 5/22**; A01N 33/26

[52] **U.S. Cl.** **424/78.27**; 525/377; 514/906; 514/2

[58] **Field of Search** 424/78.17, 78.27, 424/484, 486

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,153,094	10/1964	Reilly	564/112
4,265,714	5/1981	Nolan et al.	205/779.5
4,298,595	11/1981	Parkinson et al.	424/78.27
4,460,560	7/1984	Tokes et al.	424/78.17
4,482,533	11/1984	Keith	514/652
4,638,079	1/1987	Inskip et al.	560/4
4,659,558	4/1987	Urquhart et al.	424/486
4,708,854	11/1987	Grinstead	423/235
4,877,606	10/1989	Churchill et al.	424/486
4,888,413	12/1989	Domb	424/78.17
4,921,683	5/1990	Bedell	423/235
4,952,289	8/1990	Ciccone et al.	205/633
4,954,526	9/1990	Keefer	514/611
4,985,471	1/1991	Ohta et al.	522/27
5,039,705	8/1991	Keefer et al.	514/611
5,087,631	2/1992	Shaffer et al.	514/342
5,087,671	2/1992	Loeppky et al.	425/328.2
5,094,815	3/1992	Conboy et al.	422/52
5,405,919	4/1995	Keefer et al.	525/377

FOREIGN PATENT DOCUMENTS

PCT/US89/ 02611	6/1989	European Pat. Off. .
0 425 154 A1	10/1990	European Pat. Off. .
211 789	7/1984	Germany .

OTHER PUBLICATIONS

1991 Article by Maragos, et al., Complexes of NO with Nucleophiles as Agents for the Controlled Biological Release of Nitric Oxide. Vasorelaxant Effects, *J. Med. Chem.*, 34, 3242–3247.

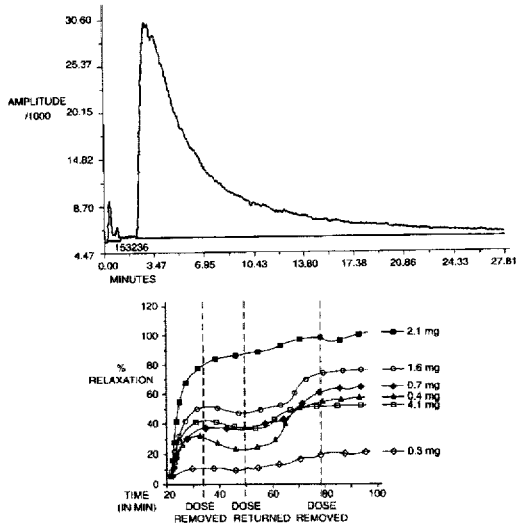
1990 Article by Myers, et al., Vasorelaxant Properties of the Endothelium–Derived Relaxing Factor more closely Resemble S–Nitrosocystein Than Nitric Oxide, *Nature*, vol. 345.

(List continued on next page.)

Primary Examiner—Peter F. Kulkosky

Attorney, Agent, or Firm—Leydig, Voit & Mayer, Ltd.

[57] **ABSTRACT**

A polymeric composition capable of releasing nitric oxide including a polymer and a nitric oxide-releasing $N_2O_2^-$ functional group bound to the polymer; pharmaceutical compositions including the polymeric composition; and methods for treating biological disorders in which dosage with nitric oxide is beneficial. The compositions can be used as and/or incorporated into implants, injectables, condoms, prosthesis coatings, patches, and the like for use in a wide variety of medical applications.

5 Claims, 2 Drawing Sheets