



US005166331A

United States Patent [19]
della Valle et al.

[11] **Patent Number:** **5,166,331**
[45] **Date of Patent:** **Nov. 24, 1992**

- [54] **HYALURONICS ACID FRACTIONS, METHODS FOR THE PREPARATION THEREOF, AND PHARMACEUTICAL COMPOSITIONS CONTAINING SAME**
- [75] Inventors: **Francesco della Valle, Padova; Aurelio Romeo, Rome; Silvana Lorenzi, Padova, all of Italy**
- [73] Assignee: **Fidia, S.p.A., Abano Terme, Italy**
- [21] Appl. No.: **452,681**
- [22] Filed: **Dec. 19, 1989**

Related U.S. Application Data

- [63] Continuation of Ser. No. 756,824, Jul. 19, 1985, abandoned, which is a continuation-in-part of Ser. No. 719,113, Apr. 2, 1985, abandoned, and a continuation-in-part of Ser. No. 669,431, Nov. 8, 1984, abandoned.

[30] **Foreign Application Priority Data**

Oct. 10, 1983 [IT]	Italy	49143 A/83
Oct. 9, 1984 [IT]	Italy	48979 A/84
Apr. 5, 1985 [IT]	Italy	47924 A/85

- [51] Int. Cl.⁵ **C07H 5/04; C07H 5/06; A01N 43/04; A61K 37/715**
- [52] U.S. Cl. **536/55.1; 514/54; 514/420; 514/576; 514/777; 514/912; 424/78.05**
- [58] Field of Search **536/55.1; 514/54, 912, 514/777, 420, 576; 424/78, 78.05**

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,870,791	3/1975	Haddad et al.	424/22
4,141,973	2/1979	Balazs	536/55.1
4,255,415	3/1981	Chrai et al.	424/78

OTHER PUBLICATIONS

- Takashi et al, The Journal of Antibiotics vo. 31 (1978) pp. 150-155.
- Cleland, Chemical Abstracts, vol. 76 (1972) No. 43075q "Molecular Weight Distribution in Hyaluronic Acid".
- Laurent et al, Chemical Abstracts, vol. 98(1983) No. 211815f "The Molecular Weight of hyaluronate in the Aqueous Humor . . .".
- Shimada et al,; J. Biochem. vol. 31 (1977) pp. 79-91 "Molecular Weight of Hyaluronic Acid from Rabbit Skin".
- Barron et al, American Journal of Ophthalmology vol 100 (1985) pp. 377-389 "Comparison of the Effects of Viscoat and Nealon".

Primary Examiner—Nathan M. Nutter
Attorney, Agent, or Firm—Birch, Stewart, Kolasch & Birch

[57] **ABSTRACT**

Two pharmaceutically useful fractions of hyaluronic acid are obtained comprising a first fraction with a molecular weight between 50,000 and 100,000 which is useful for wound healing, and a second fraction having a molecular weight between 500,000 and 730,000 which is useful for intraocular and intraarticular injections.

In addition, pharmaceutical preparations for topical administration are provided containing a pharmacologically active substance together with hyaluronic acid or a molecular weight fraction thereof. The hyaluronic acid may be in the form of the free acid or may be a salt with an alkali or alkaline earth metal, magnesium, aluminum or ammonium, or in the form of a salt with one or more pharmacologically active substances.

18 Claims, 1 Drawing Sheet