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[54] **EXCIPIENT STABILIZATION OF POLYPEPTIDES TREATED WITH ORGANIC SOLVENTS**

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[52] **U.S. Cl.** **424/85.7**; 514/21; 530/351; 530/399

[58] **Field of Search** 424/85.7; 514/21; 530/351, 399

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,664,963	5/1972	Pasin	252/316
4,297,344	10/1981	Schwinn et al.	424/101
4,652,441	3/1987	Okada et al.	424/19
4,891,319	1/1990	Roser	435/188
5,032,405	7/1991	Huang et al.	424/463
5,039,540	8/1991	Ecanon	426/385
5,096,885	3/1992	Pearlman et al.	514/12
5,100,669	3/1992	Hyon et al.	424/426
5,149,653	9/1992	Roser	435/260

FOREIGN PATENT DOCUMENTS

30771/89	7/1989	Australia	A61K 47/18
0193917	9/1985	European Pat. Off.	A61K 9/18
0303746	8/1989	European Pat. Off. .	
WO89/03671	5/1989	WIPO	A61K 9/18

OTHER PUBLICATIONS

Wang et al., J. Parenteral Sci & Tech., vol. 42, No. 25, pp. s3–s26, 1988.

"Protein Structure", A Practical Approach, Ed. T. E. Creighton, IRL Press, Chapter 14, 1989.

Manning et al., Pharm. Res., vol. 6 (11), pp. 903–918, 1989.

Pikal, Biopharm, vol. 3 (9), pp. 26–30, 1990.

Arakawa et al., "Protein–Solvent Interactions in Pharmaceutical Formulations" *Pharmaceutical Research* 8 (3) : 285–291 (1991).

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[57] **ABSTRACT**

Methods for excipient stabilization of dry or aqueous polypeptides treated with organic solvents are disclosed, wherein the polypeptide is admixed with trehalose, a polyol having a molecular weight less than about 70,000 kD.

16 Claims, No Drawings