

TABLE VIII

Stability of spray freeze-dried solid rhGH formulations in methylene chloride and ethyl acetate.					
Formulation	Soluble Protein				
	% Recovery ^a (Total)	% Recovery ^b (Soluble)	% Large Aggreg	% Dimers	% Monomer
Methylene Chloride Tests					
5 mg/ml rhGH 1.25 mg/ml trehalose 0.2% Tween @ 20	37.2	34.0	6.2	8.3	85.5
5 mg/ml rhGH 1.25 mg/ml trehalose 0.2% PEG (3350 MW)	68.8	66.8	2.3	15.8	78.8
Ethyl Acetate Tests					
5 mg/ml rhGH 1.25 mg/ml trehalose 0.2% Tween @ 20	94.6	117.7	0.5	0.9	98.7
5 mg/ml rhGH 1.25 mg/ml trehalose 10.2% PEG (3350 MW)	97.7	104.7	0.6	0.0	99.4

^aThe total recovery of protein was defined as the amount of protein extracted into buffer after treatment in the organic solvent divided by the calculated amount of protein added to the extraction buffer (0.02 mL × 5 mg/mL).

^bSEC-HPLC results for protein extracted into buffer after treatment with organic solvent. The percent recovery of soluble protein was defined as the ratio of the concentrations from the total peak area of the sample and a reference standard times 100%. Control and sample rhGH concentrations were determined by absorbance at 278 nm.

We claim:

1. A method of stabilizing a polypeptide against denaturation in an organic solvent when treated with the organic solvent, wherein the method comprises admixing the polypeptide with a polyol, wherein the molecular weight of the polyol is less than about 70,000 kD and is trehalose, to form an admixture; and treating the admixture with the organic solvent.
2. The method of claim 1, wherein the polypeptide is growth hormone.
3. The method of claim 2, wherein the growth hormone is human.
4. The method of claim 1, wherein the polypeptide is gamma interferon.
5. The method of claim 1, wherein the organic solvent is methylene chloride.
6. The method of claim 1, wherein the organic solvent is ethyl acetate.
7. The method of claim 1 wherein the polypeptide is dry.
8. The method of claim 7 wherein the polypeptide is lyophilized.
9. The method of claim 1 wherein the mass ratio of trehalose to polypeptide is from 100:1 to 1:100.
10. The method of claim 1 wherein the mass ratio of trehalose to polypeptide is from 1:1 to 1:10.

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11. The method of claim 1 wherein the mass ratio of trehalose to polypeptide is from 1:3 to 1:4.

12. A method of formulating a polypeptide using a denaturing organic solvent comprising

a) admixing the polypeptide in an aqueous solution with a polyol having a molecular weight less than about 70,000 kD, wherein the polyol is trehalose; and

b) treating the polypeptide in the aqueous solution with the organic solvent.

13. The method of claim 12, wherein the product of step a) is dried and reconstituted in an aqueous formulation.

14. The method of claim 12 further comprising formulating the polypeptide for controlled release.

15. A method of formulating a dry polypeptide for controlled release using a denaturing organic solvent comprising

a) admixing the polypeptide with an excipient, wherein said excipient is a polyol having a molecular weight less than about 70,000 kD, and the polyol is trehalose; and

b) treating the product of step a) with the organic solvent.

16. The method of claim 15, further comprising encapsulation of the polypeptide in a polymer matrix.

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