Solubility of IFN-Beta-1b in Sodium Chloride Solutions

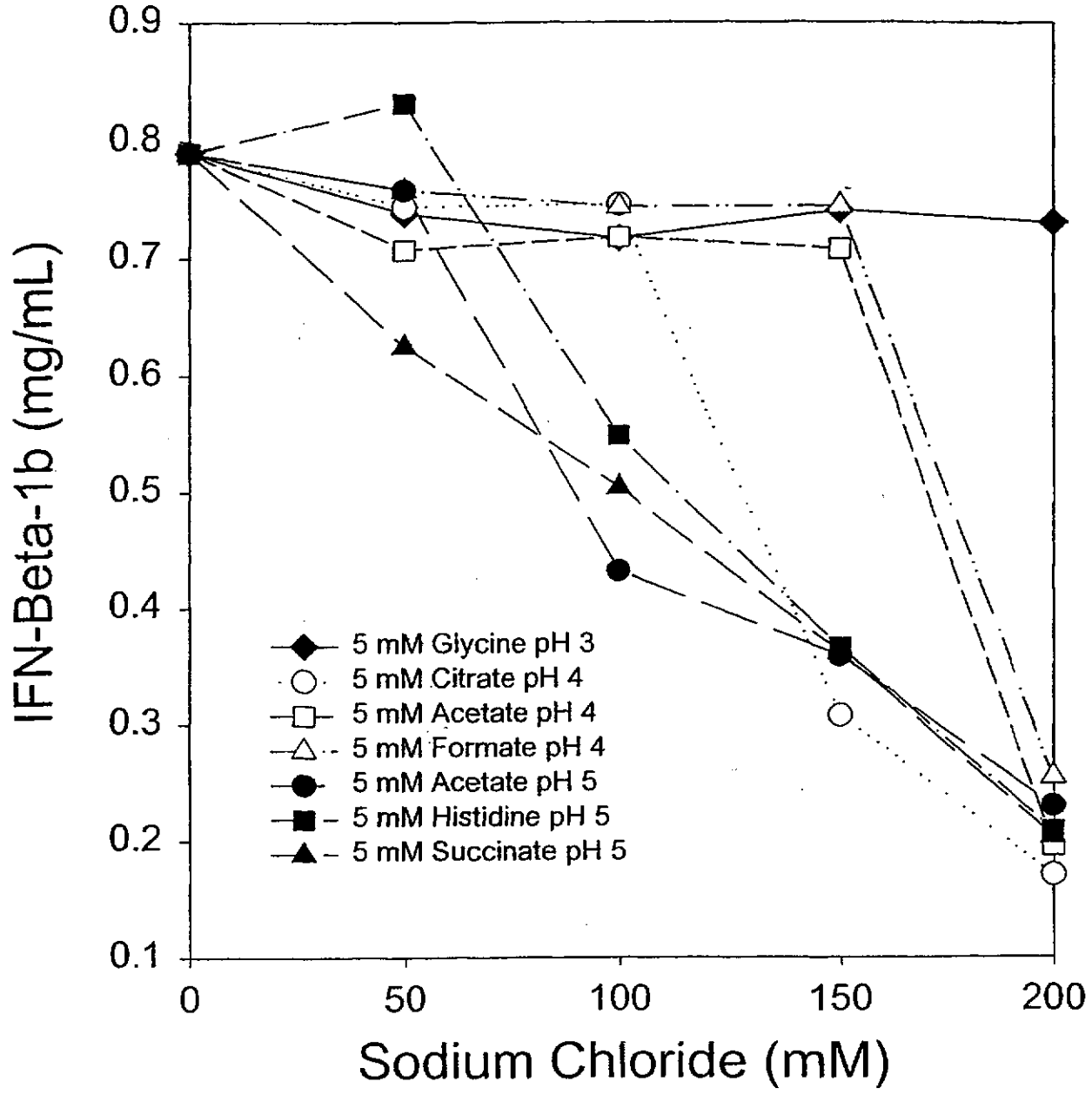


Figure 1

IFN-Beta-1b Solubility in Low-Ionic-Strength Formulations

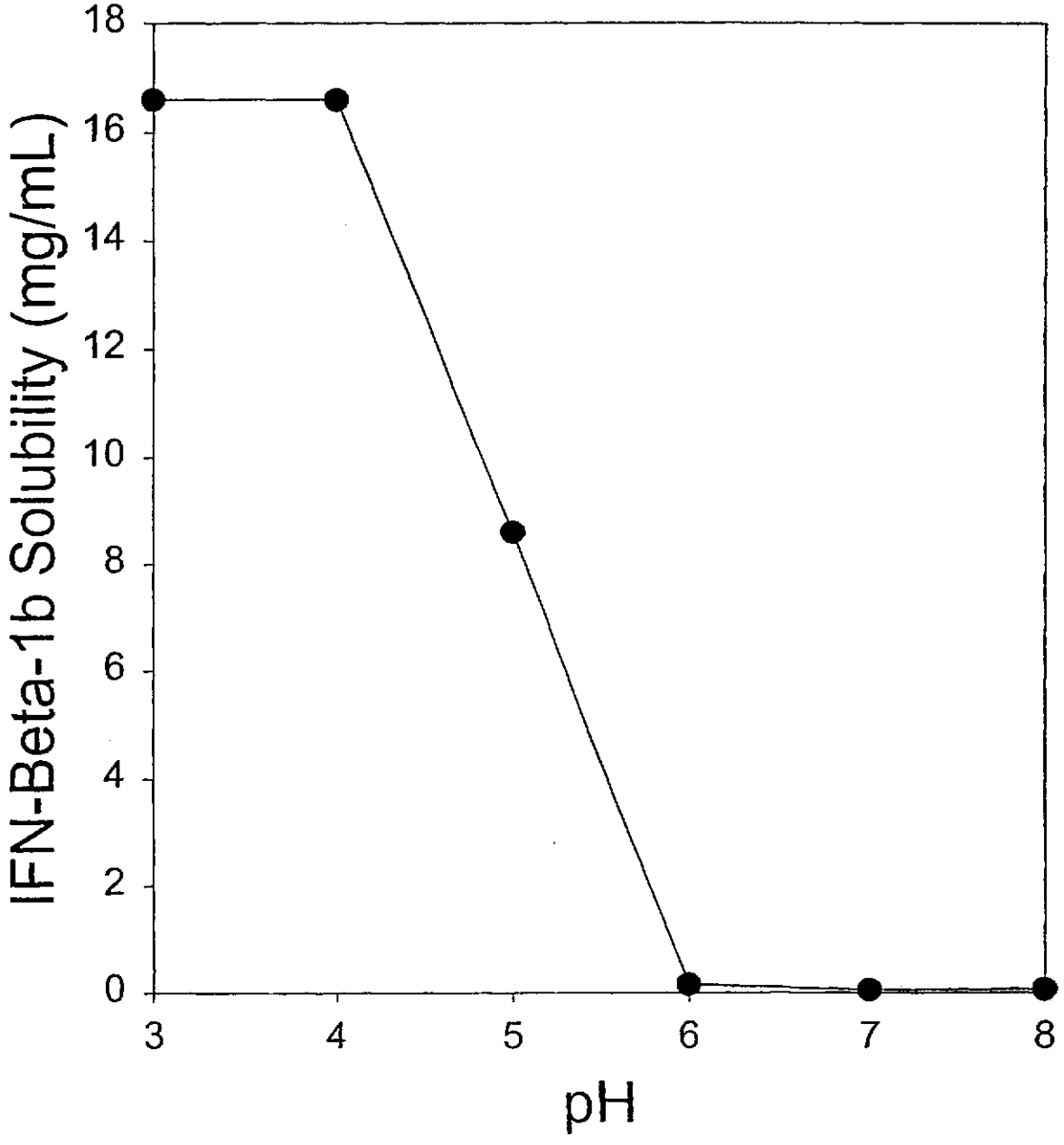


Figure 2

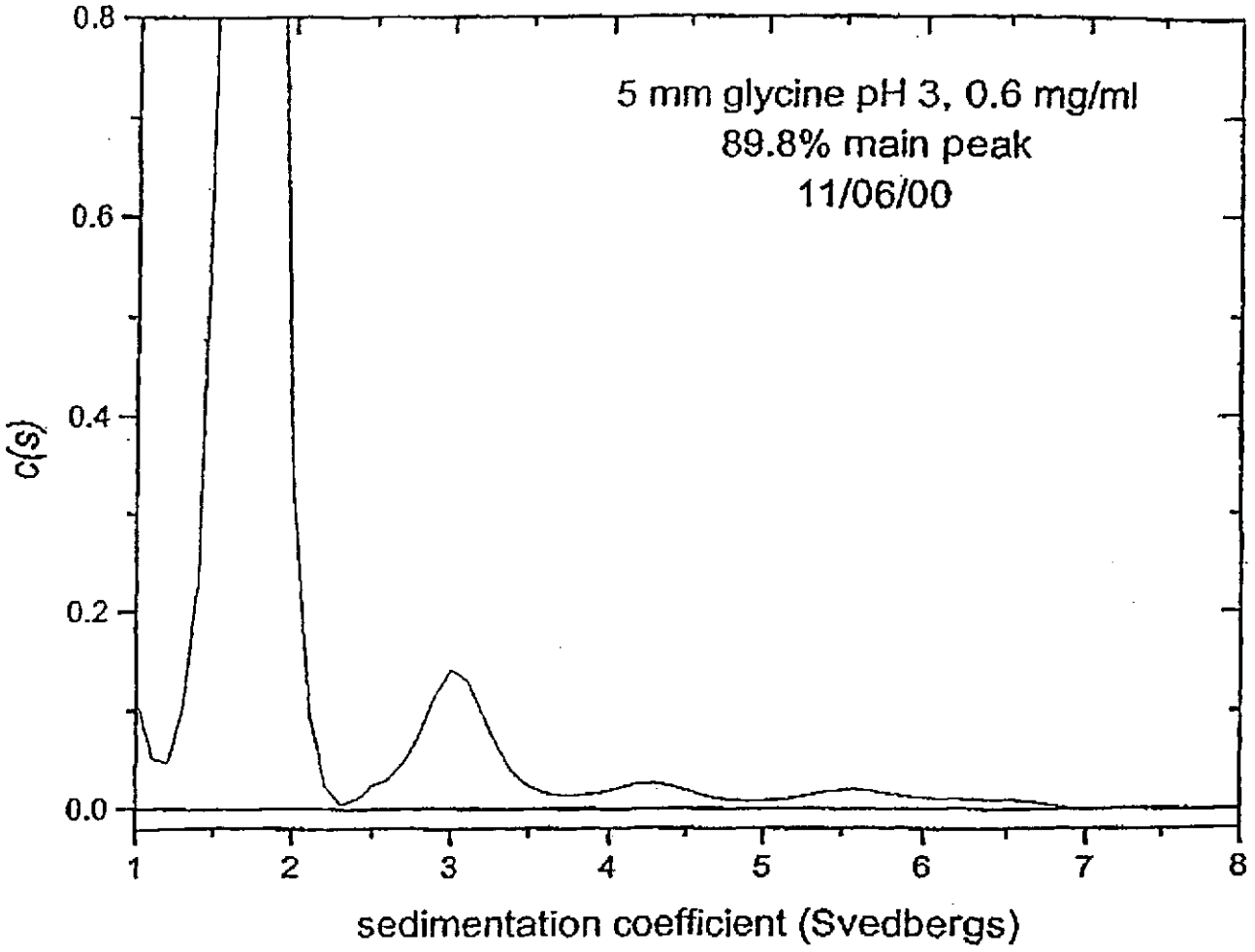

5 mm glycine pH 3, 0.6 mg/ml
89.8% main peak
11/06/00
c(s)
0.0
0.2
0.4
0.6
0.8
1
2
3
4
5
6
7
8
sedimentation coefficient (Svedbergs)

Figure 3

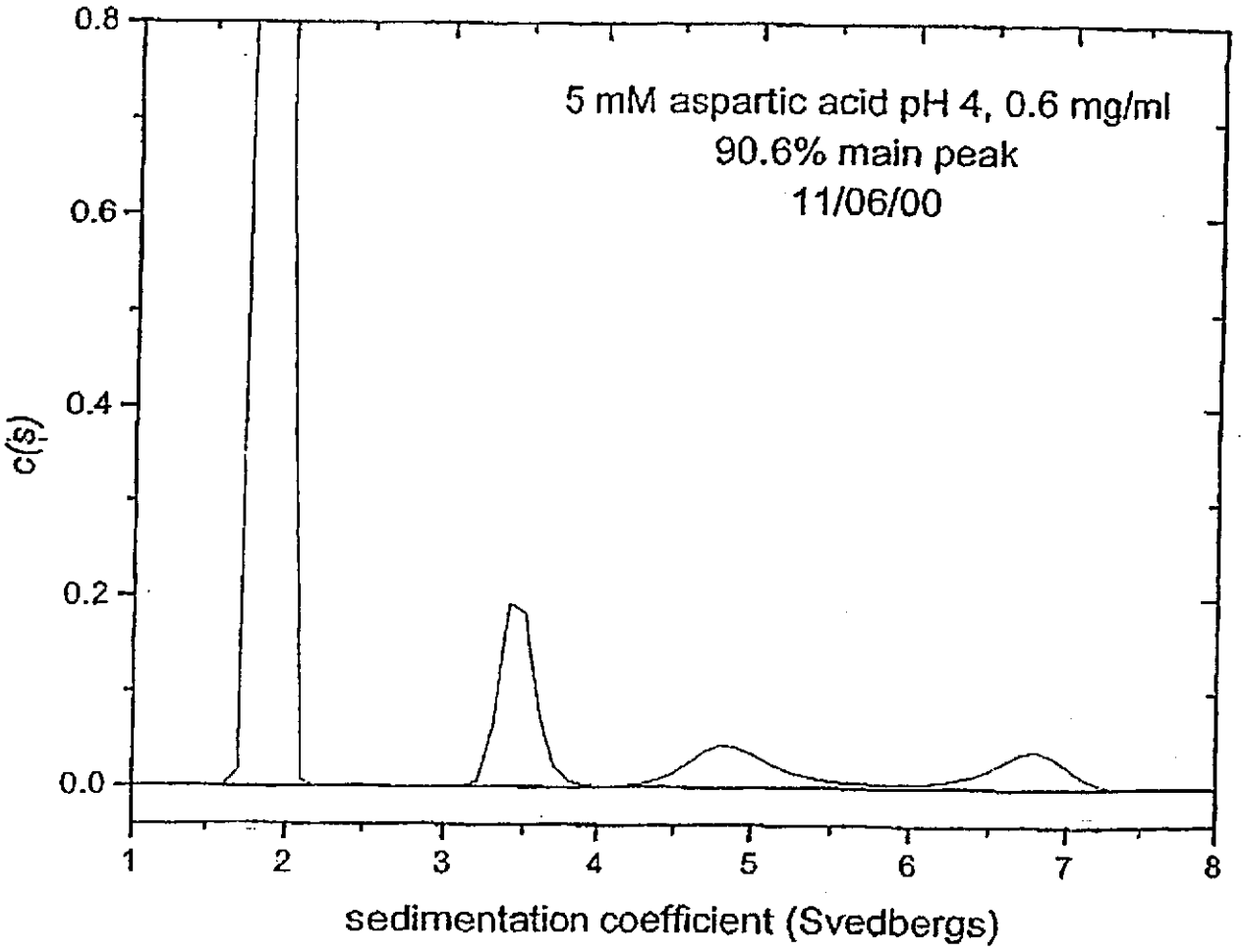

5 mM aspartic acid pH 4, 0.6 mg/ml
90.6% main peak
11/06/00
c(s)
0.0
0.2
0.4
0.6
0.8
1
2
3
4
5
6
7
8
sedimentation coefficient (Svedbergs)

Figure 4

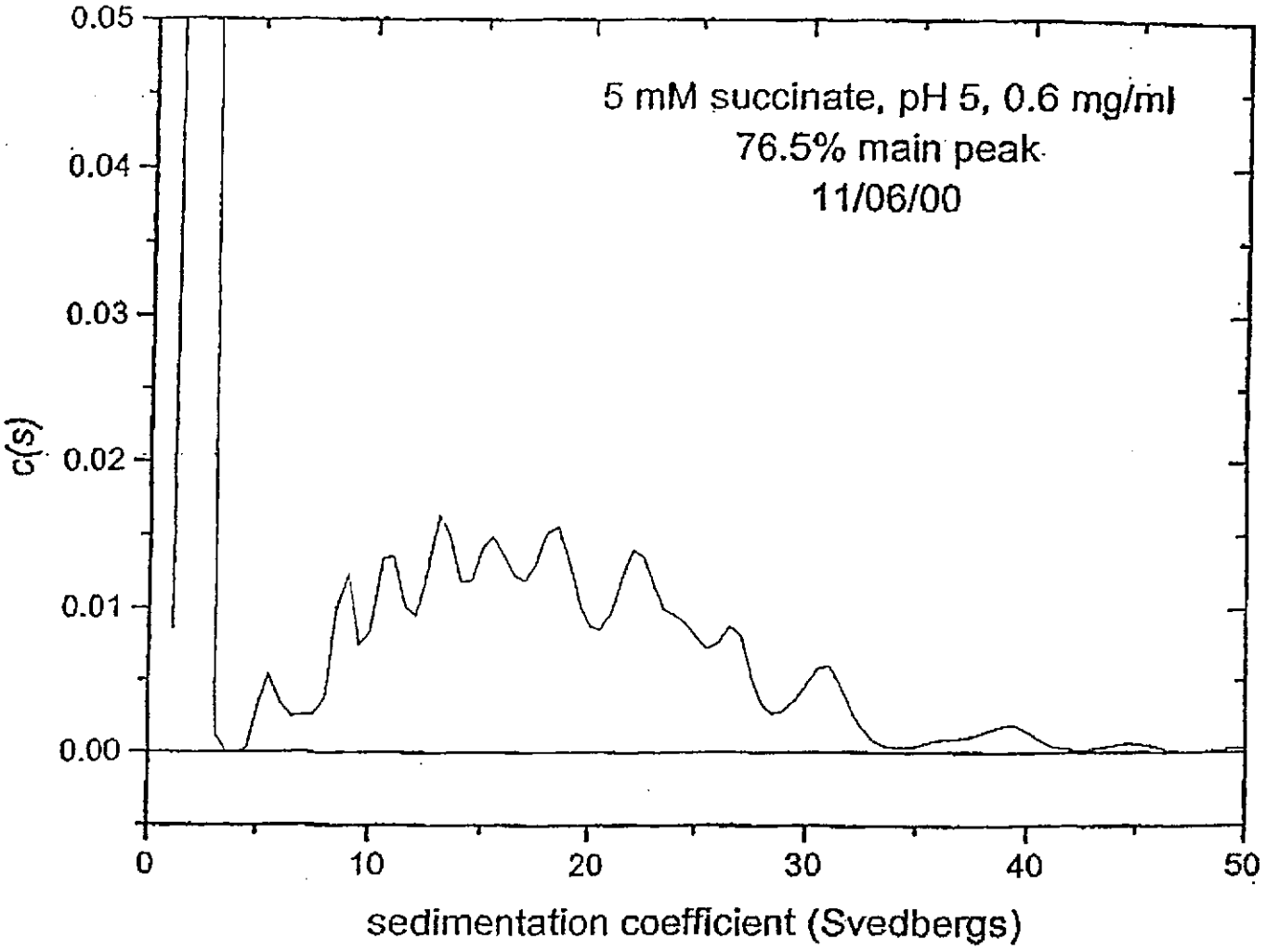

5 mM succinate, pH 5, 0.6 mg/ml
76.5% main peak
11/06/00
c(s)
0.05
0.04
0.03
0.02
0.01
0.00
0
10
20
30
40
50
sedimentation coefficient (Svedbergs)

Figure 5

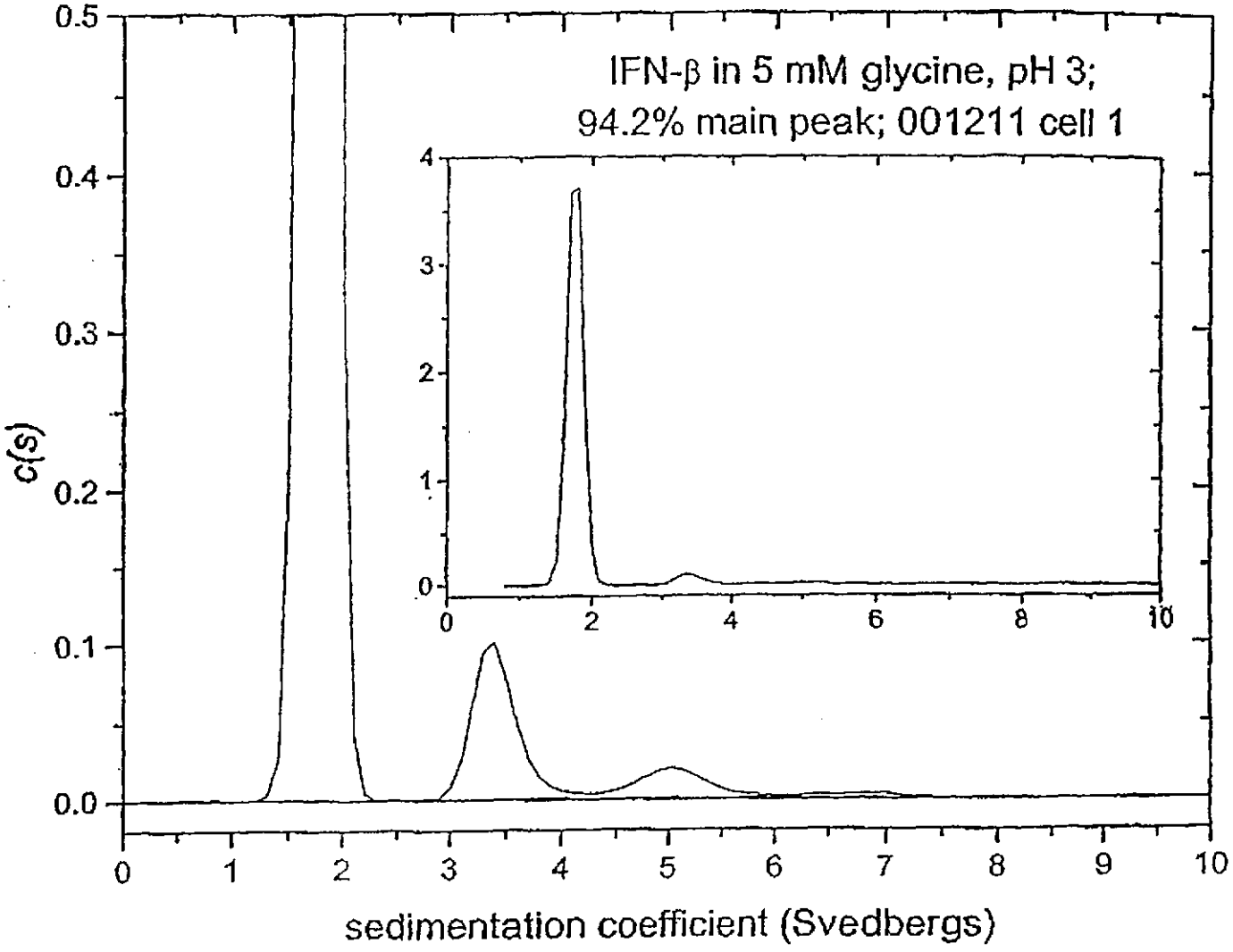

IFN-β in 5 mM glycine, pH 3;
94.2% main peak; 001211 cell 1
c(s)
sedimentation coefficient (Svedbergs)

Figure 6

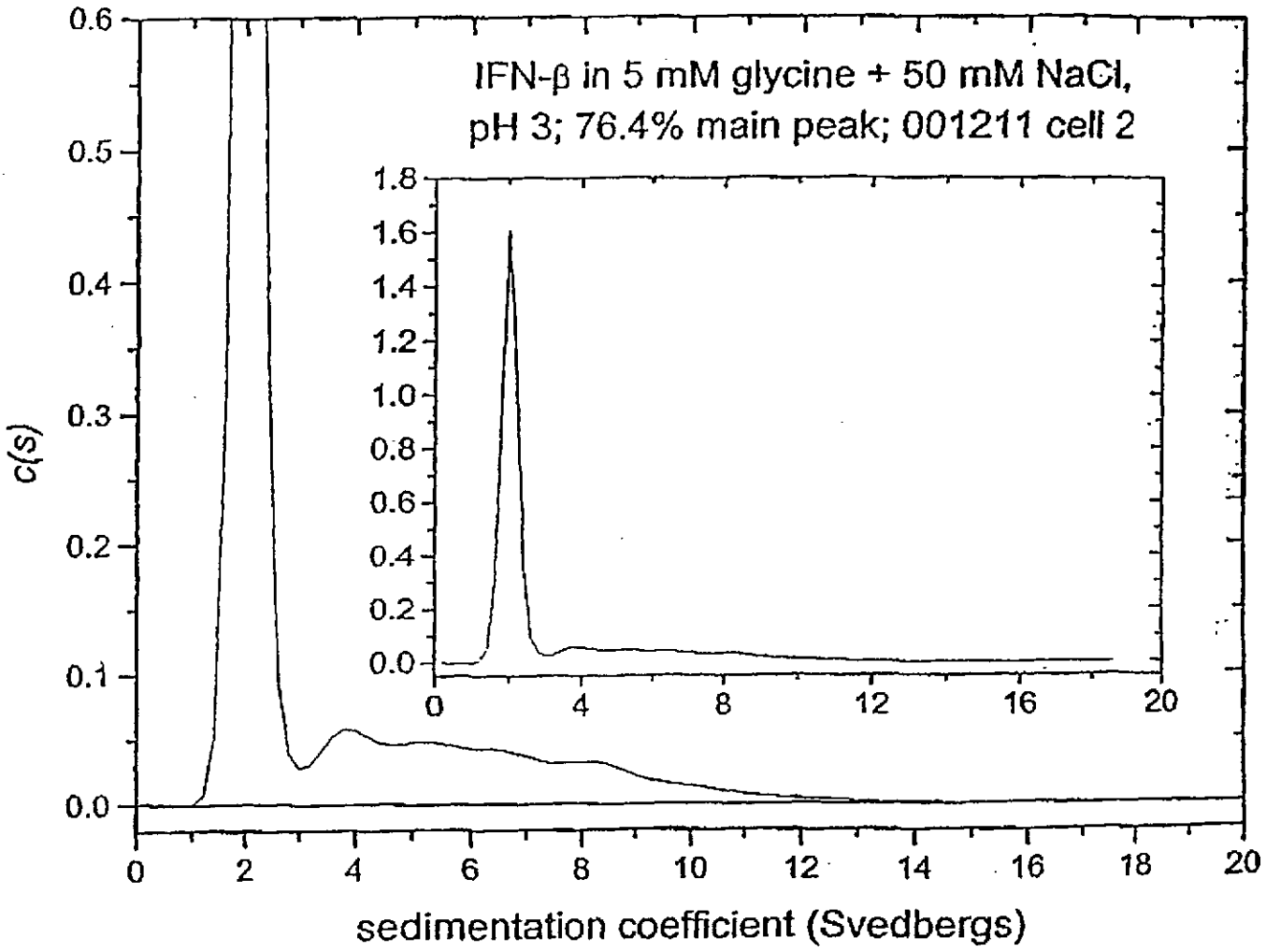

IFN-β in 5 mM glycine + 50 mM NaCl,
pH 3; 76.4% main peak; 001211 cell 2
c(s)
sedimentation coefficient (Svedbergs)

Figure 7

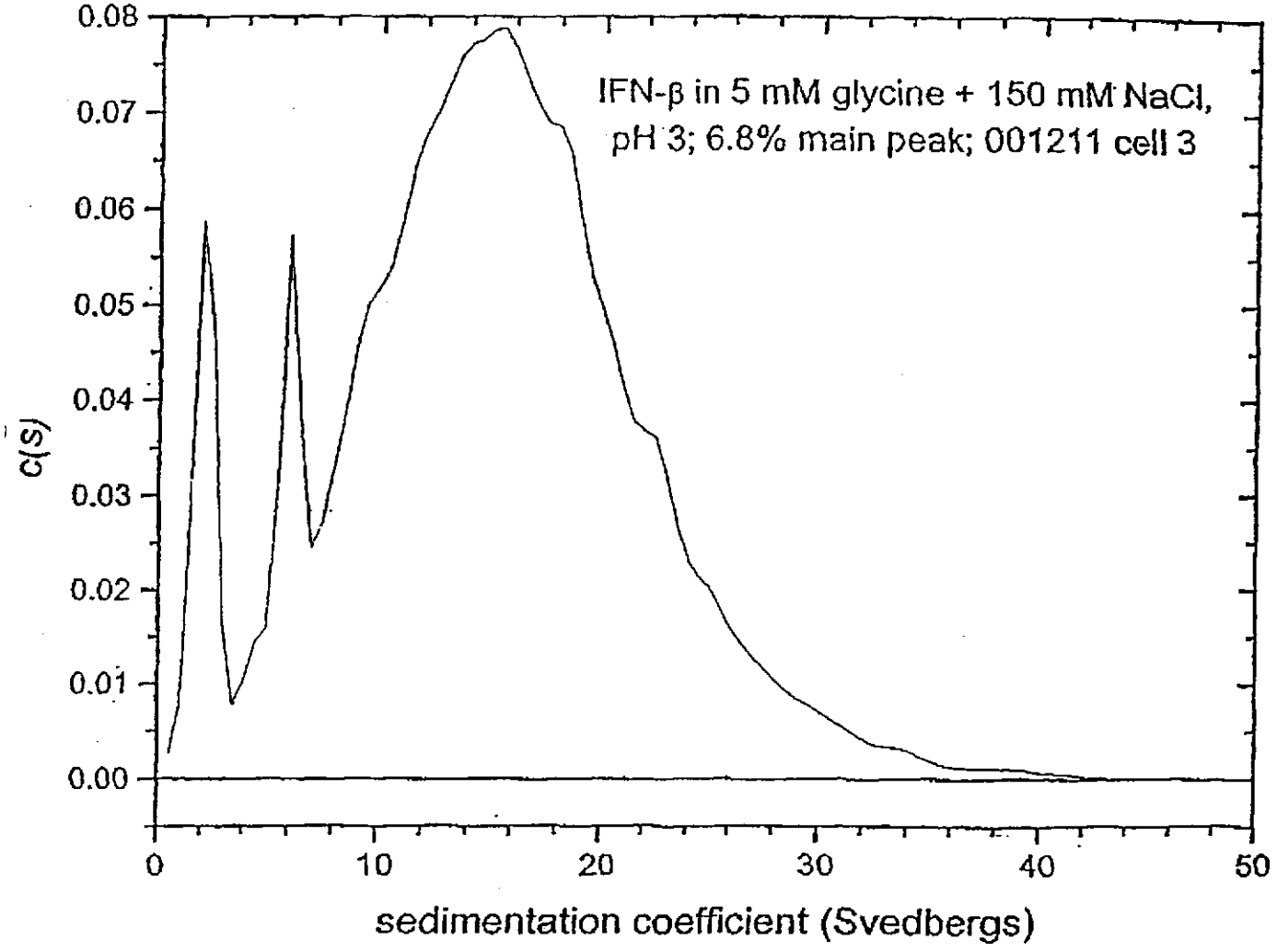

IFN-β in 5 mM glycine + 150 mM NaCl,
pH 3; 6.8% main peak; 001211 cell 3
c(s)
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0
10
20
30
40
50
sedimentation coefficient (Svedbergs)

Figure 8

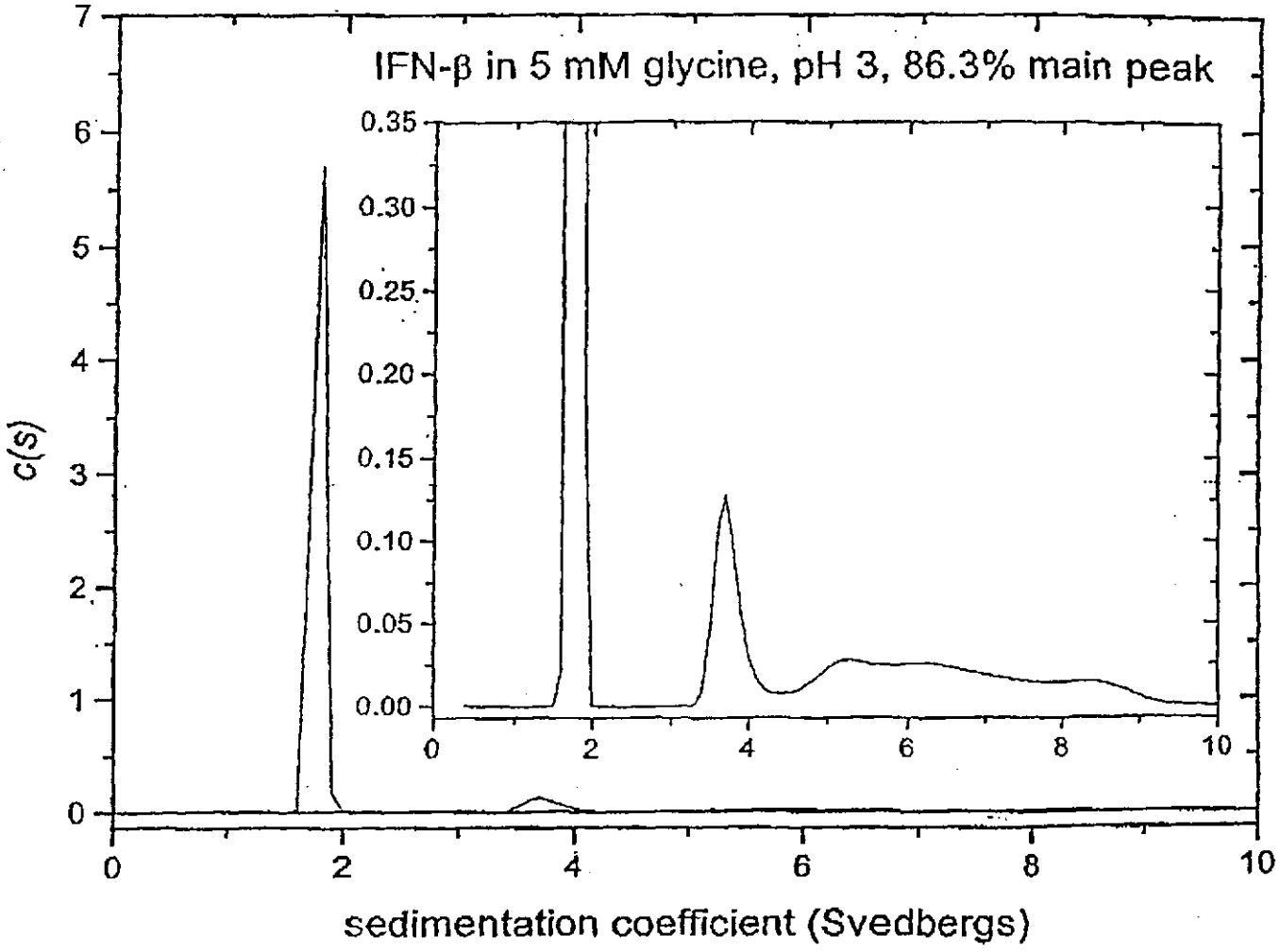

IFN-β in 5 mM glycine, pH 3, 86.3% main peak
c(s)
sedimentation coefficient (Svedbergs)
0
1
2
3
4
5
6
7
0
2
4
6
8
10
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35

Figure 9

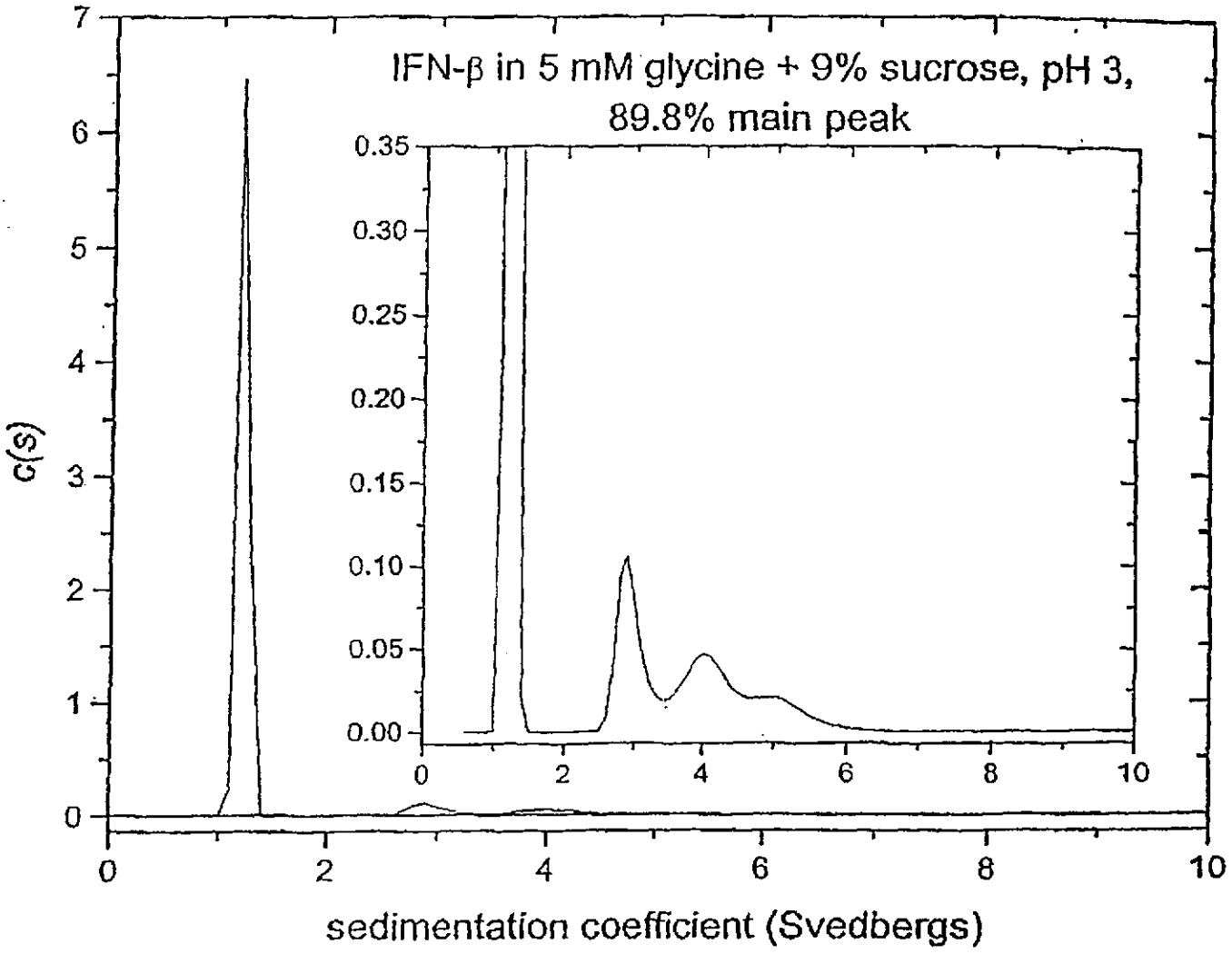

IFN-β in 5 mM glycine + 9% sucrose, pH 3,
89.8% main peak
c(s)
sedimentation coefficient (Svedbergs)

Figure 10

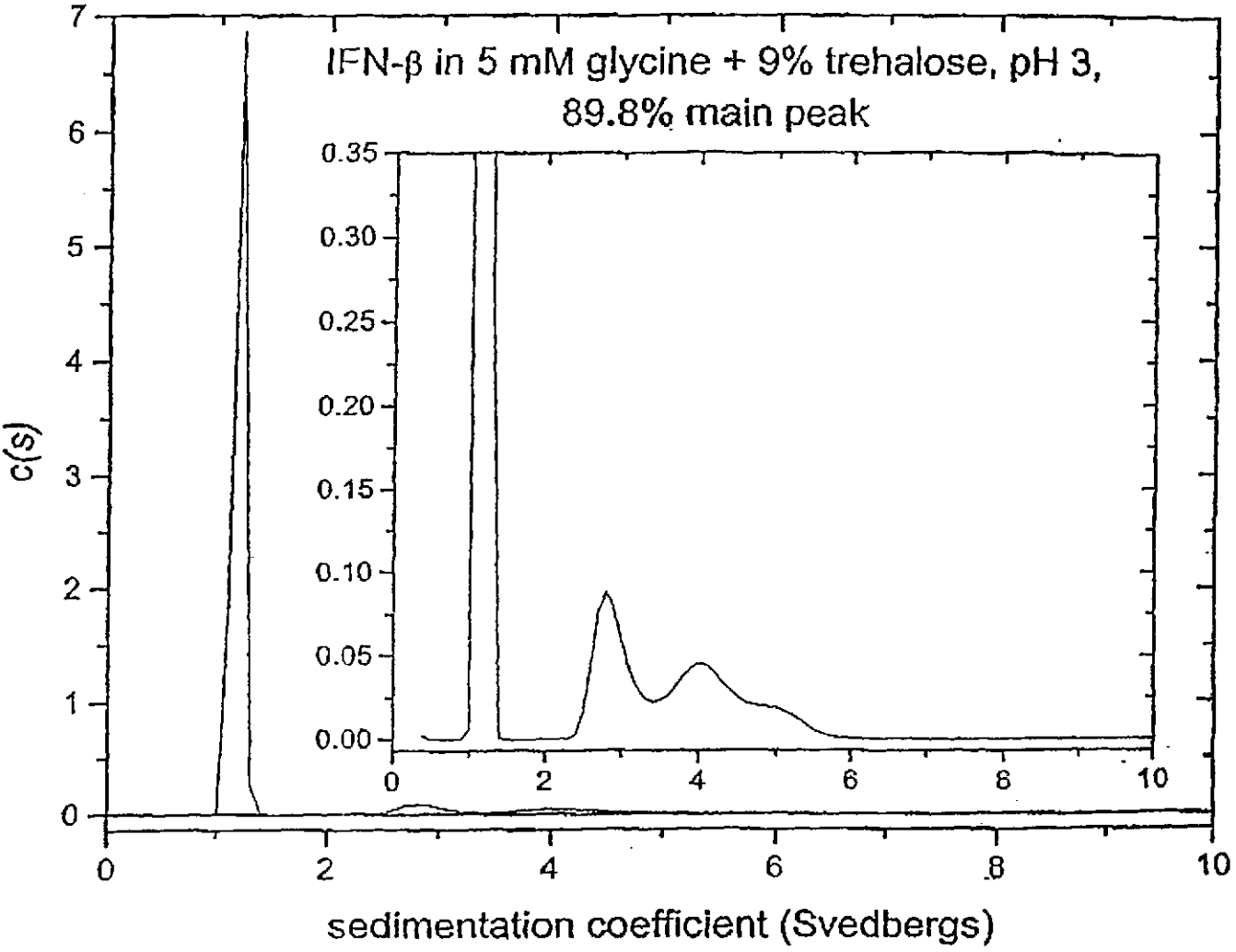

IFN-β in 5 mM glycine + 9% trehalose, pH 3,
89.8% main peak
c(s)
sedimentation coefficient (Svedbergs)
0
1
2
3
4
5
6
7
0
2
4
6
8
10
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35

Figure 11

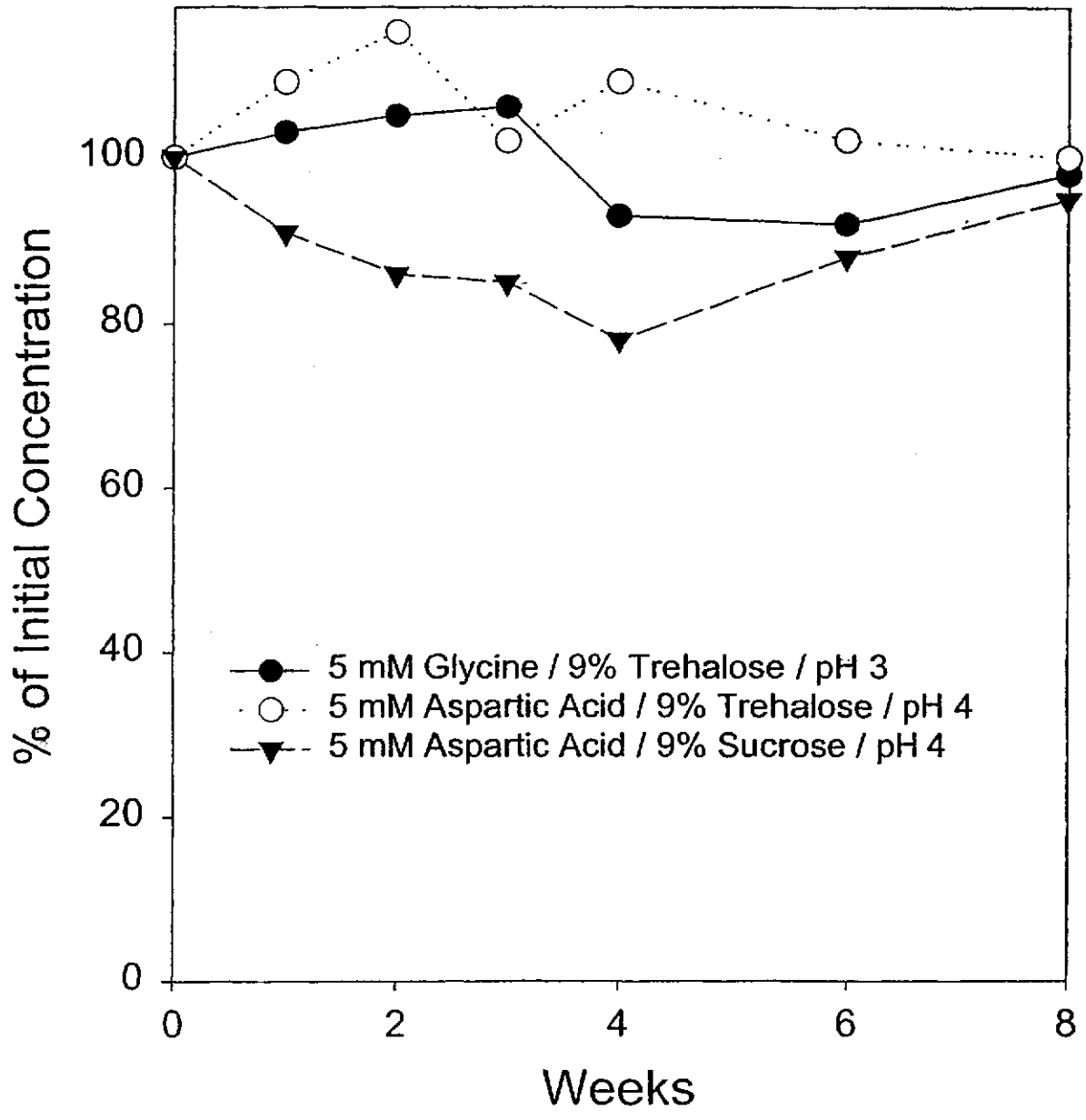

IFN-Beta-1b
Lyophilized Formulations
% of Initial Concentration
UV Absorption
40°C
% of Initial Concentration
100
80
60
40
20
0
0
2
4
6
8
Weeks
5 mM Glycine / 9% Trehalose / pH 3
5 mM Aspartic Acid / 9% Trehalose / pH 4
5 mM Aspartic Acid / 9% Sucrose / pH 4

Figure 12

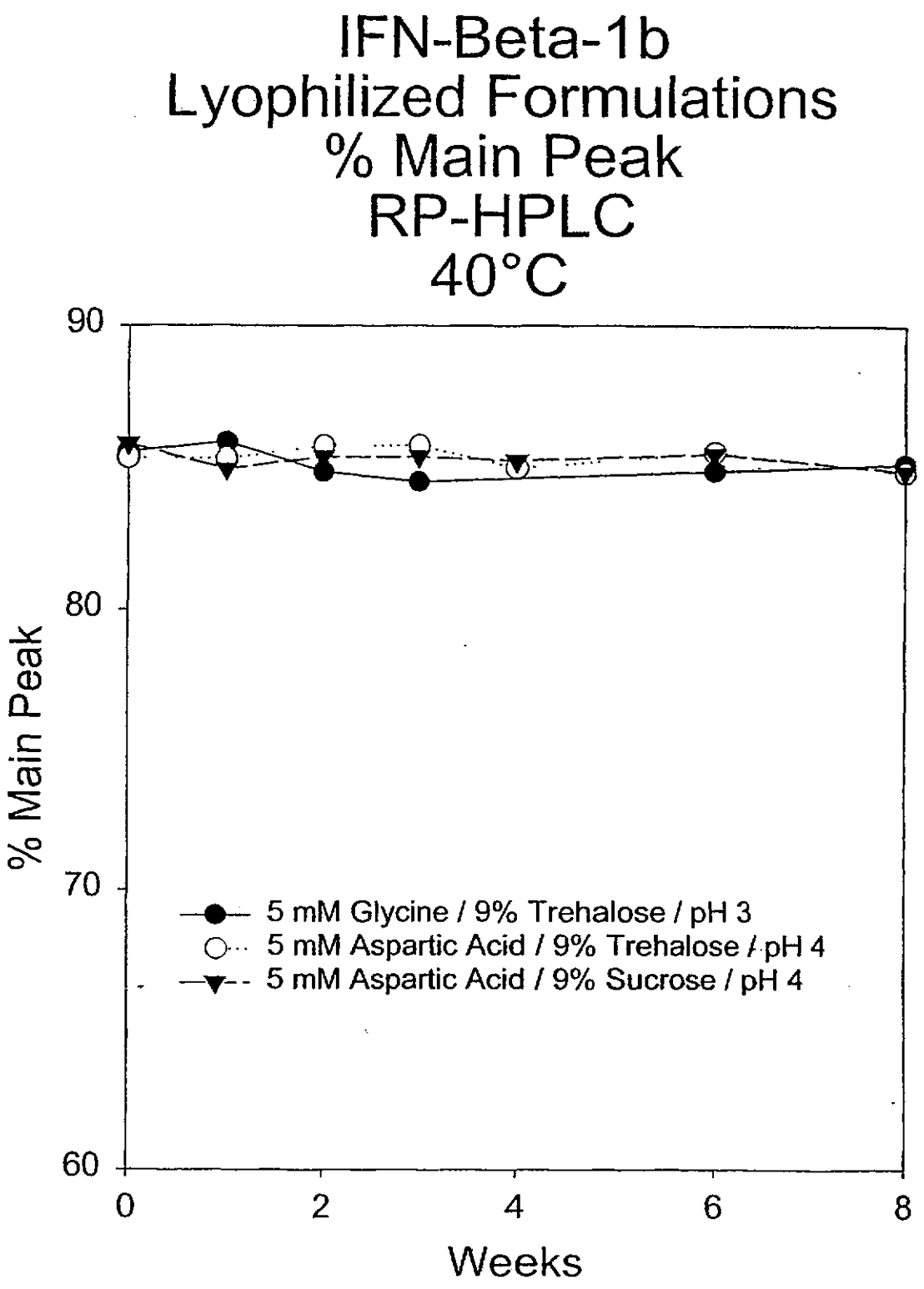

IFN-Beta-1b
Lyophilized Formulations
% Main Peak
RP-HPLC
40°C
90
80
70
60
% Main Peak
0
2
4
6
8
Weeks
5 mM Glycine / 9% Trehalose / pH 3
5 mM Aspartic Acid / 9% Trehalose / pH 4
5 mM Aspartic Acid / 9% Sucrose / pH 4

Figure 13

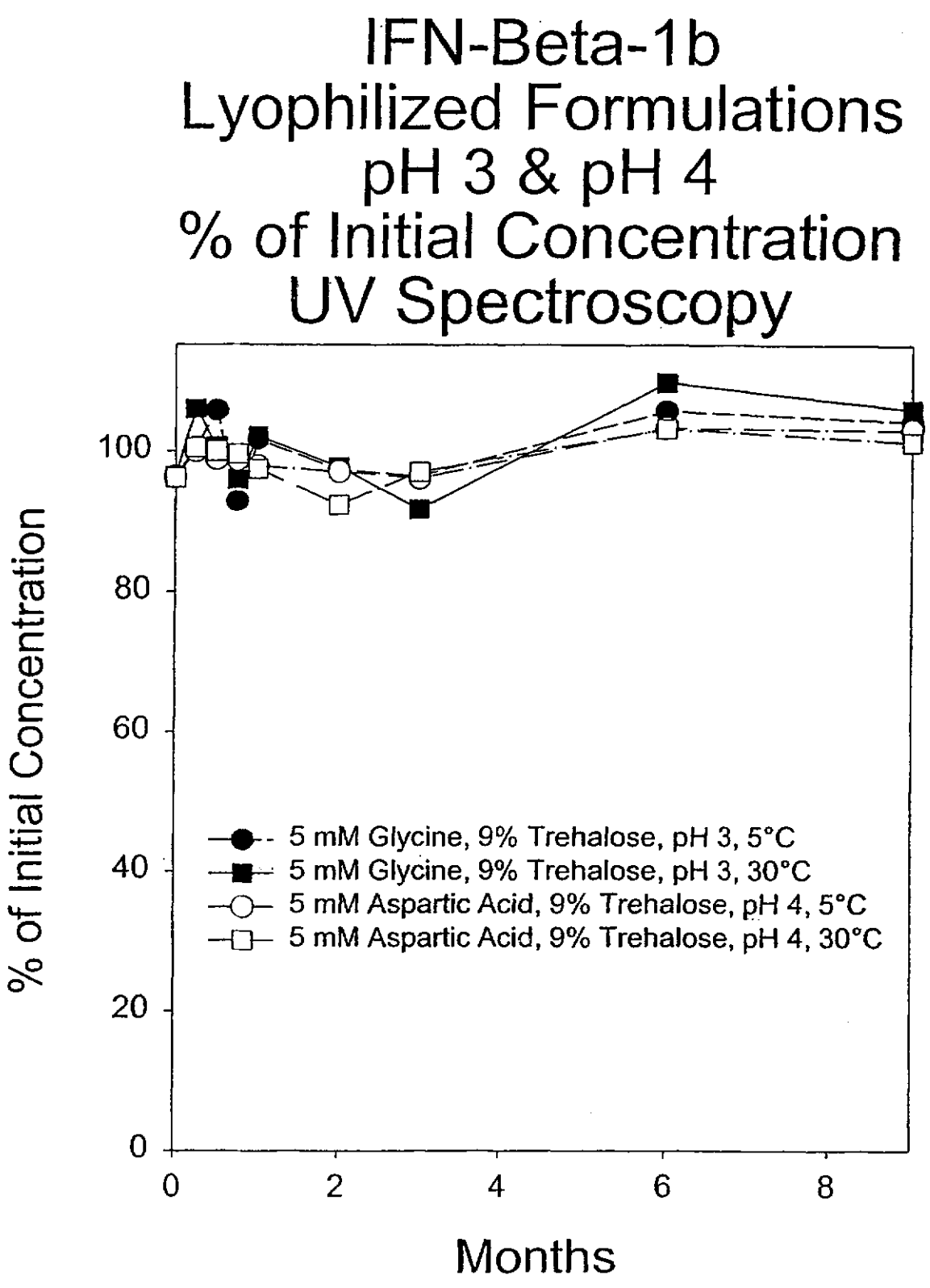

IFN-Beta-1b
Lyophilized Formulations
pH 3 & pH 4
% of Initial Concentration
UV Spectroscopy
% of Initial Concentration
100
80
60
40
20
0
0
2
4
6
8
Months
5 mM Glycine, 9% Trehalose, pH 3, 5°C
5 mM Glycine, 9% Trehalose, pH 3, 30°C
5 mM Aspartic Acid, 9% Trehalose, pH 4, 5°C
5 mM Aspartic Acid, 9% Trehalose, pH 4, 30°C

Figure 14

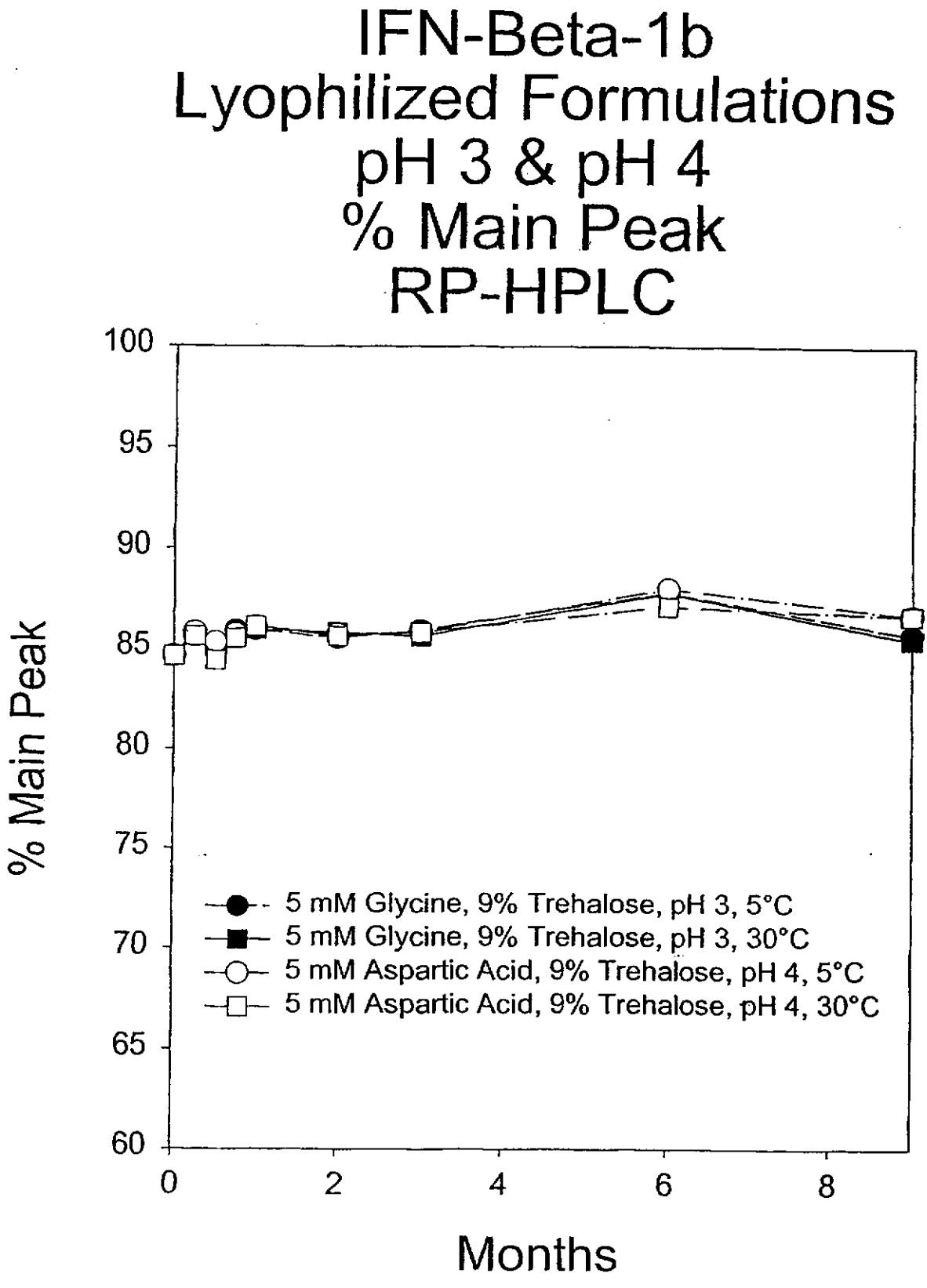

IFN-Beta-1b
Lyophilized Formulations
pH 3 & pH 4
% Main Peak
RP-HPLC
% Main Peak
100
95
90
85
80
75
70
65
60
0
2
4
6
8
Months
5 mM Glycine, 9% Trehalose, pH 3, 5°C
5 mM Glycine, 9% Trehalose, pH 3, 30°C
5 mM Aspartic Acid, 9% Trehalose, pH 4, 5°C
5 mM Aspartic Acid, 9% Trehalose, pH 4, 30°C

Figure 15

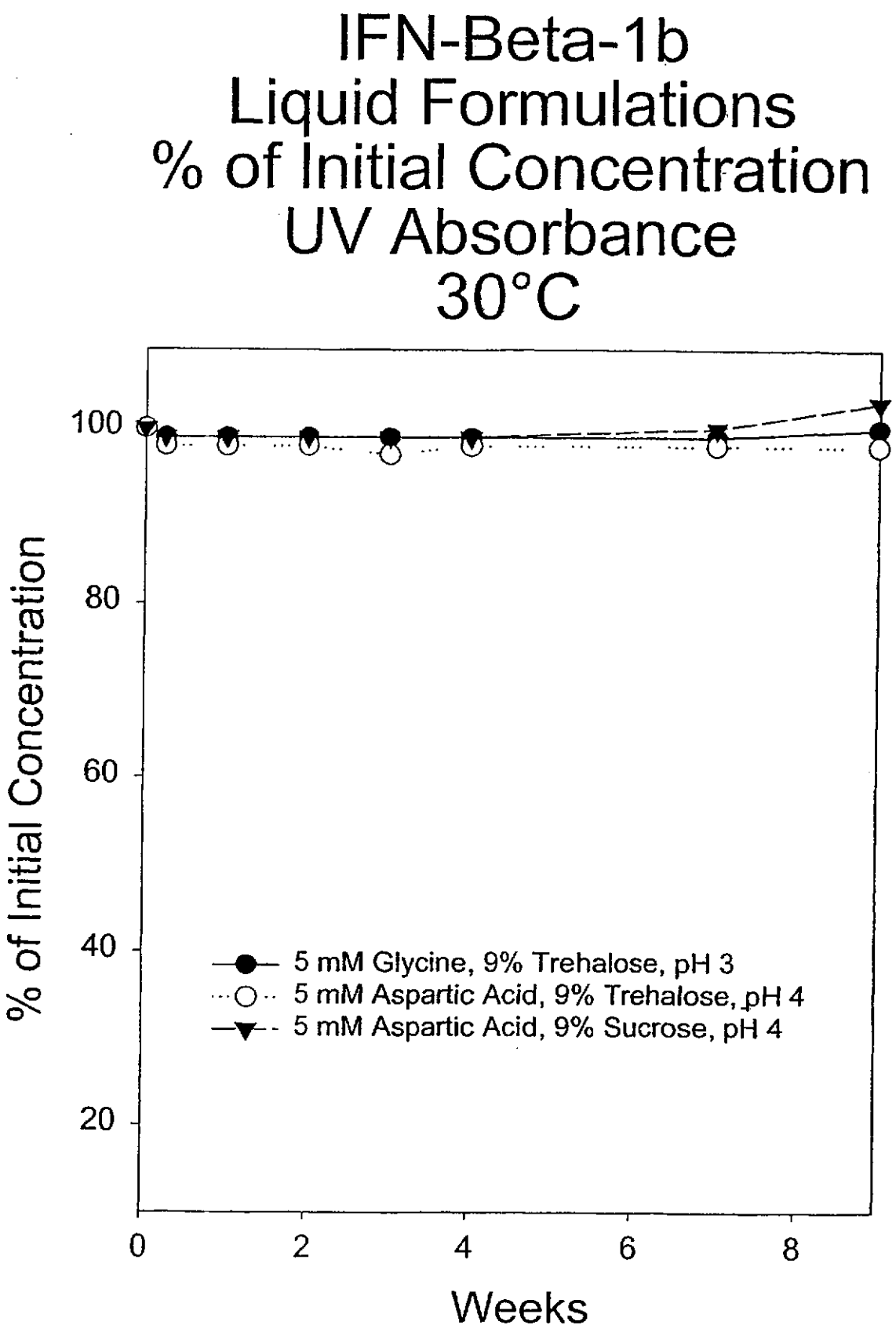

IFN-Beta-1b
Liquid Formulations
% of Initial Concentration
UV Absorbance
30°C
% of Initial Concentration
100
80
60
40
20
0
2
4
6
8
Weeks
5 mM Glycine, 9% Trehalose, pH 3
5 mM Aspartic Acid, 9% Trehalose, pH 4
5 mM Aspartic Acid, 9% Sucrose, pH 4

Figure 16

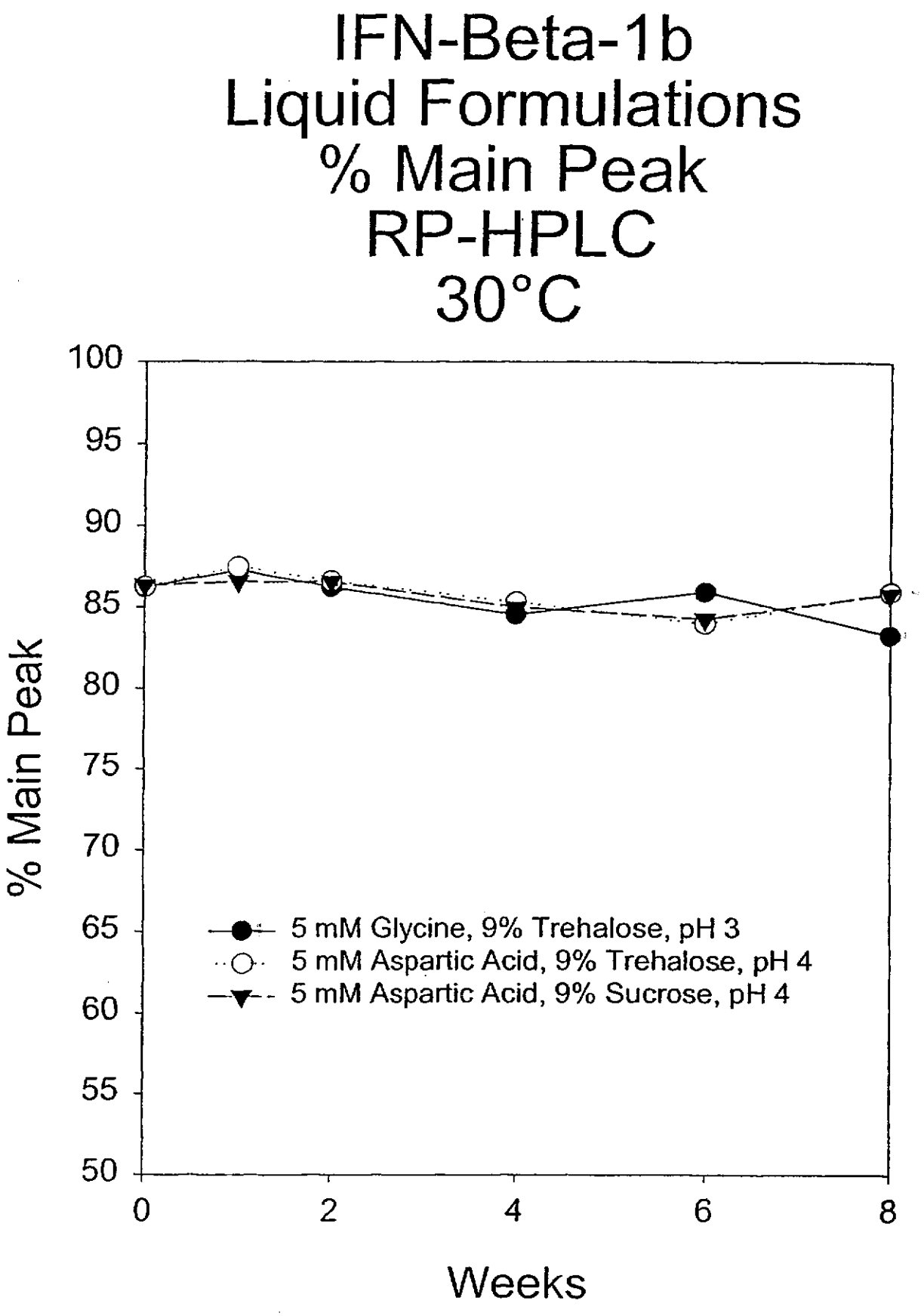

IFN-Beta-1b
Liquid Formulations
% Main Peak
RP-HPLC
30°C
% Main Peak
100
95
90
85
80
75
70
65
60
55
50
0
2
4
6
8
Weeks
5 mM Glycine, 9% Trehalose, pH 3
5 mM Aspartic Acid, 9% Trehalose, pH 4
5 mM Aspartic Acid, 9% Sucrose, pH 4

Figure 17

IFN-Beta-1b
Liquid Formulations in Vials
% of Initial Concentration
UV Spectroscopy
5°C

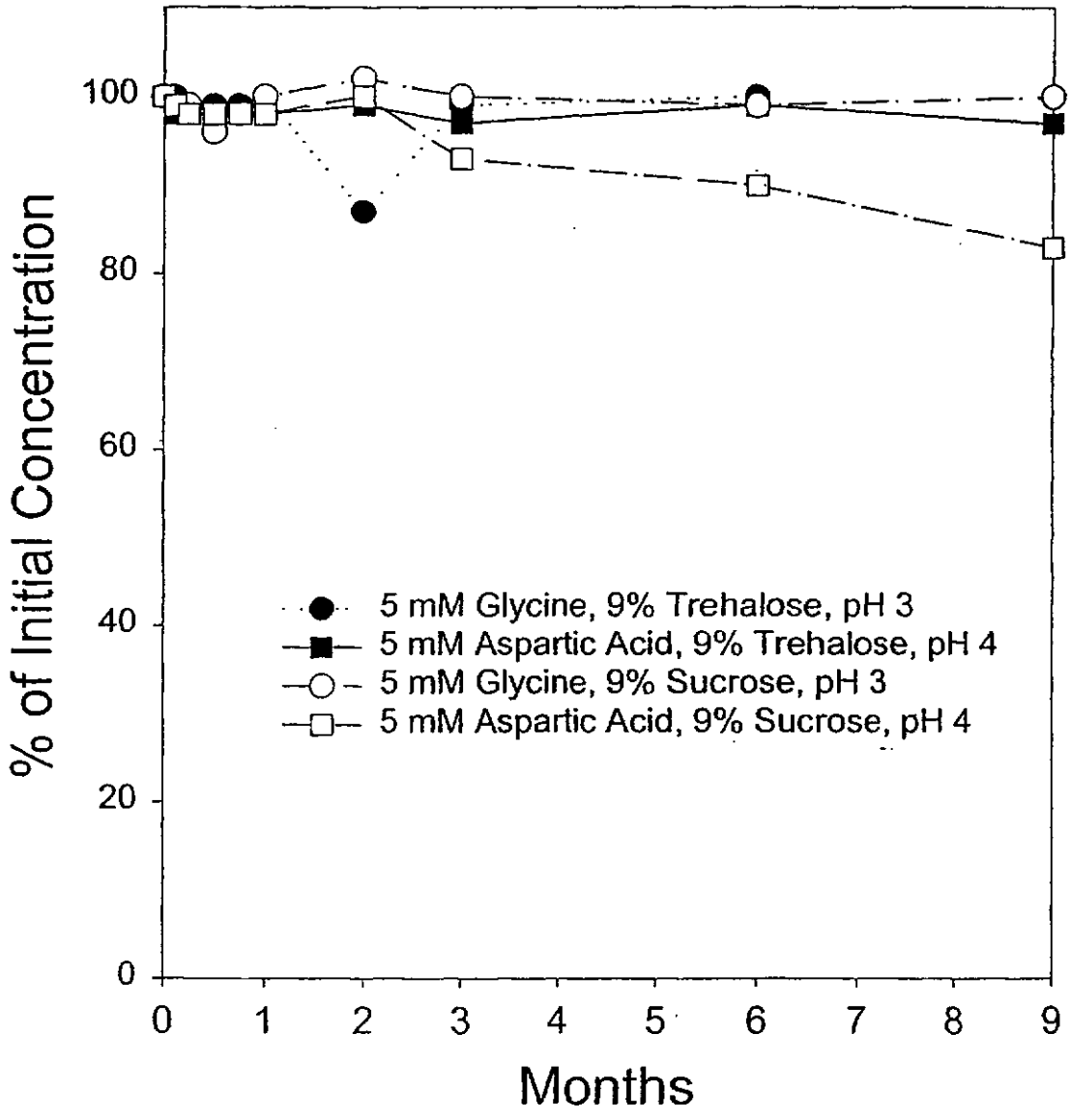


Figure 18

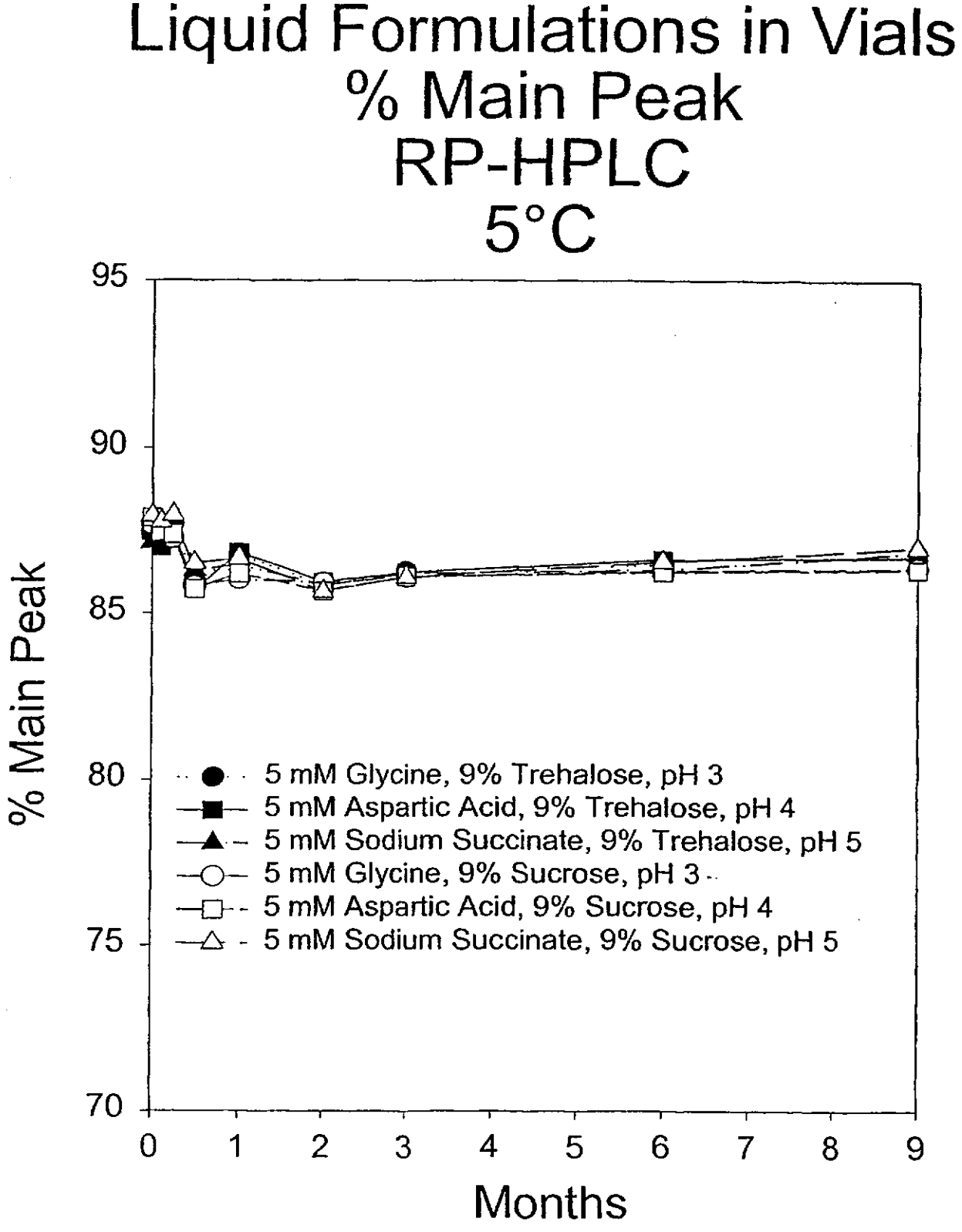

IFN-Beta-1b
Liquid Formulations in Vials
% Main Peak
RP-HPLC
5°C
% Main Peak
95
90
85
80
75
70
0
1
2
3
4
5
6
7
8
9
Months
5 mM Glycine, 9% Trehalose, pH 3
5 mM Aspartic Acid, 9% Trehalose, pH 4
5 mM Sodium Succinate, 9% Trehalose, pH 5
5 mM Glycine, 9% Sucrose, pH 3
5 mM Aspartic Acid, 9% Sucrose, pH 4
5 mM Sodium Succinate, 9% Sucrose, pH 5

Figure 19

IFN-Beta-1b Liquid Formulations Containing Trehalose or Sucrose % of Initial Concentration UV Spectroscopy 30°C

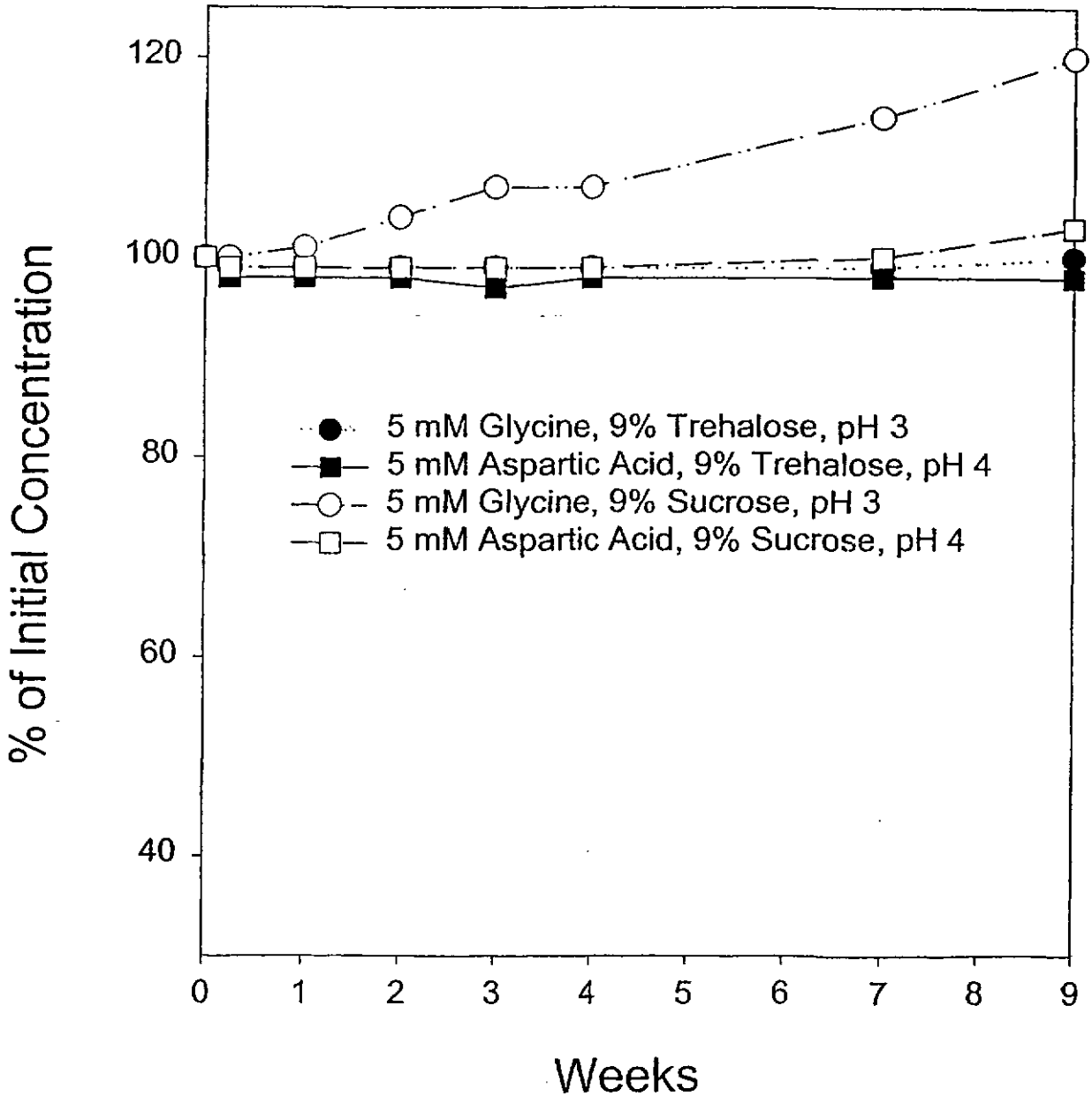


Figure 20

IFN-β-1b Lyophilized Formulations % of Initial Concentration Containing Trehalose or Sucrose pH 3 & 4 40°C

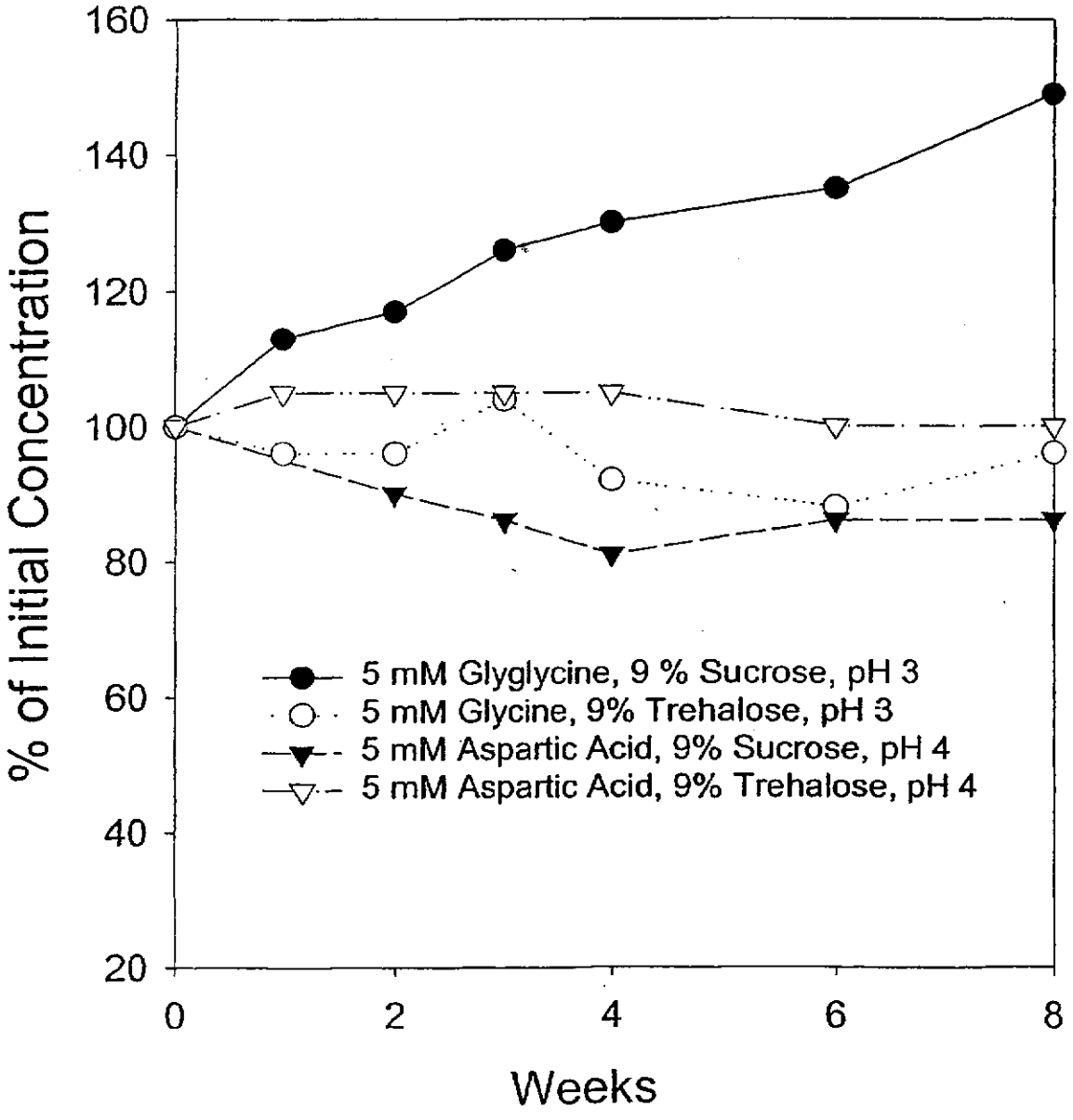


Figure 21

IFN-Beta-1b
Liquid Formulations Containing Mannitol
% of Initial Concentration
UV Spectroscopy
5°C

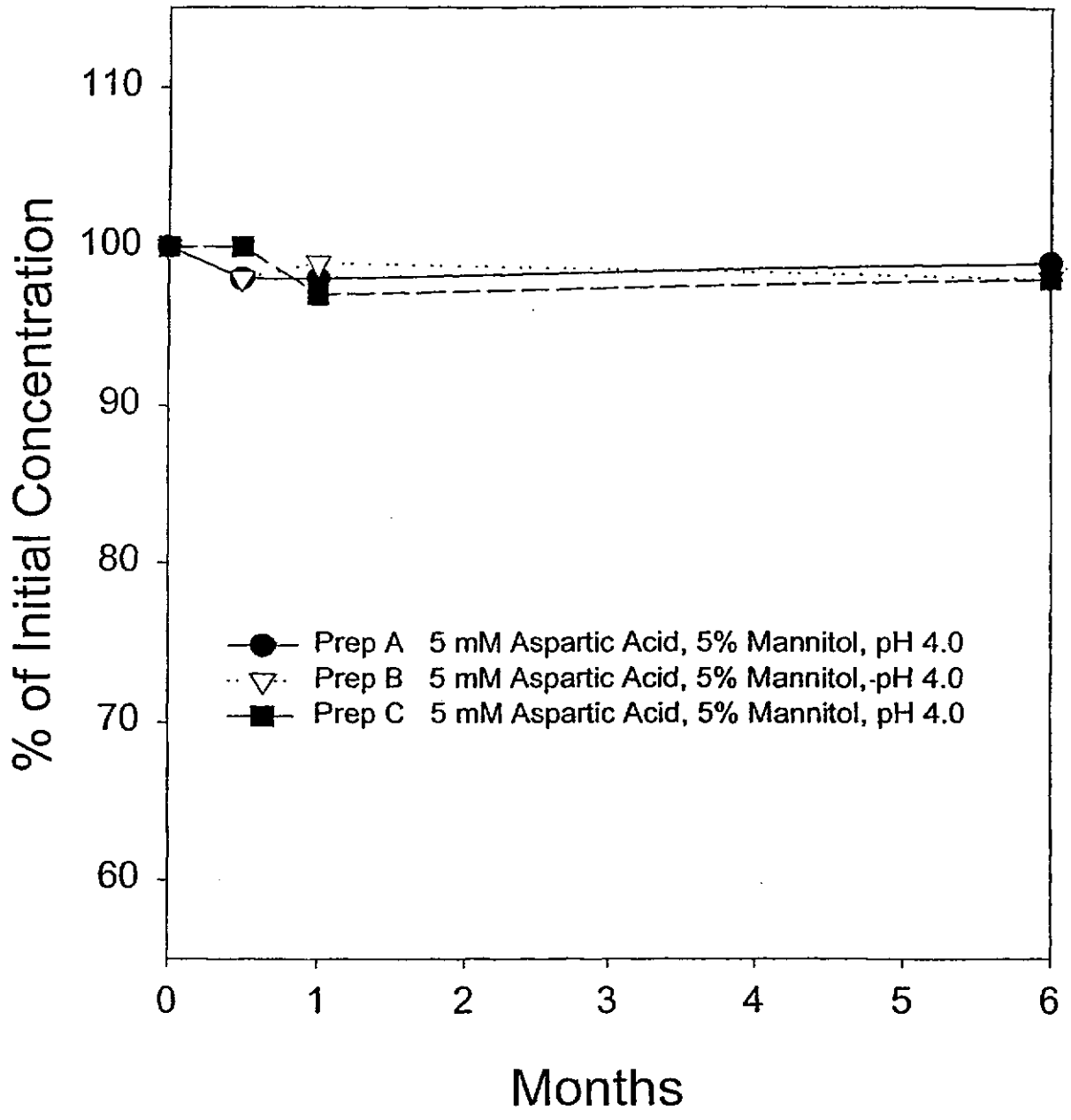


Figure 22

IFN-Beta-1b
Liquid Formulations Containing Mannitol
% Main Peak
RP-HPLC
5°C

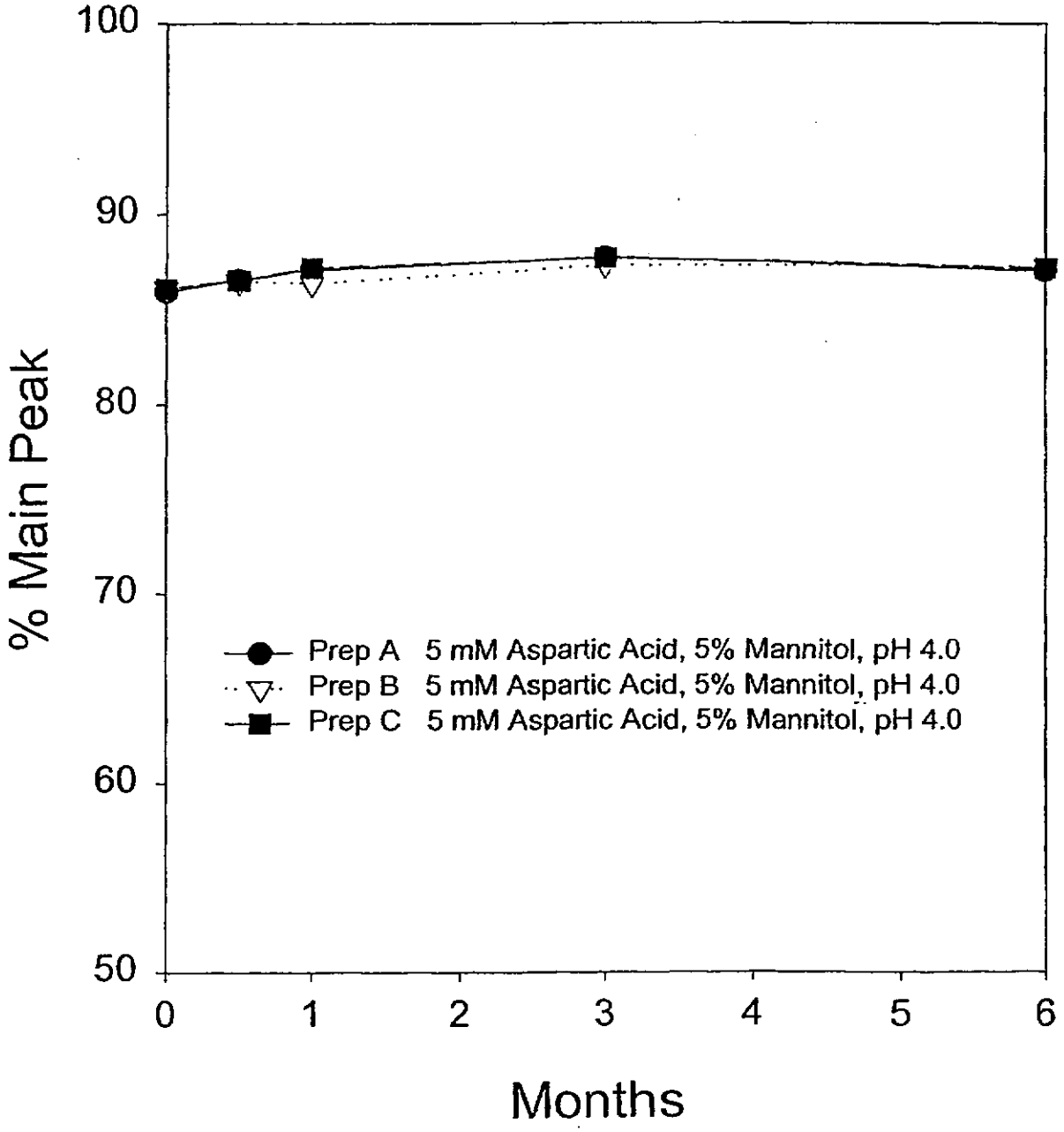


Figure 23