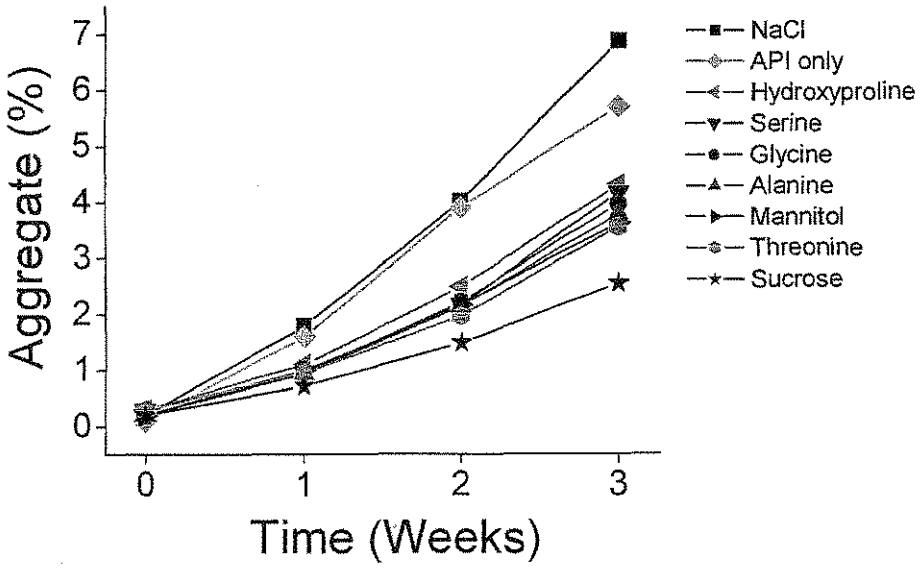

Aggregate (%)
0
1
2
3
4
5
6
7
Time (Weeks)
0
1
2
3
NaCl
API only
Hydroxyproline
Serine
Glycine
Alanine
Mannitol
Threonine
Sucrose

FIG. 1

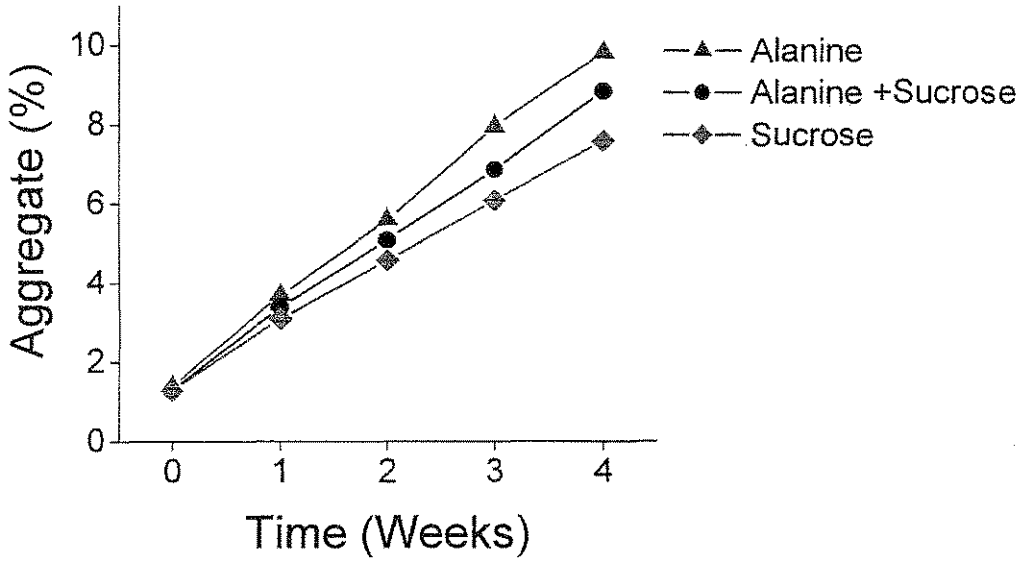

Aggregate (%)
10
8
6
4
2
0
0
1
2
3
4
Time (Weeks)
Alanine
Alanine +Sucrose
Sucrose

FIG. 2

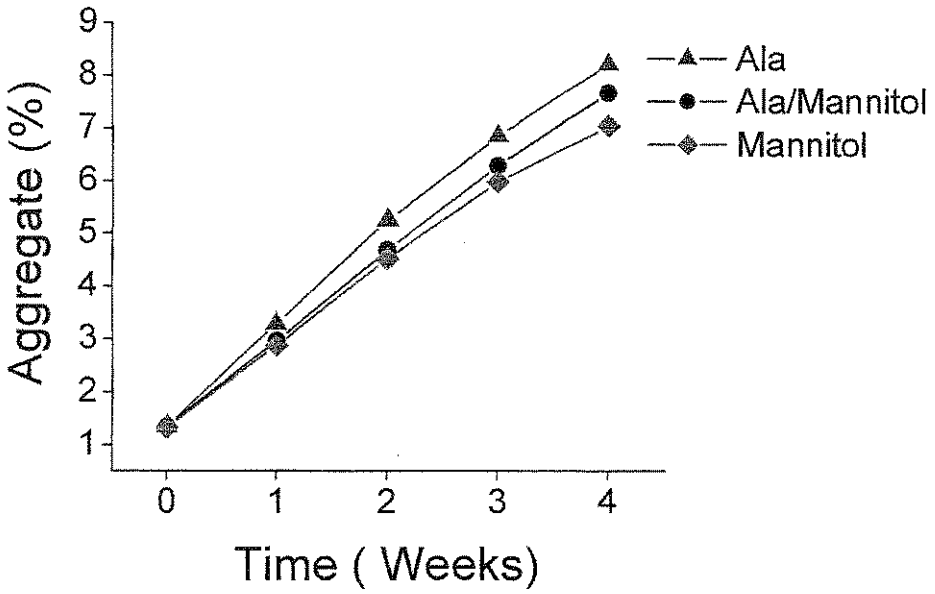

Aggregate (%)
9
8
7
6
5
4
3
2
1
0
1
2
3
4
Time (Weeks)
Ala
Ala/Mannitol
Mannitol

FIG. 3

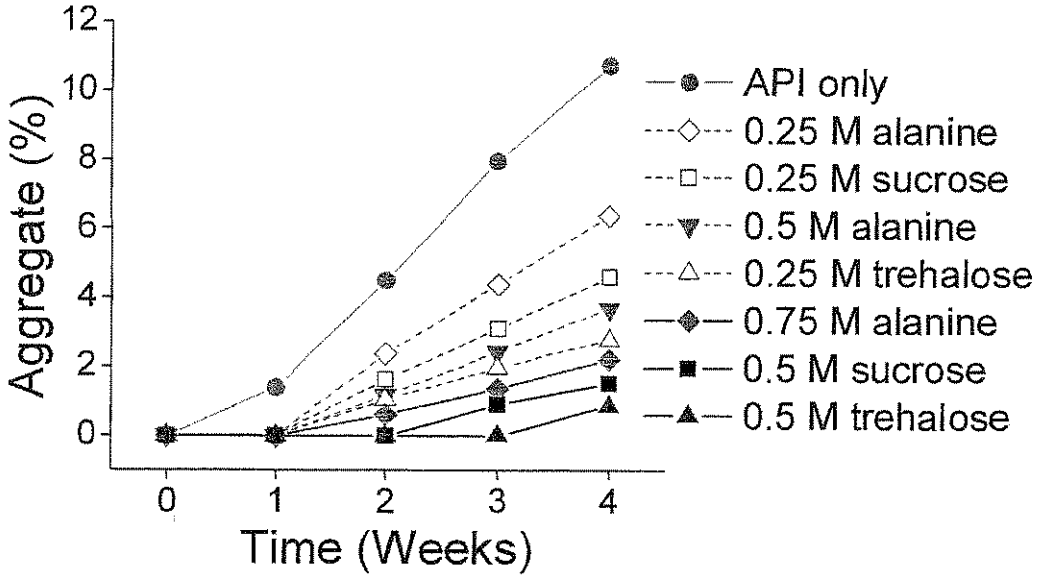

Aggregate (%)
12
10
8
6
4
2
0
0
1
2
3
4
Time (Weeks)
API only
0.25 M alanine
0.25 M sucrose
0.5 M alanine
0.25 M trehalose
0.75 M alanine
0.5 M sucrose
0.5 M trehalose

FIG.4

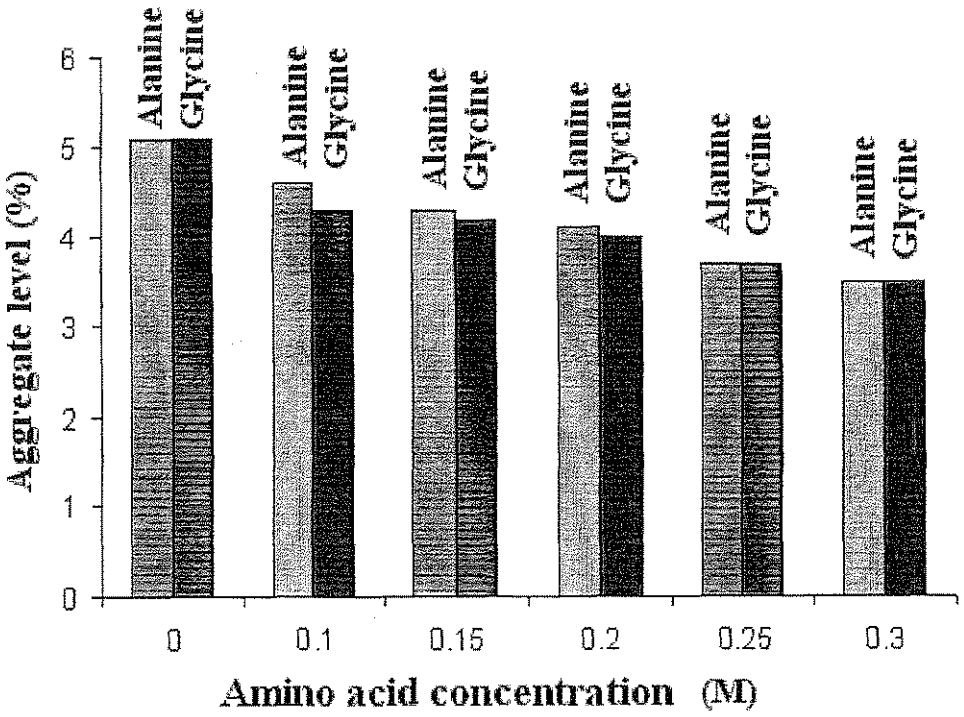

Aggregate level (%)
0
1
2
3
4
5
6
Alanine
Glycine
0
0.1
0.15
0.2
0.25
0.3
Amino acid concentration (M)

FIG. 5

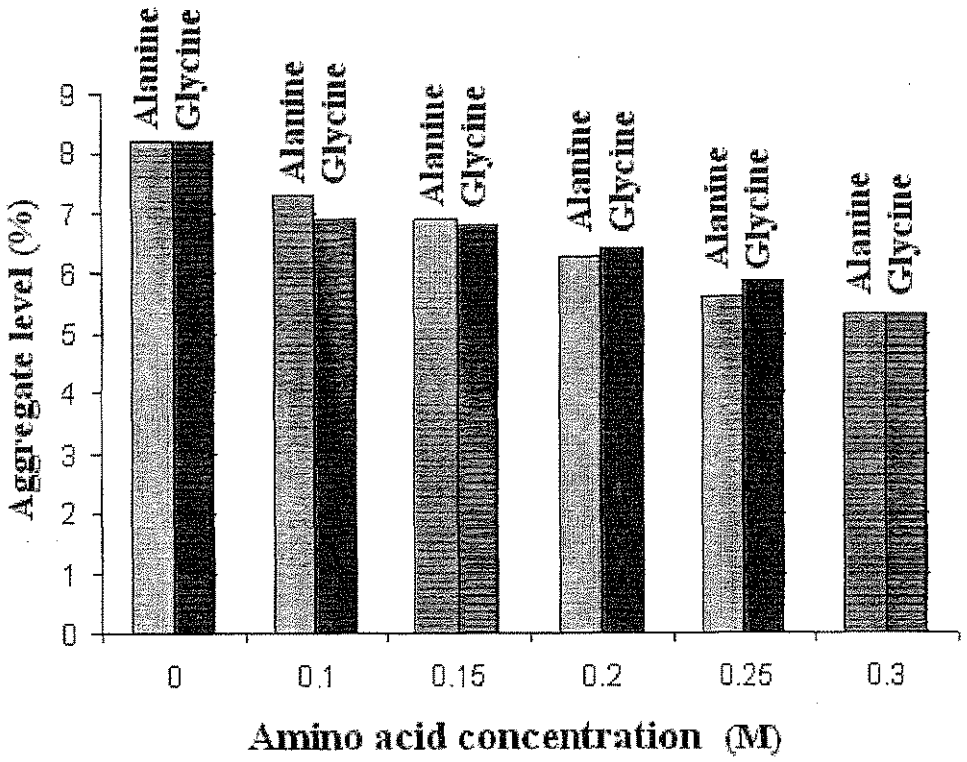

Aggregate level (%)
0
1
2
3
4
5
6
7
8
9
Alanine
Glycine
0
0.1
0.15
0.2
0.25
0.3
Amino acid concentration (M)

FIG. 6

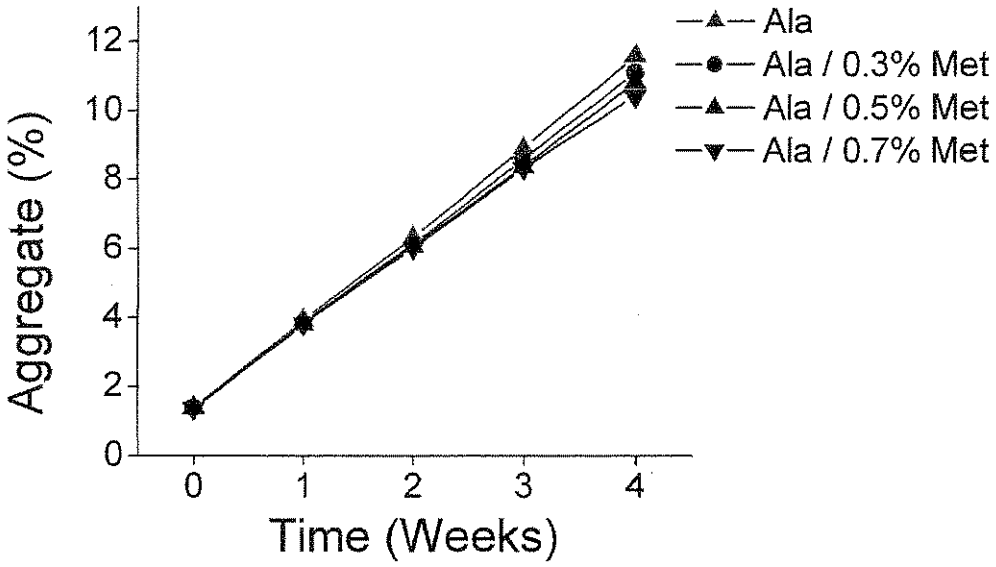

Aggregate (%)
0
2
4
6
8
10
12
0
1
2
3
4
Time (Weeks)
Ala
Ala / 0.3% Met
Ala / 0.5% Met
Ala / 0.7% Met

FIG. 7

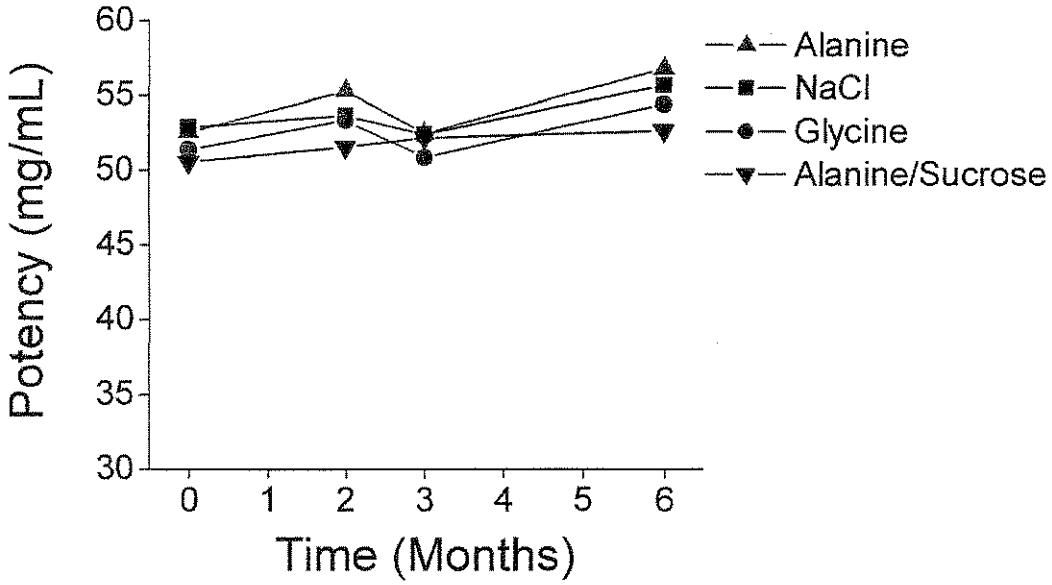

Potency (mg/mL)
60
55
50
45
40
35
30
0
1
2
3
4
5
6
Time (Months)
Alanine
NaCl
Glycine
Alanine/Sucrose

FIG. 8

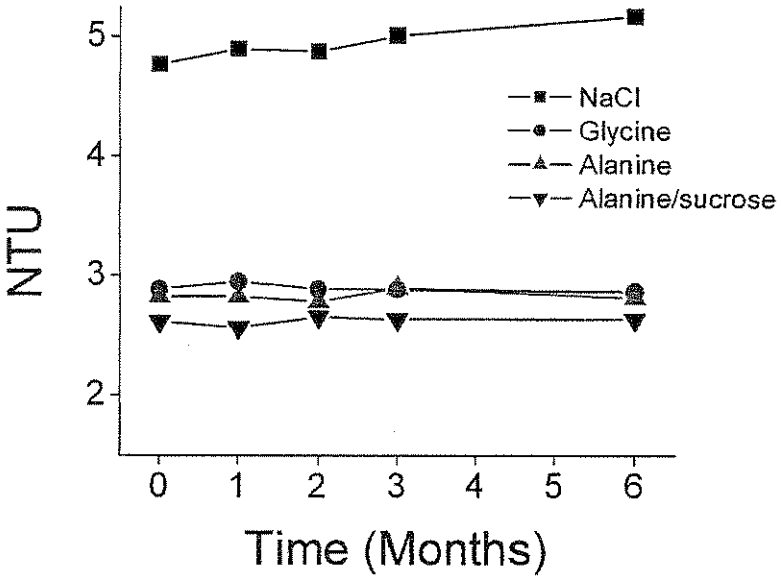

NTU
5
4
3
2
0
1
2
3
4
5
6
Time (Months)
NaCl
Glycine
Alanine
Alanine/sucrose

FIG. 9

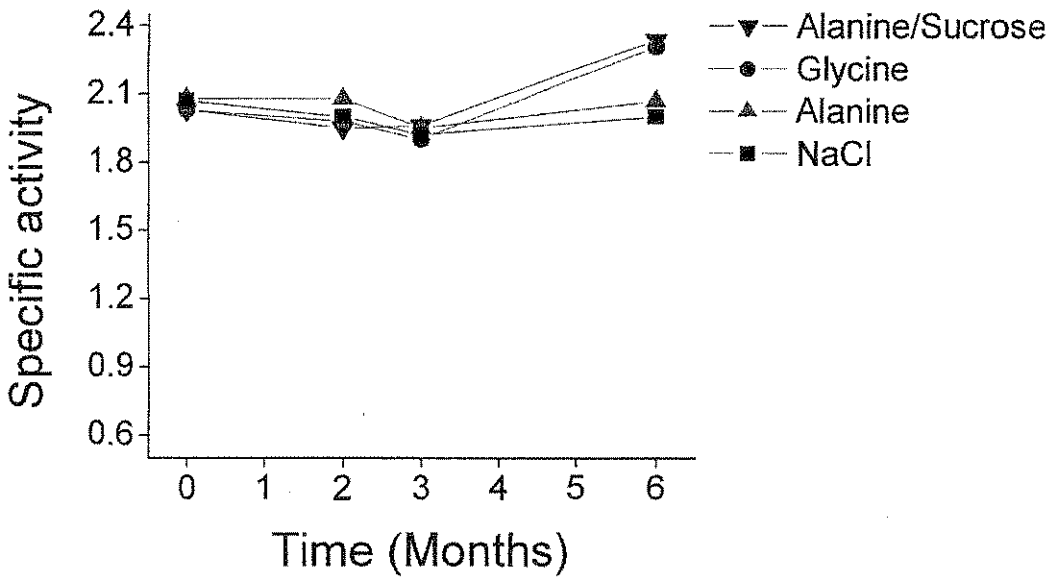

Specific activity
2.4
2.1
1.8
1.5
1.2
0.9
0.6
0
1
2
3
4
5
6
Time (Months)
Alanine/Sucrose
Glycine
Alanine
NaCl

FIG. 10

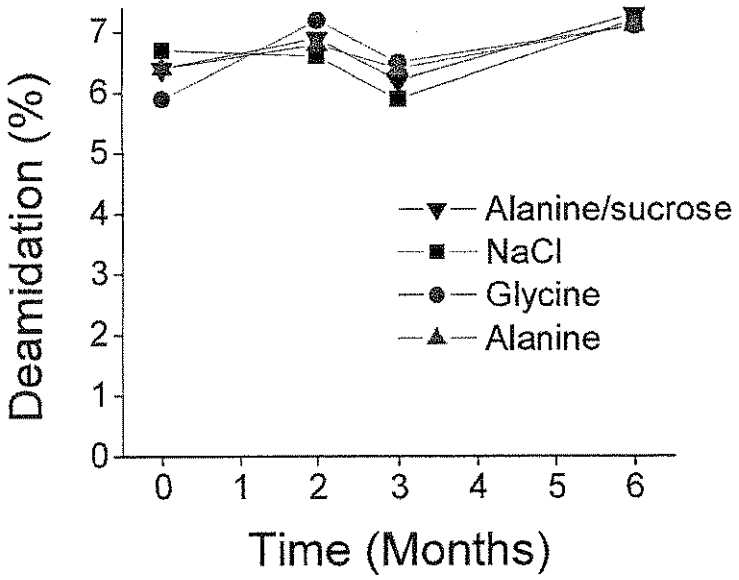

Deamidation (%)
0
1
2
3
4
5
6
7
0
1
2
3
4
5
6
Time (Months)
Alanine/sucrose
NaCl
Glycine
Alanine

FIG. 11

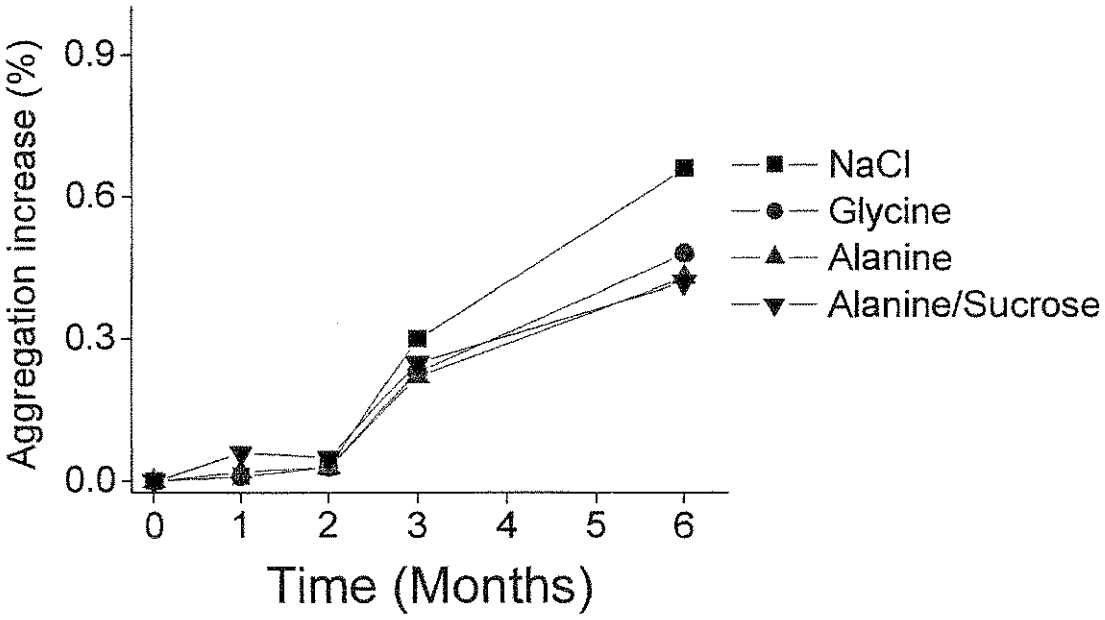

Aggregation increase (%)
0.9
0.6
0.3
0.0
0
1
2
3
4
5
6
Time (Months)
NaCl
Glycine
Alanine
Alanine/Sucrose

FIG. 12

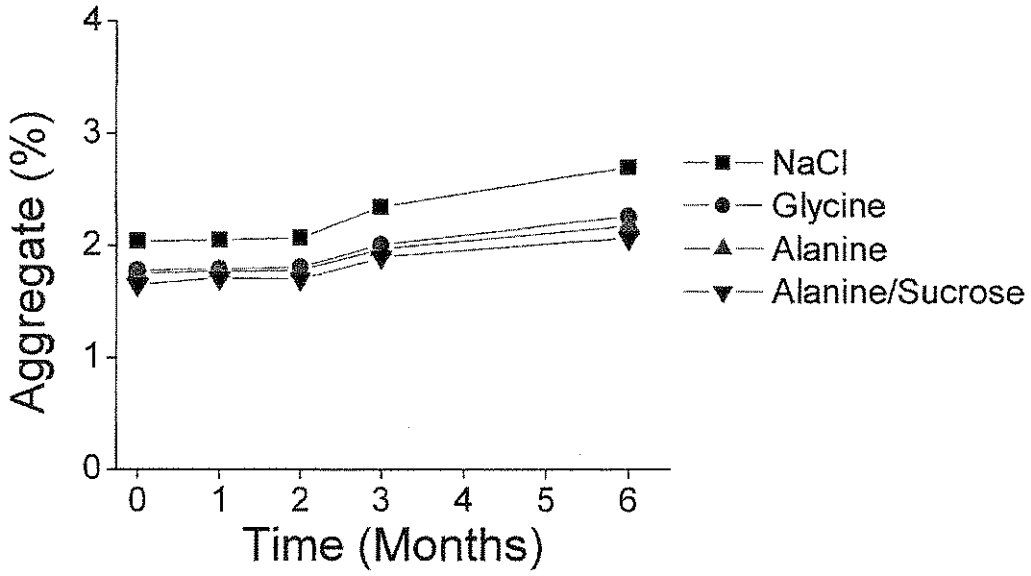

Aggregate (%)
0
1
2
3
4
0
1
2
3
4
5
6
Time (Months)
NaCl
Glycine
Alanine
Alanine/Sucrose

FIG. 13

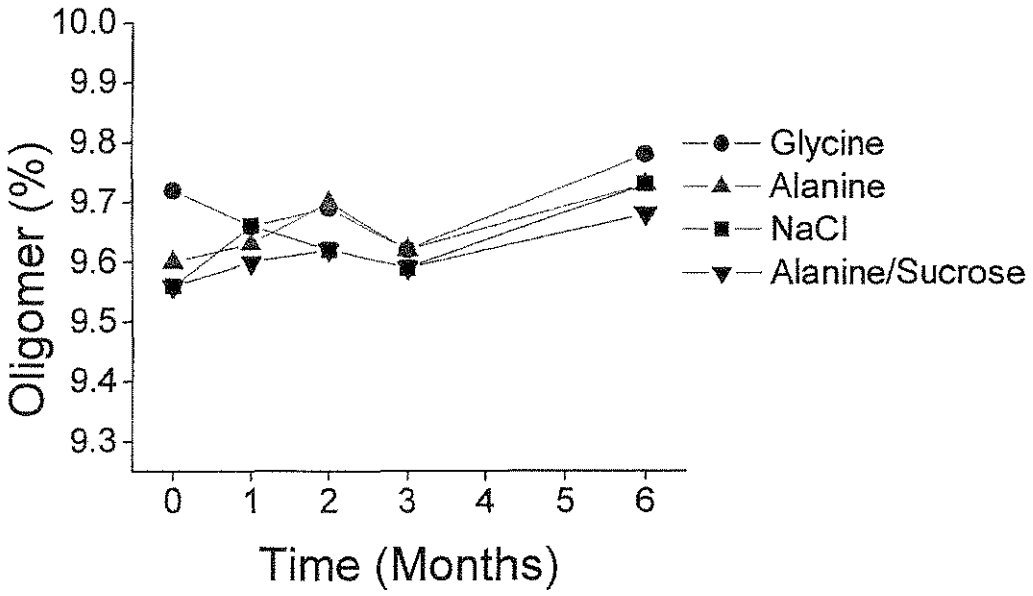

10.0
9.9
9.8
9.7
9.6
9.5
9.4
9.3
Oligomer (%)
0
1
2
3
4
5
6
Time (Months)
Glycine
Alanine
NaCl
Alanine/Sucrose

FIG. 14

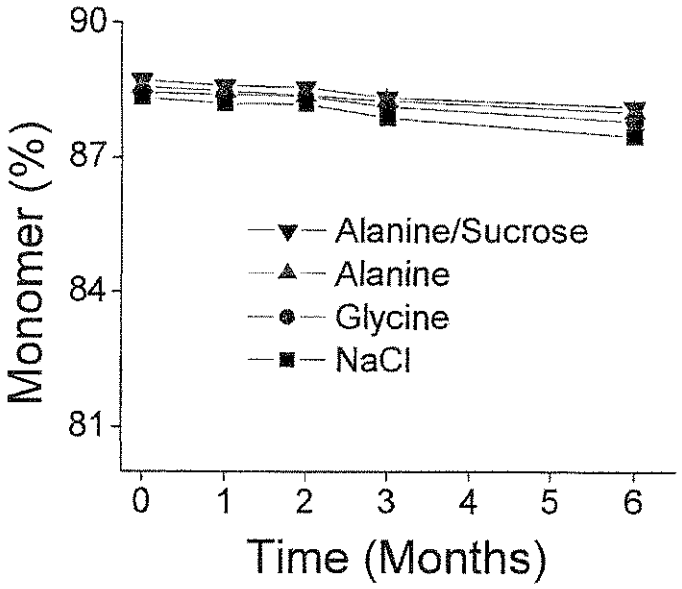

90
87
84
81
Monomer (%)
Alanine/Sucrose
Alanine
Glycine
NaCl
0
1
2
3
4
5
6
Time (Months)

FIG. 15

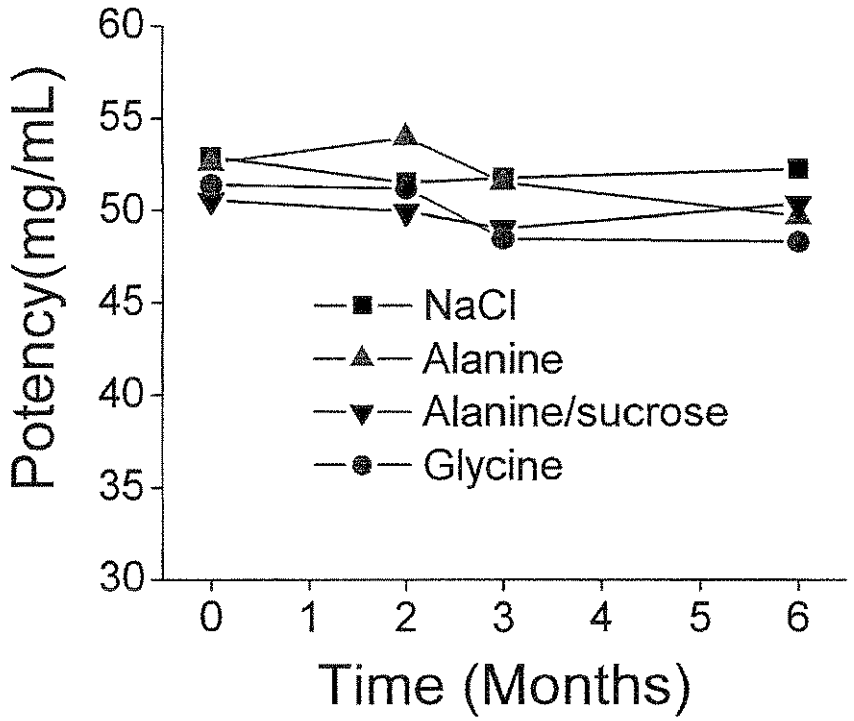

Potency(mg/mL)
60
55
50
45
40
35
30
0
1
2
3
4
5
6
Time (Months)
NaCl
Alanine
Alanine/sucrose
Glycine

FIG. 16

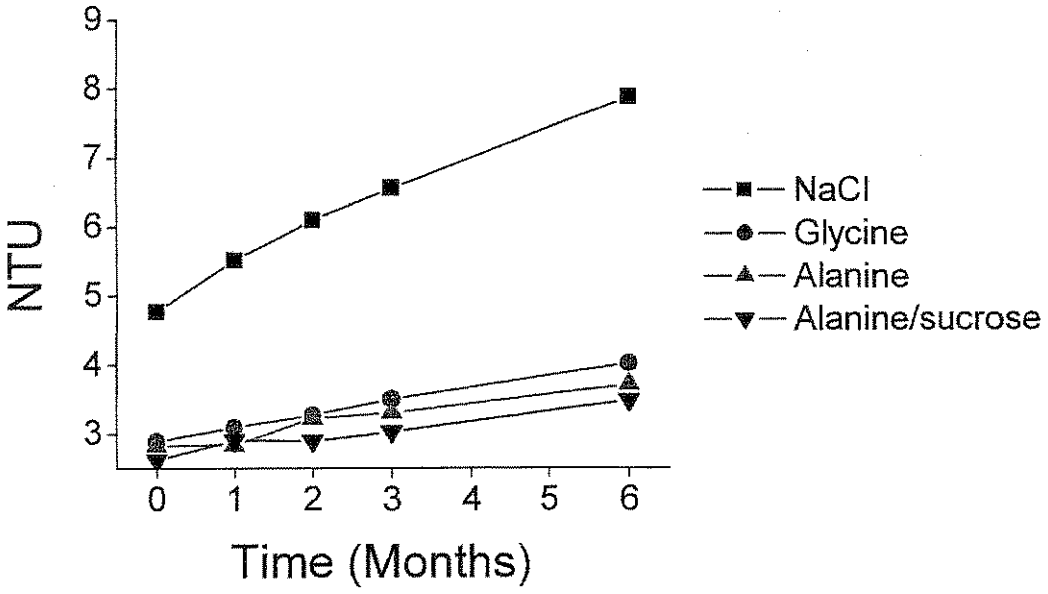

NTU
9
8
7
6
5
4
3
0
1
2
3
4
5
6
Time (Months)
NaCl
Glycine
Alanine
Alanine/sucrose

FIG. 17

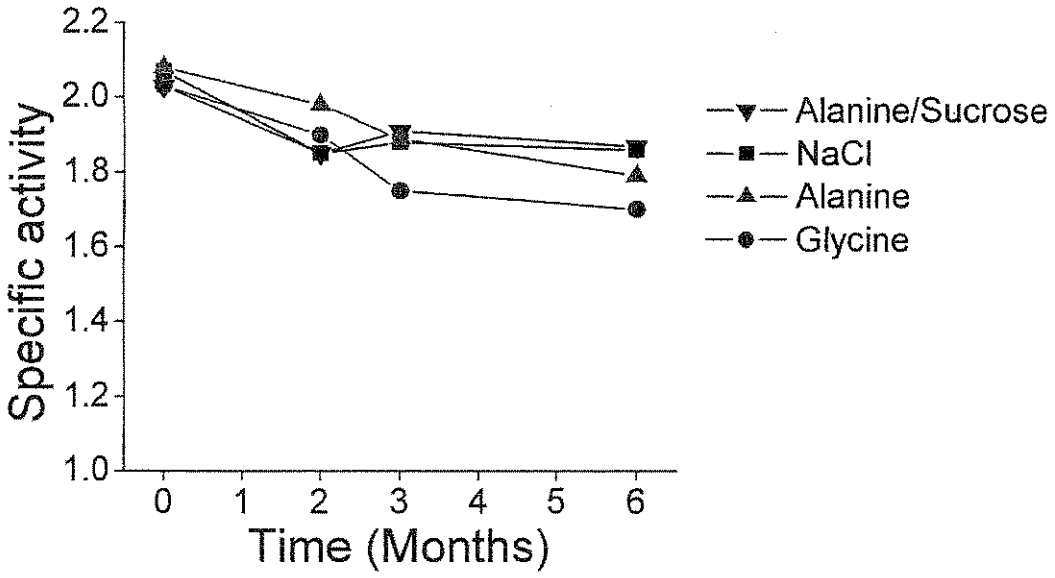

Specific activity
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0
1
2
3
4
5
6
Time (Months)
Alanine/Sucrose
NaCl
Alanine
Glycine

FIG. 18

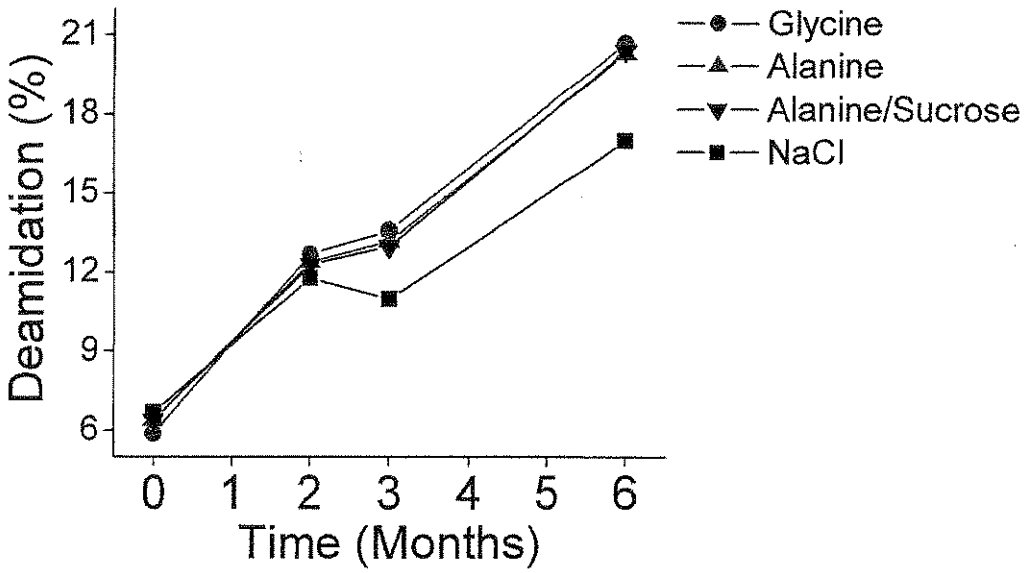

Deamidation (%)
21
18
15
12
9
6
0
1
2
3
4
5
6
Time (Months)
Glycine
Alanine
Alanine/Sucrose
NaCl

FIG. 19

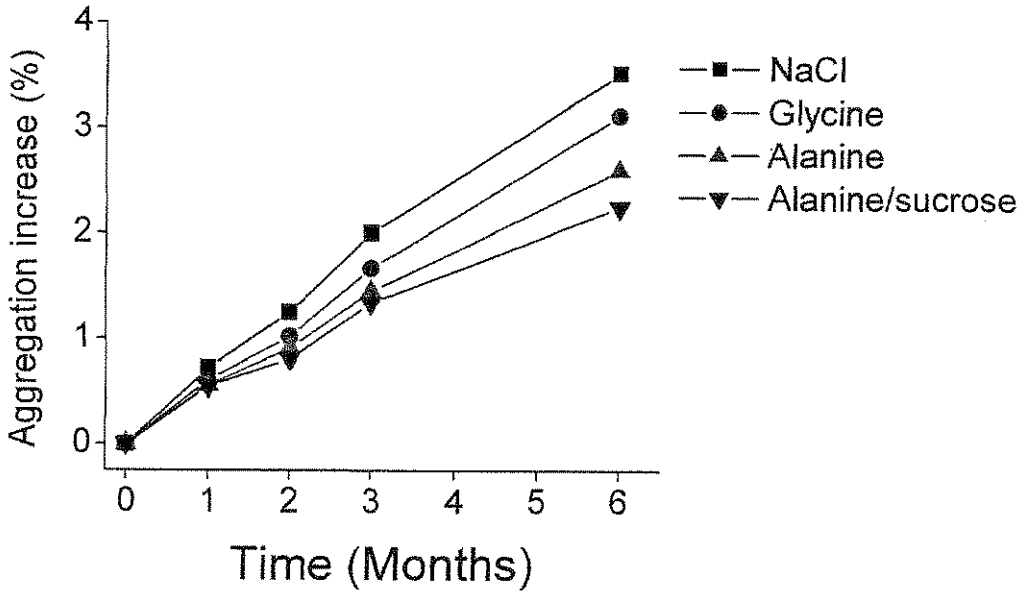

Aggregation increase (%)
0
1
2
3
4
0
1
2
3
4
5
6
Time (Months)
NaCl
Glycine
Alanine
Alanine/sucrose

FIG. 20

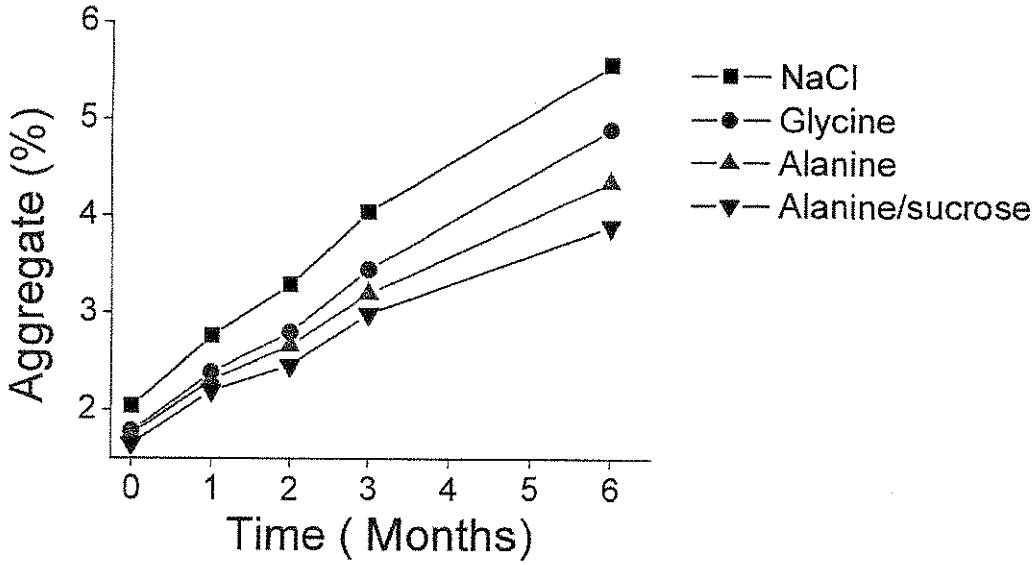

Aggregate (%)
6
5
4
3
2
0
1
2
3
4
5
6
Time (Months)
NaCl
Glycine
Alanine
Alanine/sucrose

FIG. 21

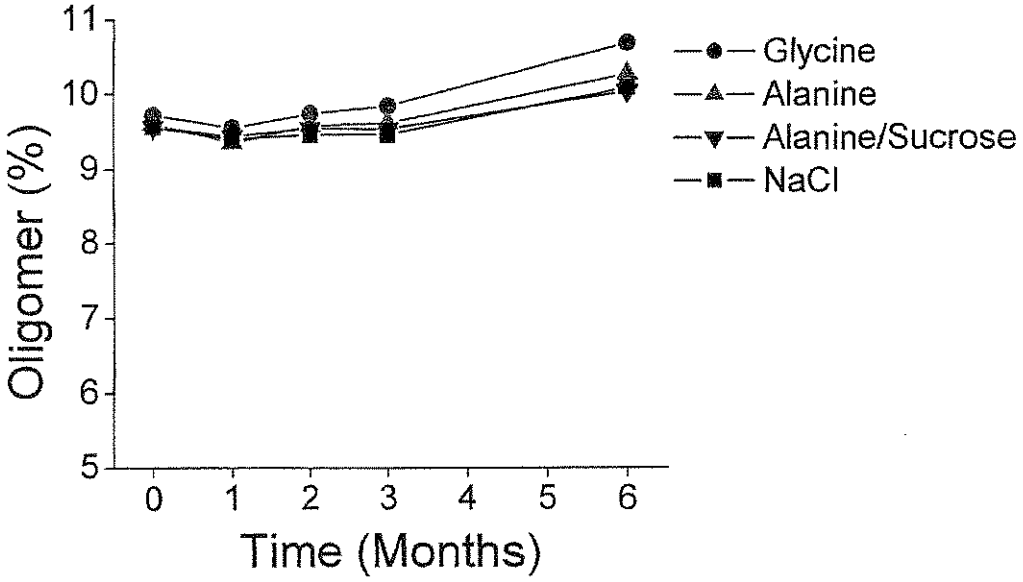

11
10
9
8
7
6
5
Oligomer (%)
0
1
2
3
4
5
6
Time (Months)
Glycine
Alanine
Alanine/Sucrose
NaCl

FIG. 22

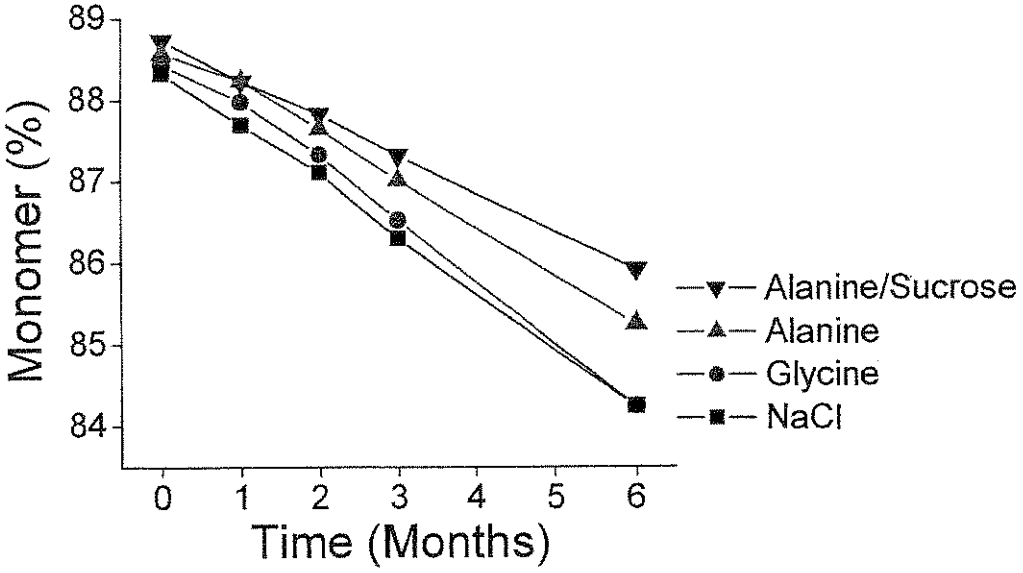
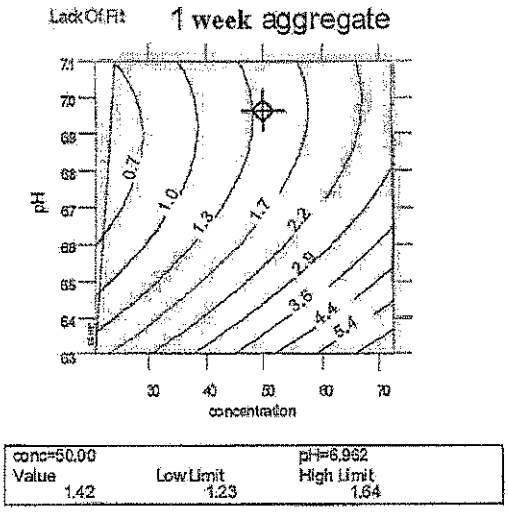
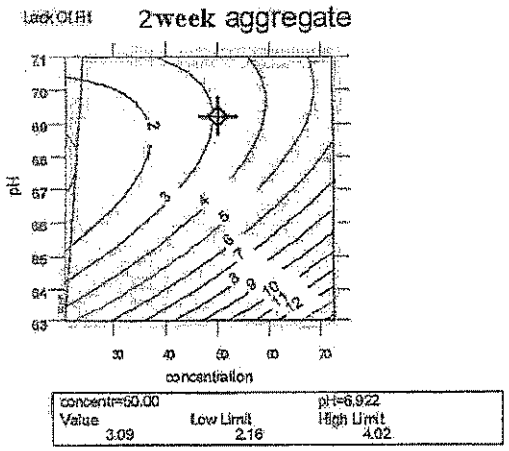

89
88
87
86
85
84
Monomer (%)
0
1
2
3
4
5
6
Time (Months)
Alanine/Sucrose
Alanine
Glycine
NaCl

FIG. 23


Lack Of Fit
1 week aggregate
pH
concentration
0.7
1.0
1.3
1.7
2.2
2.9
3.5
4.4
5.4
conc=50.00
pH=6.962
Value
Low Limit
High Limit
1.42
1.23
1.64


Lack Of Fit
2week aggregate
pH
concentration
2
3
4
5
6
7
8
9
10
11
12
concentr=50.00
pH=6.922
Value
Low Limit
High Limit
3.09
2.16
4.02

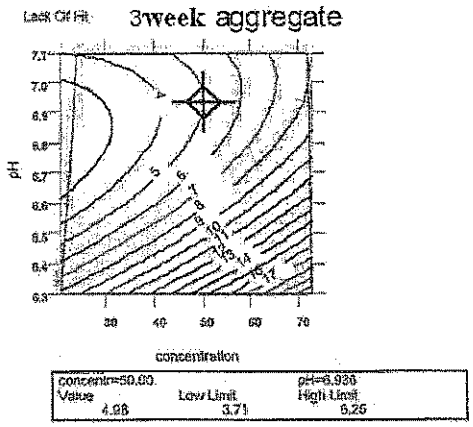
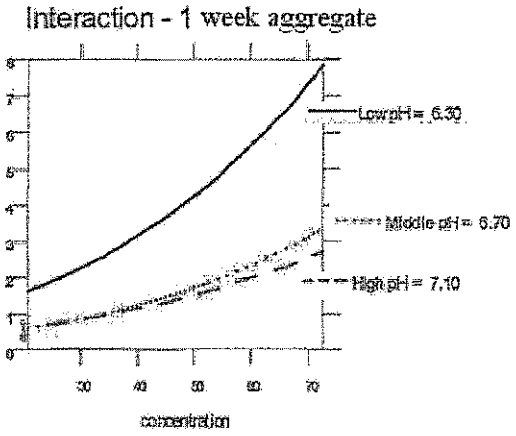
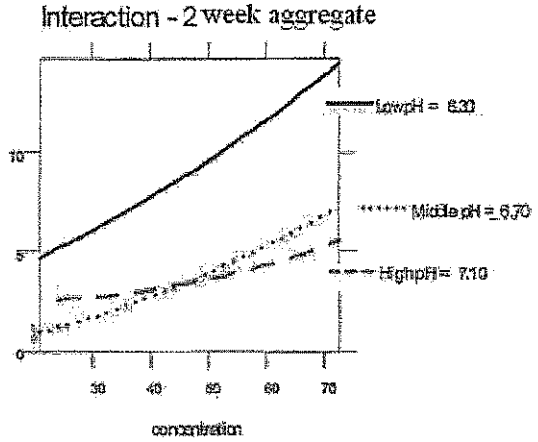

Lack Of Fit
3week aggregate
pH
concentration
4
5
6
7
8
9
10
11
concentr=50.00
pH=6.936
Value
Low Limit
High Limit
4.98
3.71
6.25

FIG. 24


Interaction - 1 week aggregate
LowpH= 6.30
Middle pH= 6.70
High pH = 7.10
concentration


Interaction - 2 week aggregate
LowpH = 6.30
Middle pH = 6.70
HighpH= 7.10
concentration

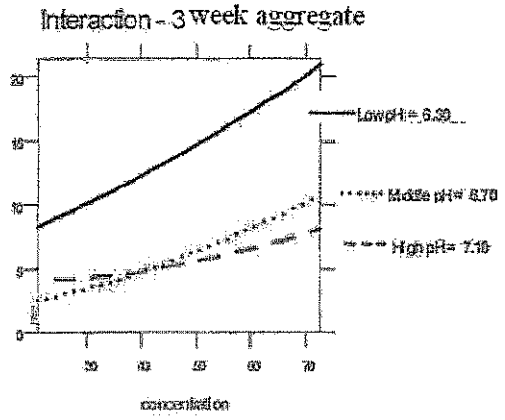

Interaction - 3 week aggregate
LowpH= 6.30
Middle pH= 6.70
High pH= 7.10
concentration

FIG. 25

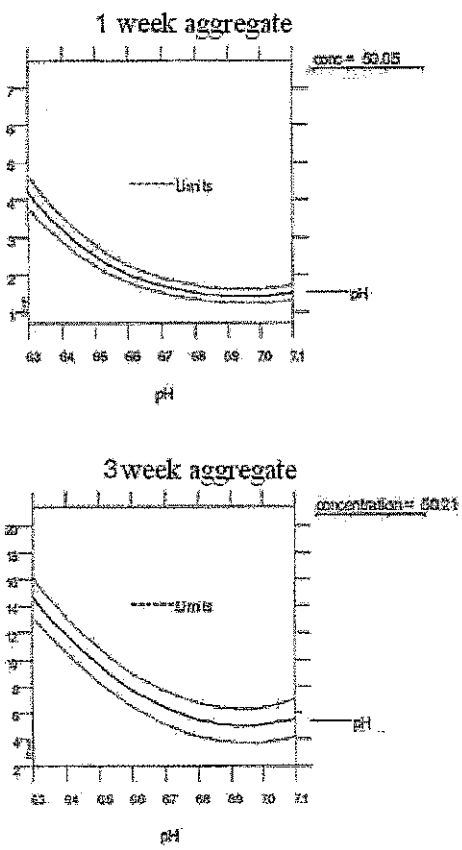

1 week aggregate
conc = 50.05
Limits
pH
pH
2 week aggregate
concentration = 50.05
Limits
pH
pH
3 week aggregate
concentration = 50.21
Limits
pH
pH

FIG. 26

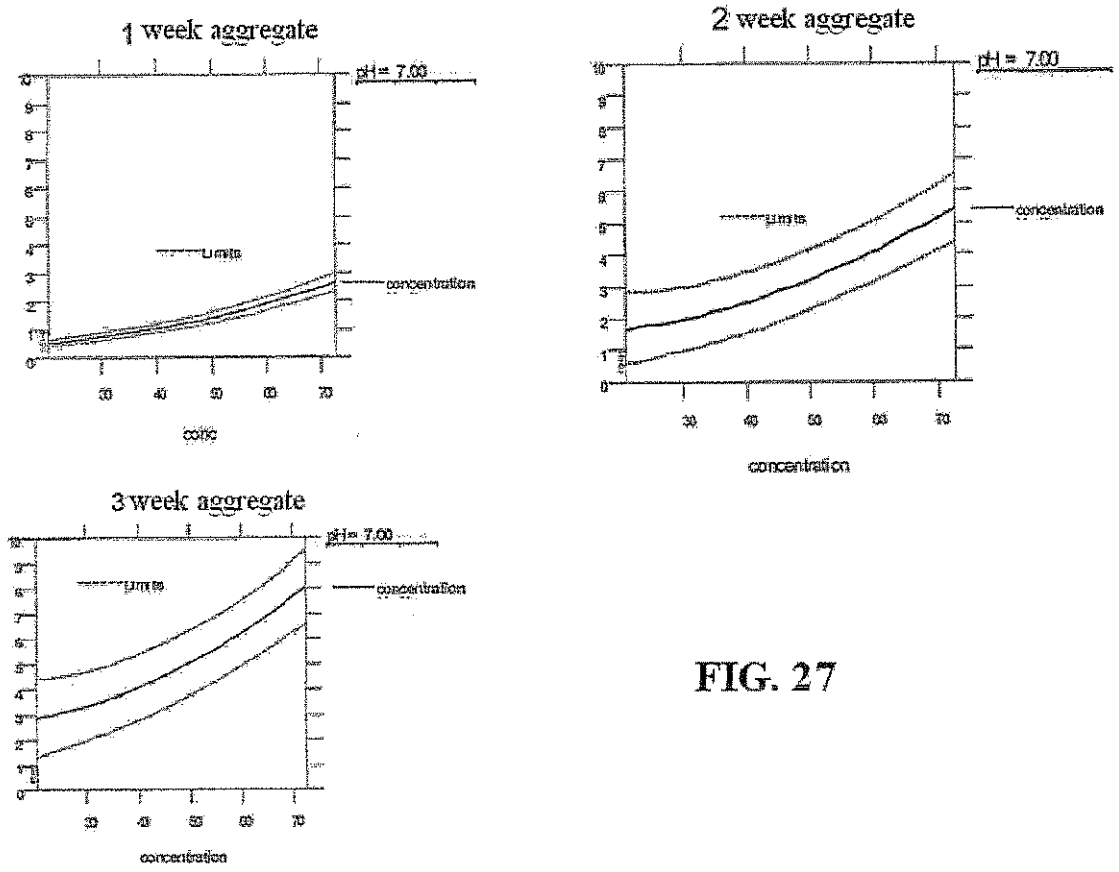

1 week aggregate
pH = 7.00
Limits
concentration
conc
2 week aggregate
pH = 7.00
Limits
concentration
concentration
3 week aggregate
pH = 7.00
Limits
concentration
concentration

FIG. 27