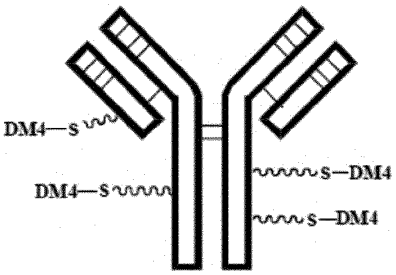
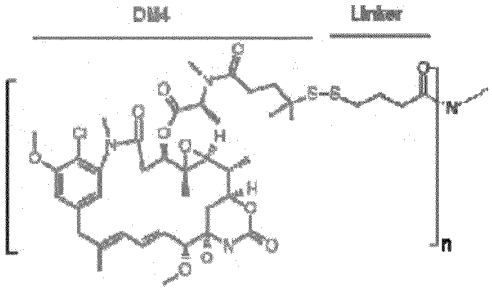
General representation



Structure of the chemical portion



n is about 3.8 drug linked per antibody molecule

huMAb2-3-SPDB-DM4

FIG. 1

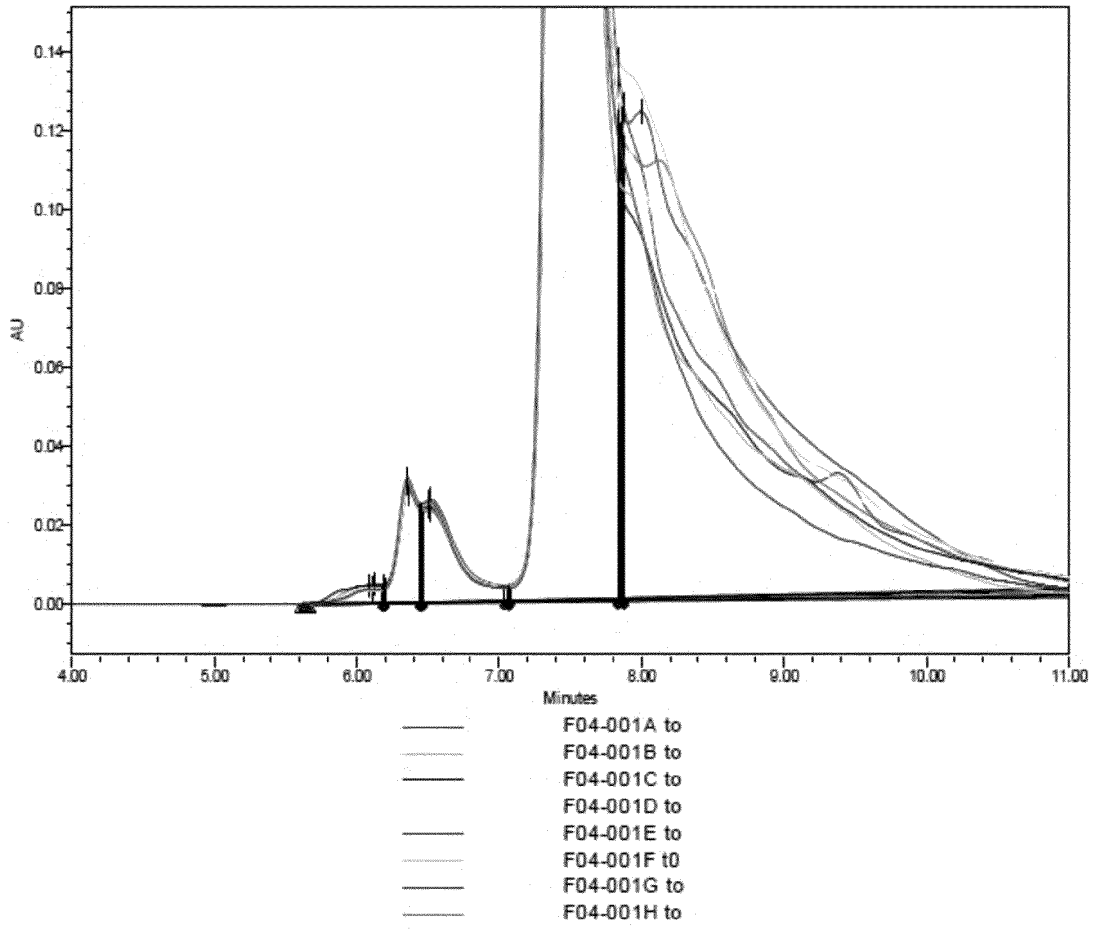

0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
AU
4.00
5.00
6.00
7.00
8.00
9.00
10.00
11.00
Minutes
F04-001A to
F04-001B to
F04-001C to
F04-001D to
F04-001E to
F04-001F t0
F04-001G to
F04-001H to

FIG. 2

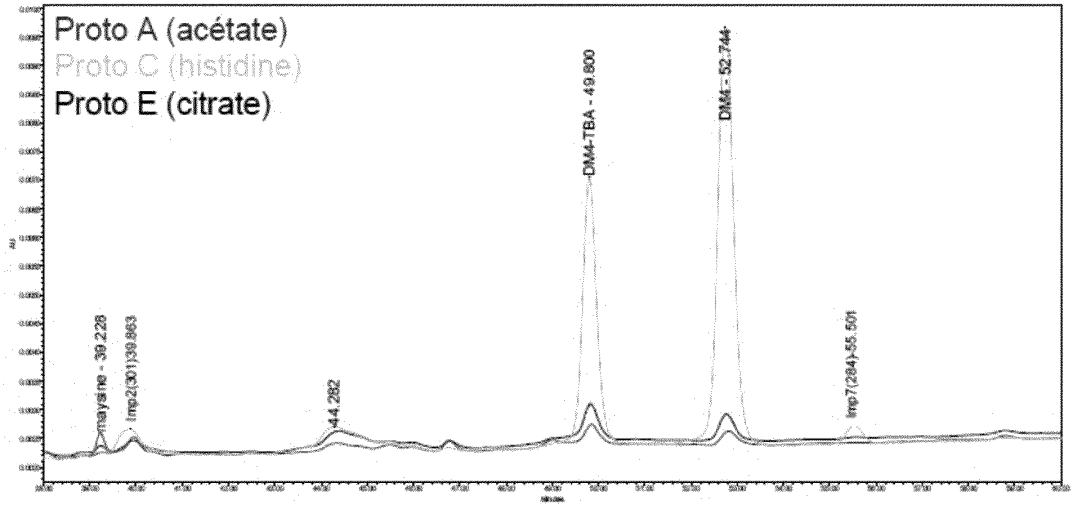

Proto A (acétate)
Proto C (histidine)
Proto E (citrate)
maysine - 39.228
Imp2(301)39.863
44.282
DM4-TBA - 49.800
DM4 - 52.744
Imp7(284)-55.501

FIG. 3

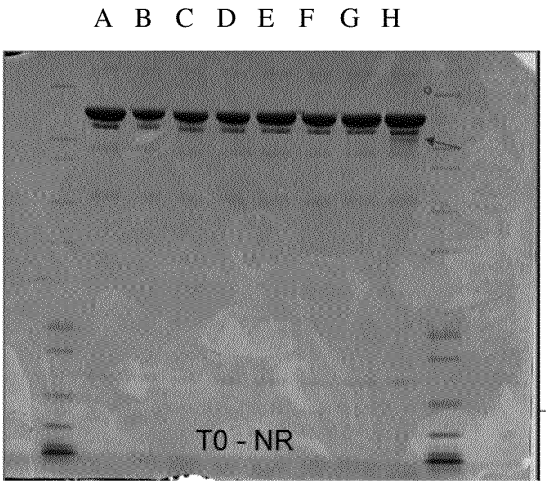


FIG. 4A

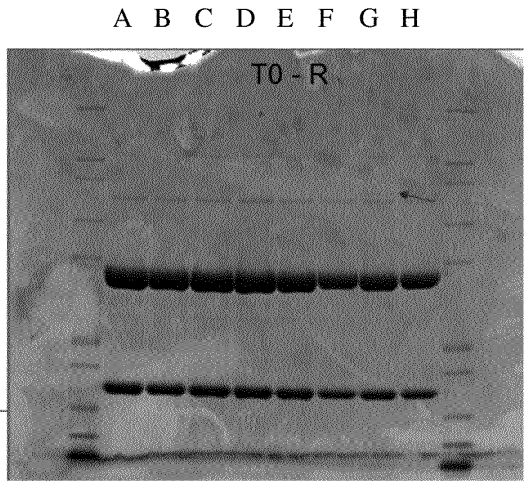


FIG. 4B

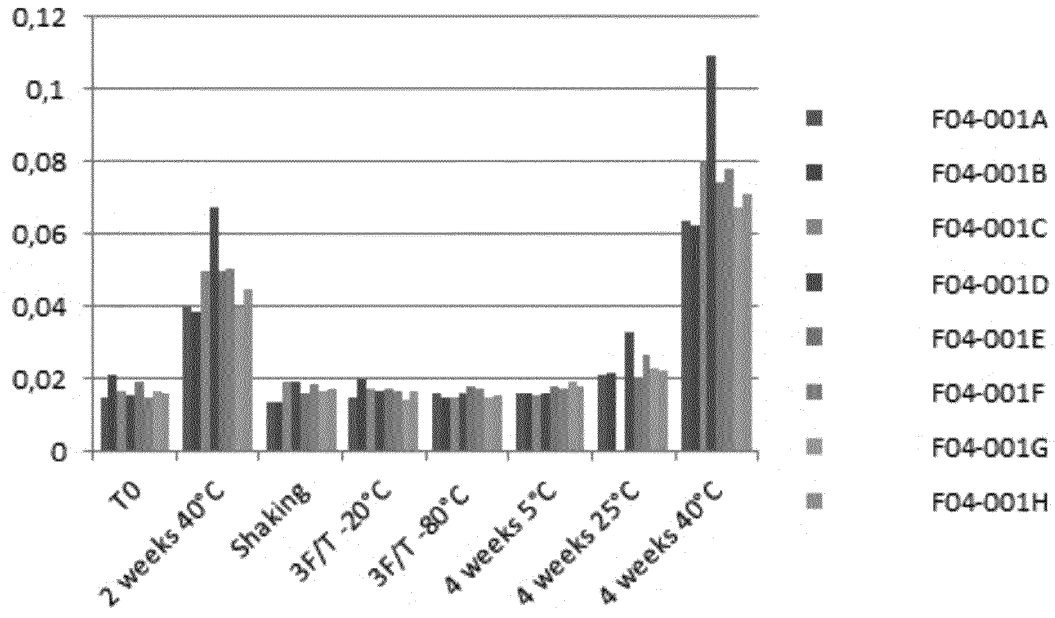

0,12
0,1
0,08
0,06
0,04
0,02
0
T0
2 weeks 40°C
Shaking
3F/T -20°C
3F/T -80°C
4 weeks 5°C
4 weeks 25°C
4 weeks 40°C
F04-001A
F04-001B
F04-001C
F04-001D
F04-001E
F04-001F
F04-001G
F04-001H

FIG. 5

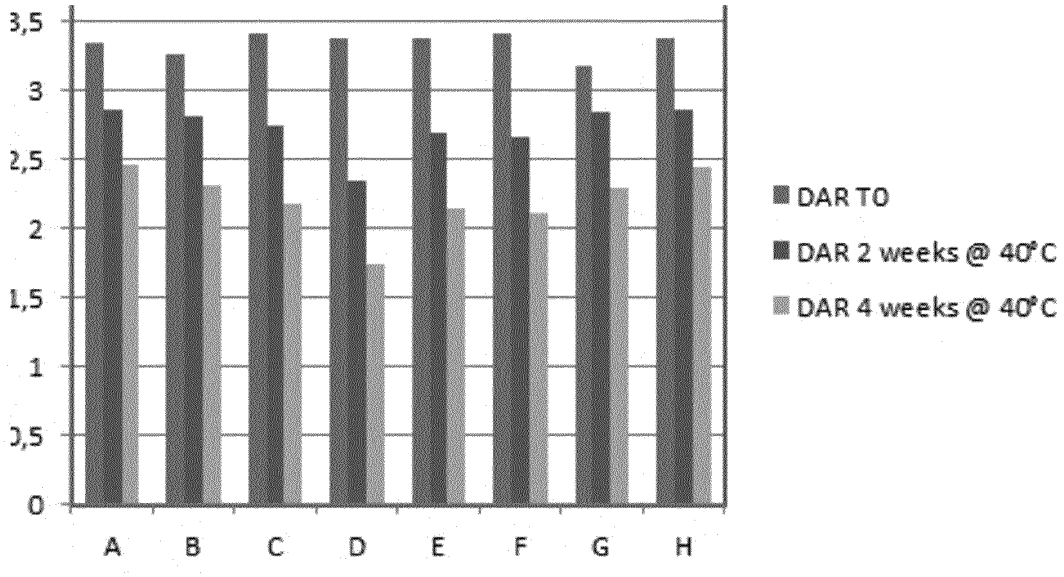


FIG. 6

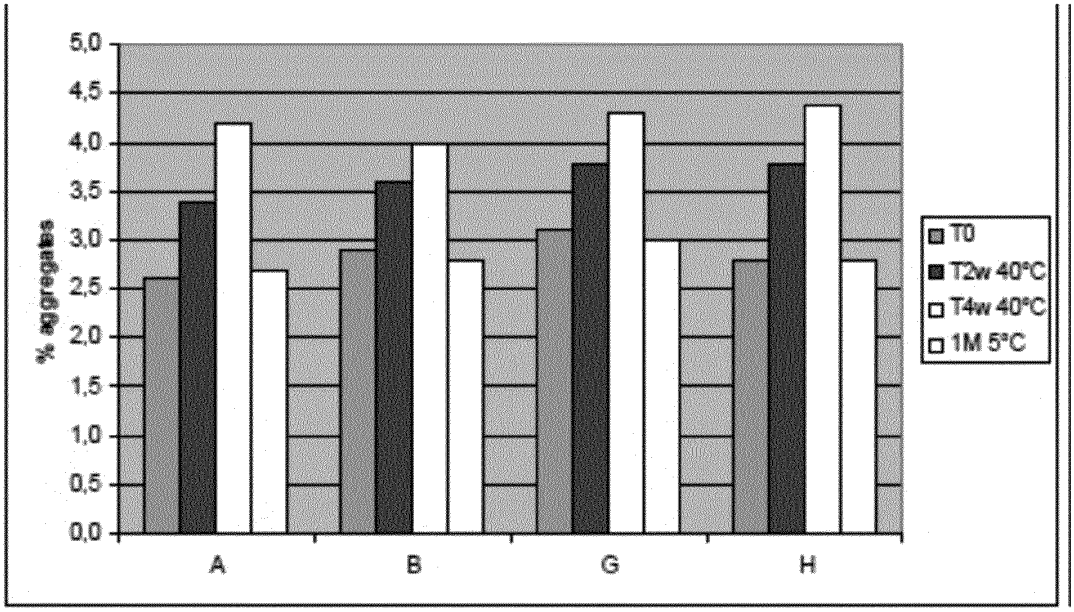

5,0
4,5
4,0
3,5
3,0
2,5
2,0
1,5
1,0
0,5
0,0
% aggregates
A
B
G
H
T0
T2w 40°C
T4w 40°C
1M 5°C

FIG. 7

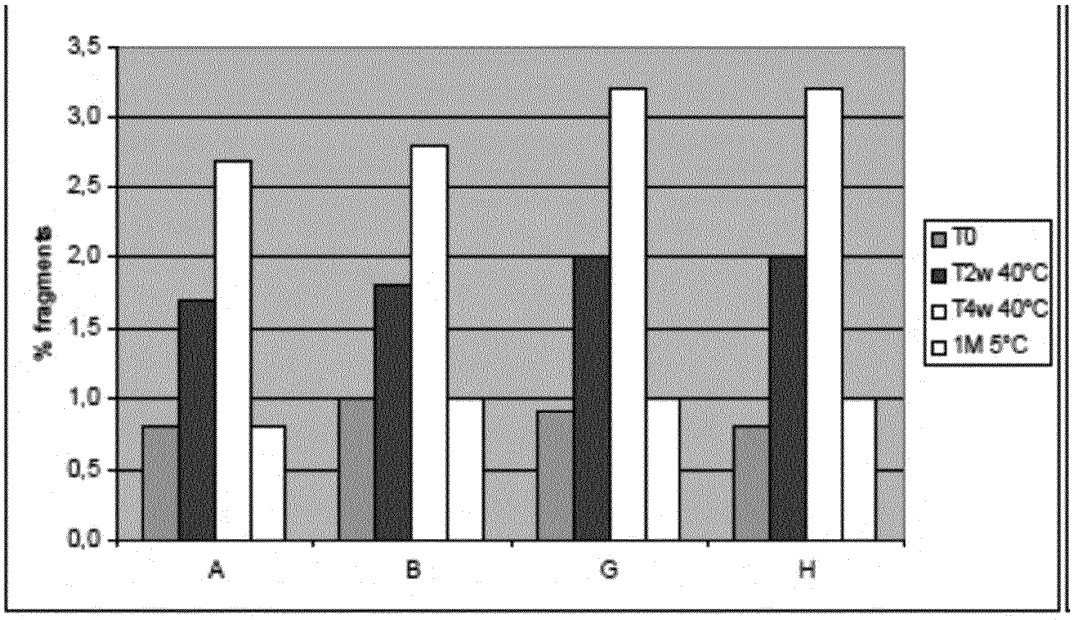


FIG. 8

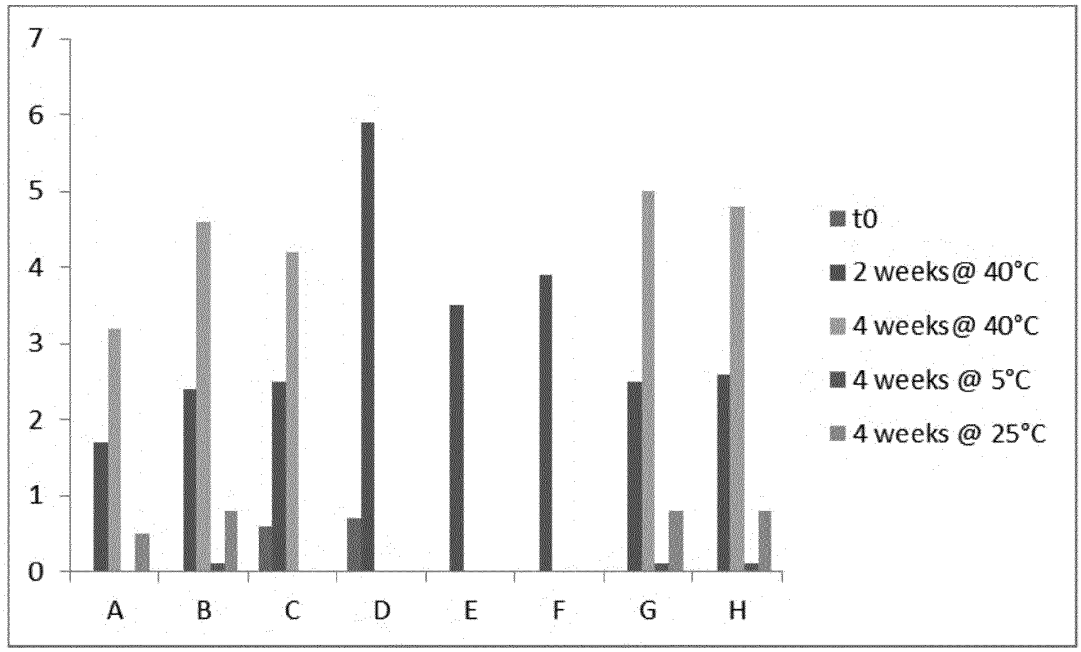

7
6
5
4
3
2
1
0
A
B
C
D
E
F
G
H
t0
2 weeks@ 40°C
4 weeks@ 40°C
4 weeks @ 5°C
4 weeks @ 25°C

FIG. 9

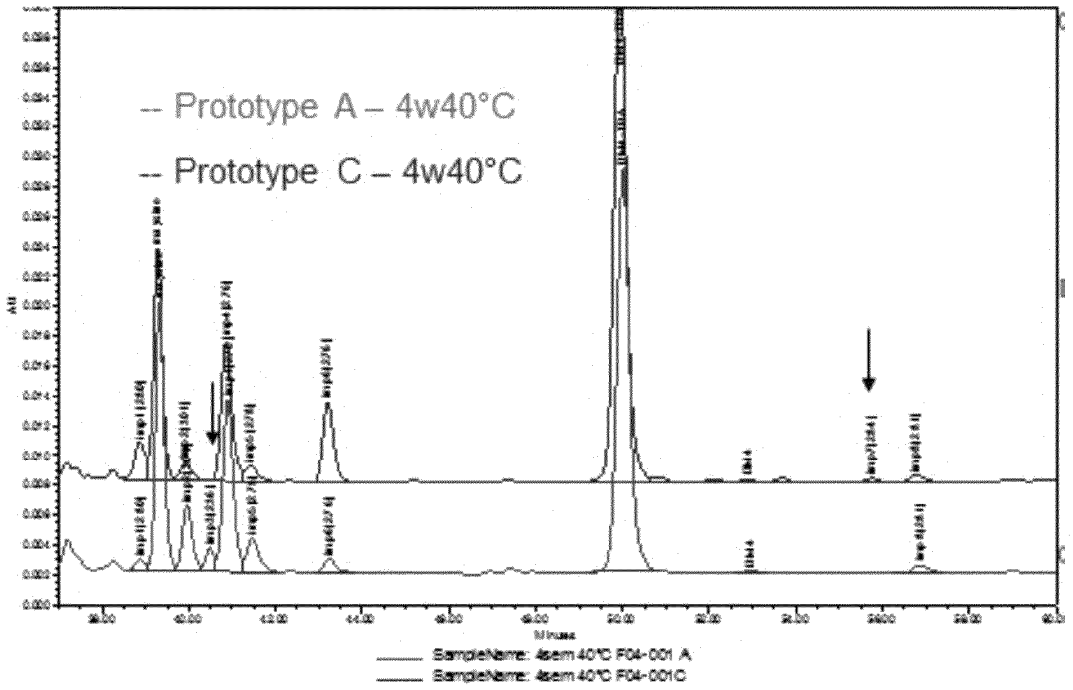

-- Prototype A – 4w40°C
-- Prototype C – 4w40°C
AU
Minutes
SampleName: 4sem 40°C F04-001 A
SampleName: 4sem 40°C F04-001C

FIG. 10

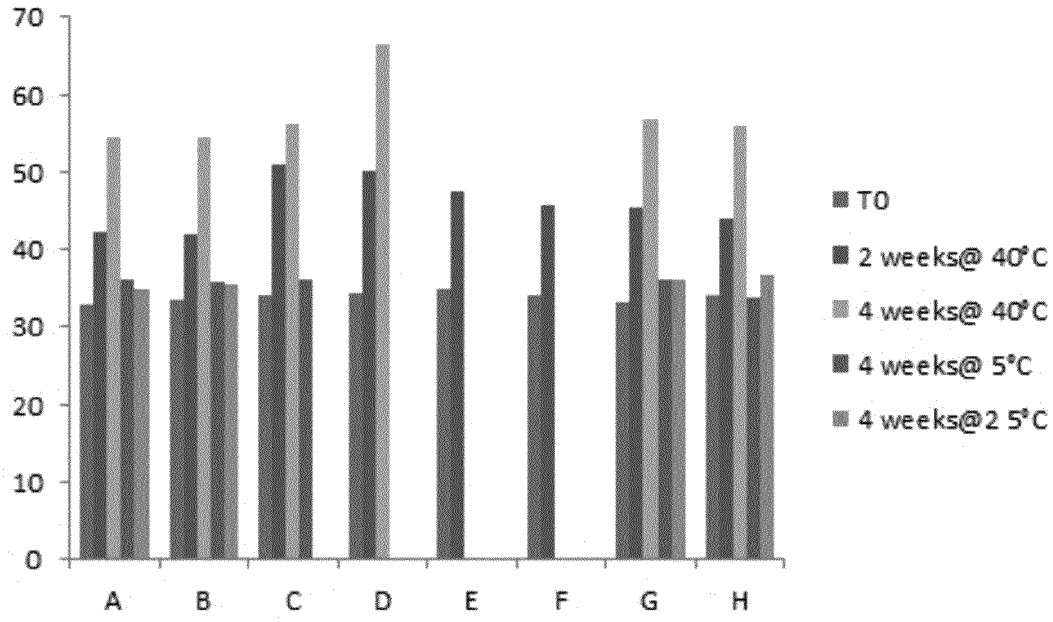

70
60
50
40
30
20
10
0
A
B
C
D
E
F
G
H
T0
2 weeks@ 40°C
4 weeks@ 40°C
4 weeks@ 5°C
4 weeks@2 5°C

FIG. 11

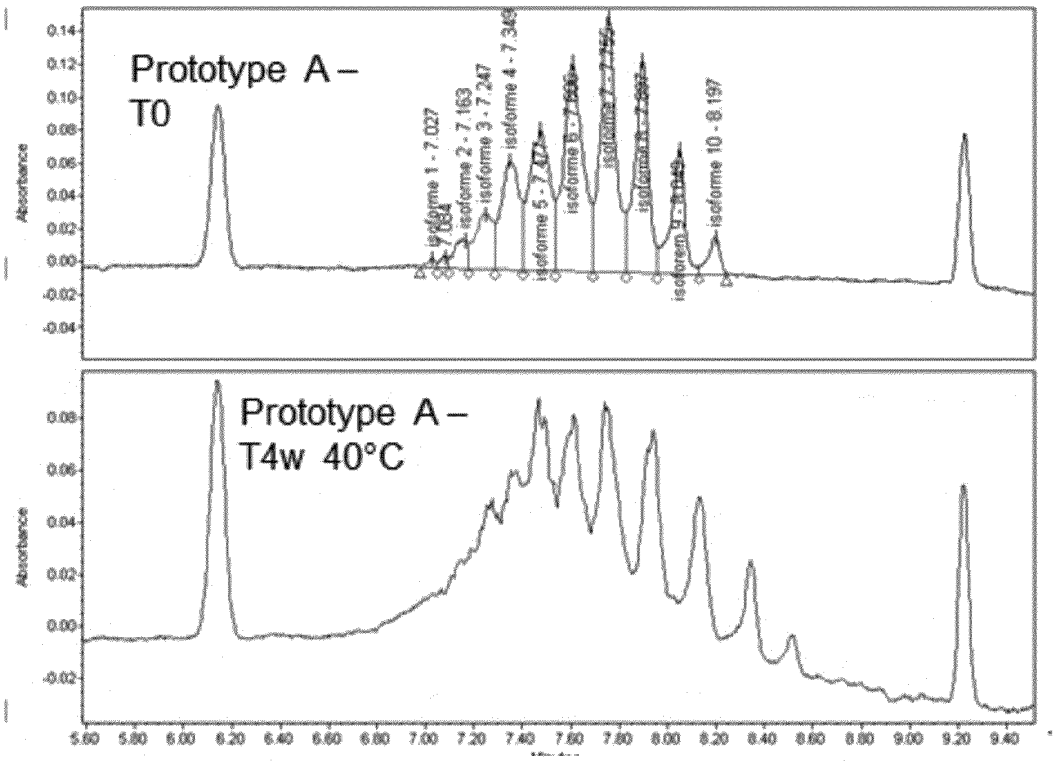

Prototype A – T0
isoforme 1 - 7.027
isoforme 2 - 7.163
isoforme 3 - 7.247
isoforme 4 - 7.345
isoforme 10 - 8.197
Absorbance
Prototype A – T4w 40°C
Absorbance
5.60 5.80 6.00 6.20 6.40 6.60 6.80 7.00 7.20 7.40 7.60 7.80 8.00 8.20 8.40 8.60 8.80 9.00 9.20 9.40

FIG. 12

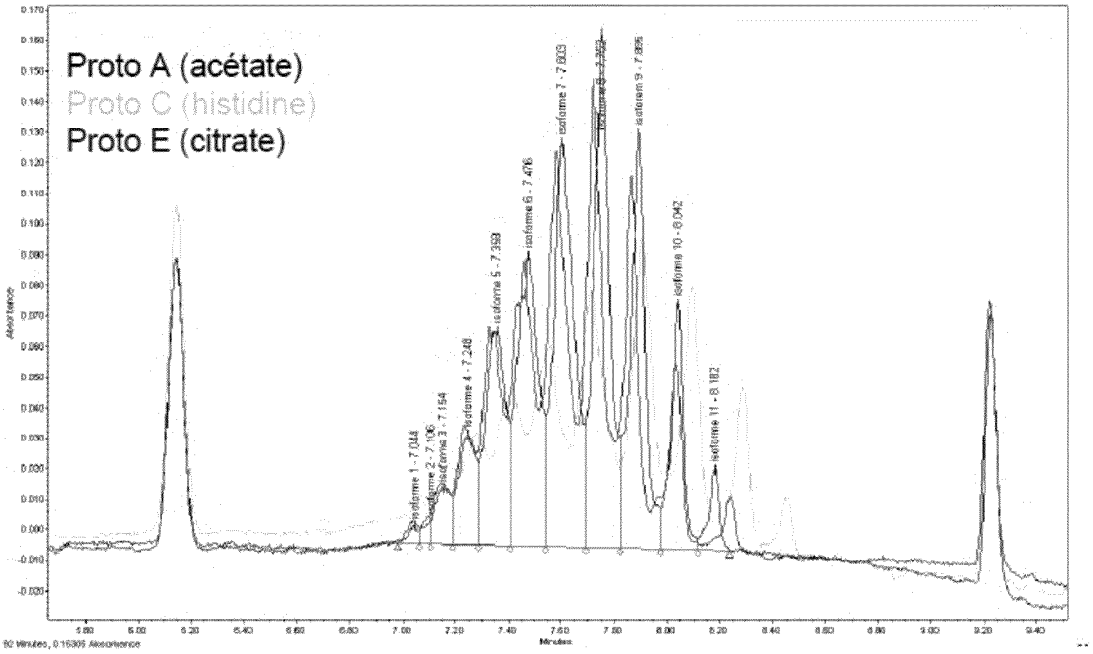

Proto A (acétate)
Proto C (histidine)
Proto E (citrate)
Absorbance
Minutes
isoforme 1 - 7.044
isoforme 2 - 7.106
isoforme 3 - 7.154
isoforme 4 - 7.248
isoforme 5 - 7.393
isoforme 6 - 7.476
isoforme 7 - 7.603
isoforme 8 - 7.755
isoforme 9 - 7.895
isoforme 10 - 8.042
isoforme 11 - 8.182

FIG. 13

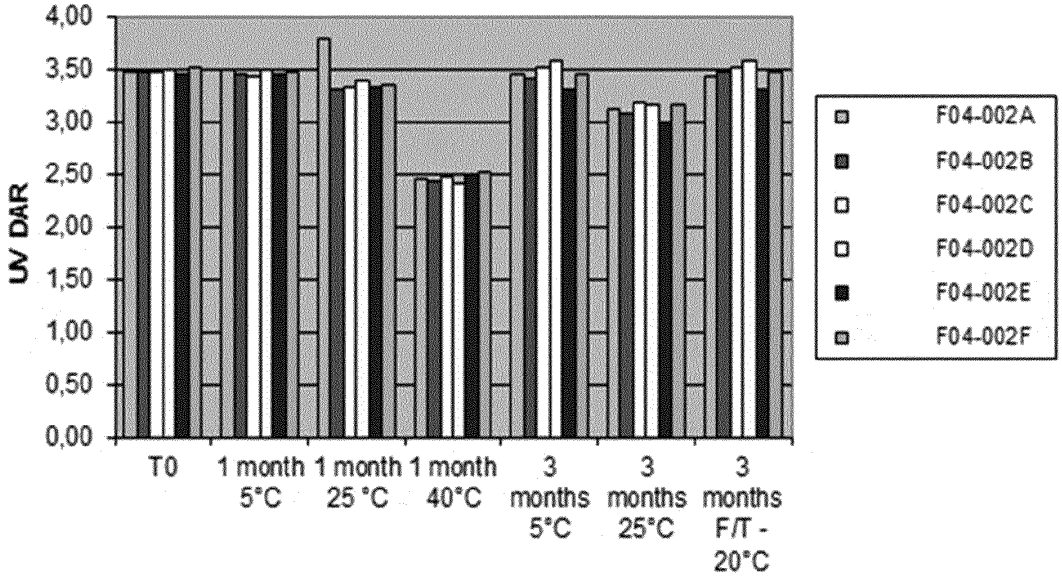

4,00
3,50
3,00
2,50
2,00
1,50
1,00
0,50
0,00
UV DAR
T0
1 month 5°C
1 month 25 °C
1 month 40°C
3 months 5°C
3 months 25°C
3 months F/T - 20°C
F04-002A
F04-002B
F04-002C
F04-002D
F04-002E
F04-002F

FIG. 14

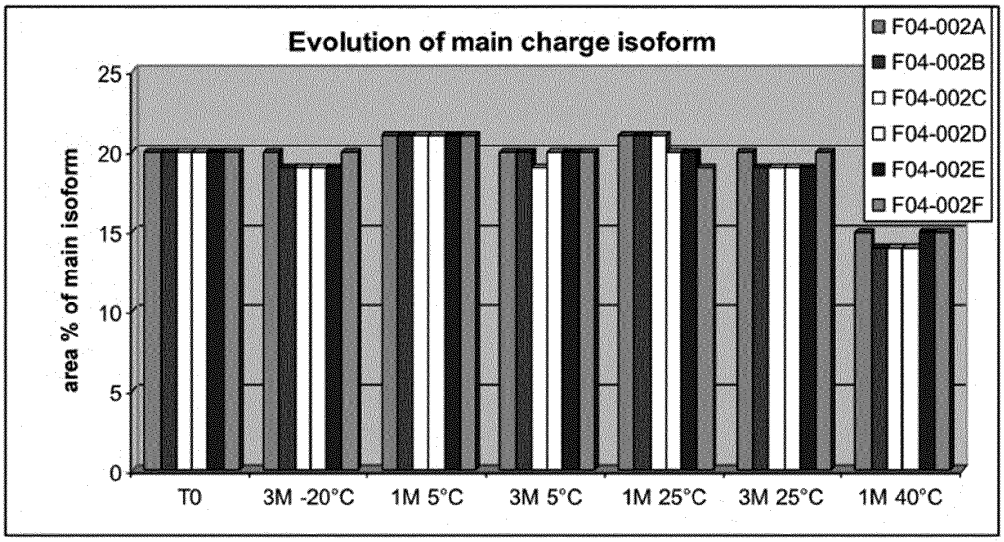

Evolution of main charge isoform
area % of main isoform
25
20
15
10
5
0
T0
3M -20°C
1M 5°C
3M 5°C
1M 25°C
3M 25°C
1M 40°C
F04-002A
F04-002B
F04-002C
F04-002D
F04-002E
F04-002F

FIG. 15

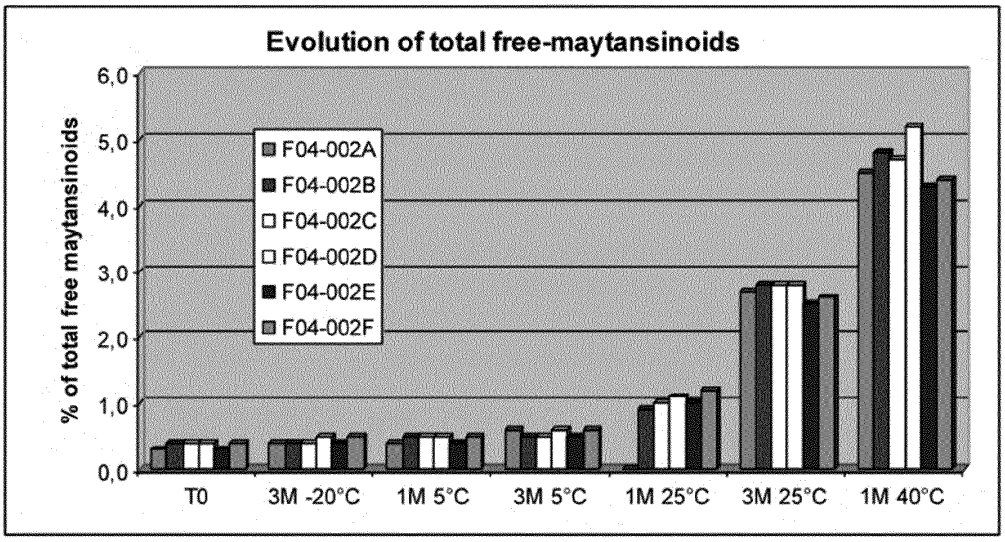

Evolution of total free-maytansinoids
% of total free maytansinoids
6,0
5,0
4,0
3,0
2,0
1,0
0,0
F04-002A
F04-002B
F04-002C
F04-002D
F04-002E
F04-002F
T0
3M -20°C
1M 5°C
3M 5°C
1M 25°C
3M 25°C
1M 40°C

FIG. 16

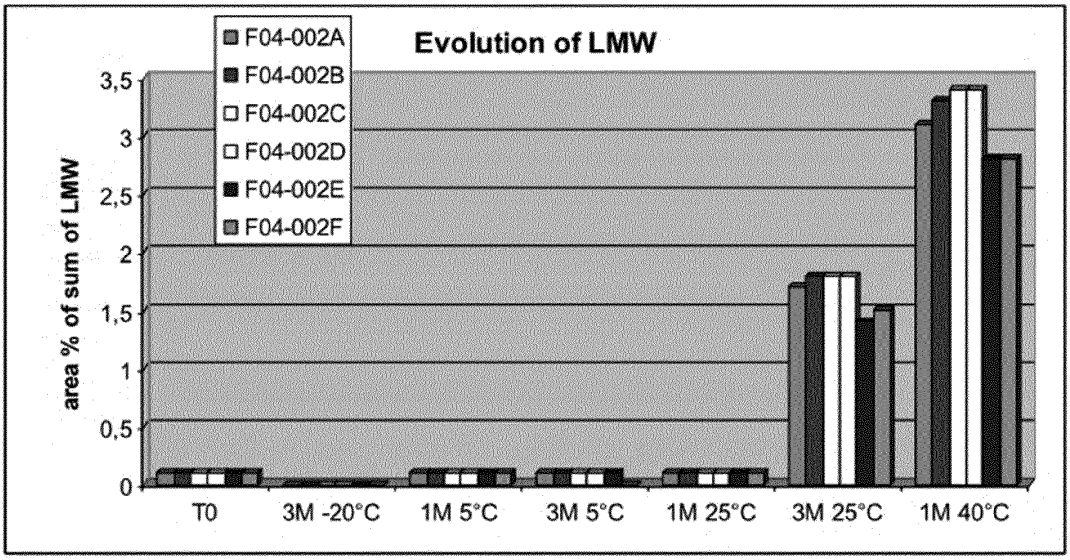

Evolution of LMW
F04-002A
F04-002B
F04-002C
F04-002D
F04-002E
F04-002F
area % of sum of LMW
3,5
3
2,5
2
1,5
1
0,5
0
T0
3M -20°C
1M 5°C
3M 5°C
1M 25°C
3M 25°C
1M 40°C

FIG. 17

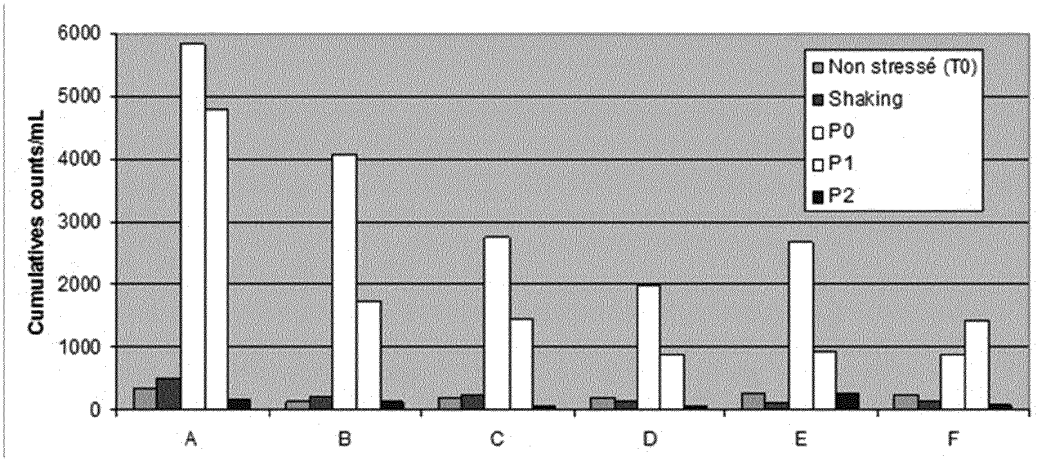

6000
5000
4000
3000
2000
1000
0
Cumulatives counts/mL
A
B
C
D
E
F
Non stressé (T0)
Shaking
P0
P1
P2

FIG. 18

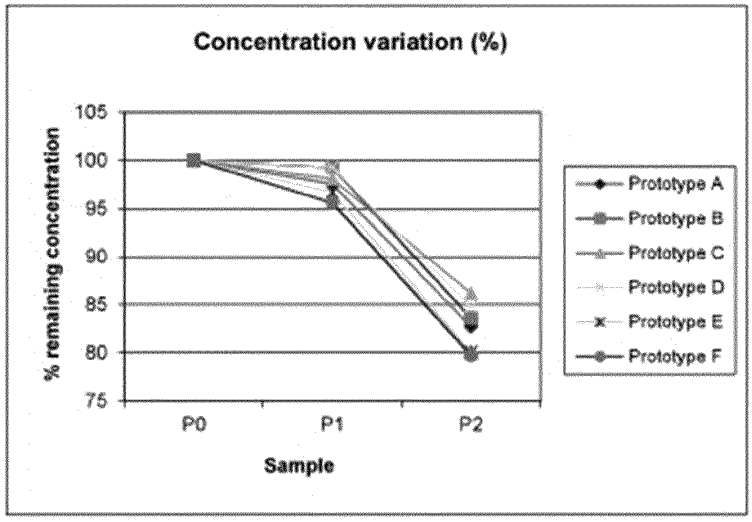


FIG. 19A

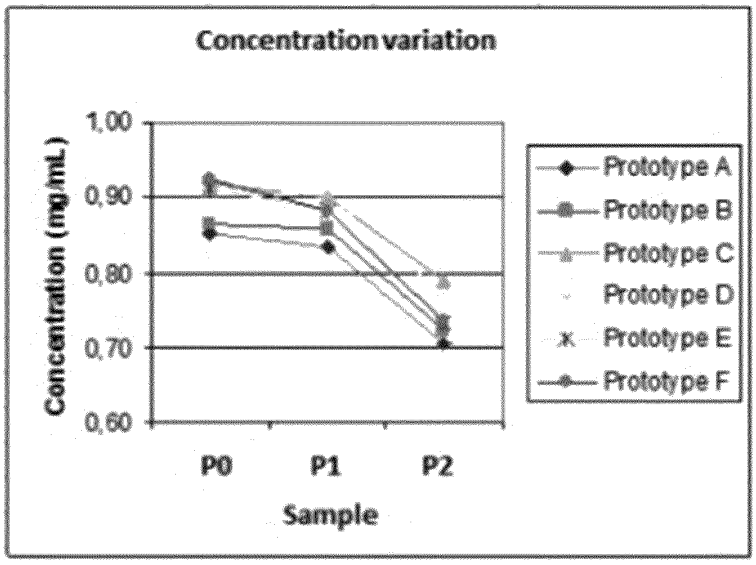


FIG. 19B

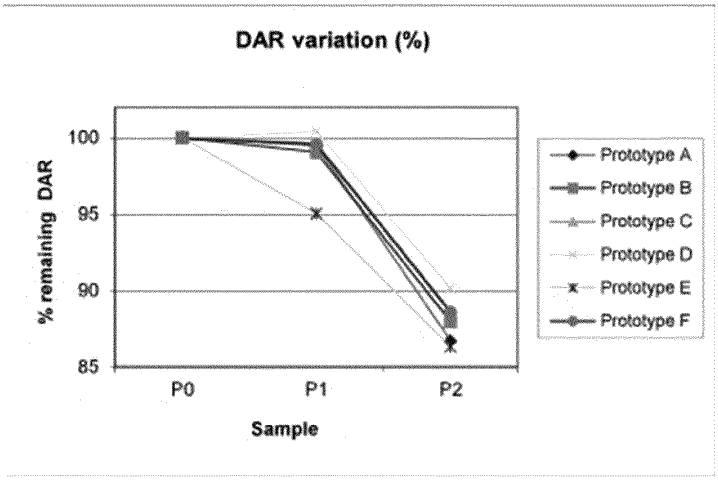


FIG. 20A

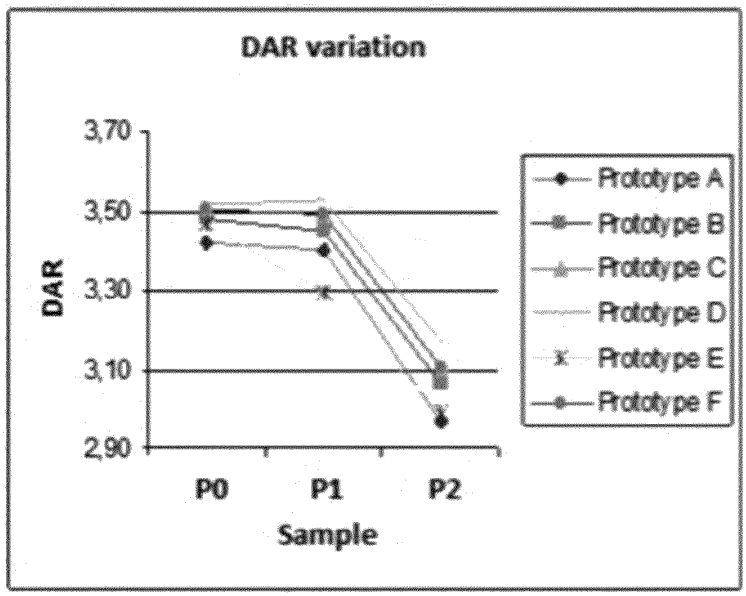


FIG. 20B

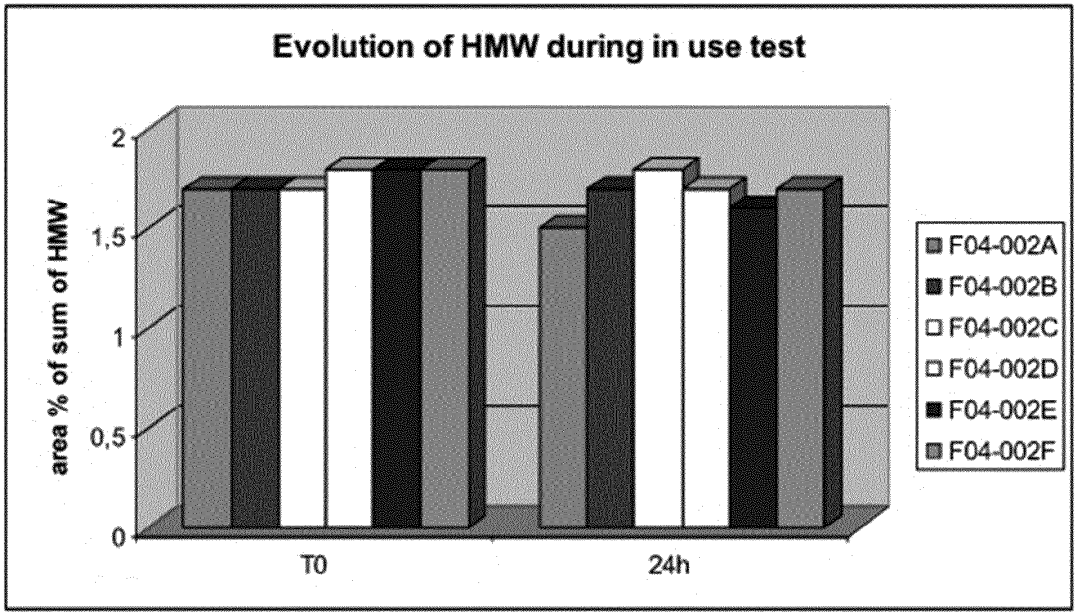

Evolution of HMW during in use test
area % of sum of HMW
2
1,5
1
0,5
0
T0
24h
F04-002A
F04-002B
F04-002C
F04-002D
F04-002E
F04-002F

FIG. 21

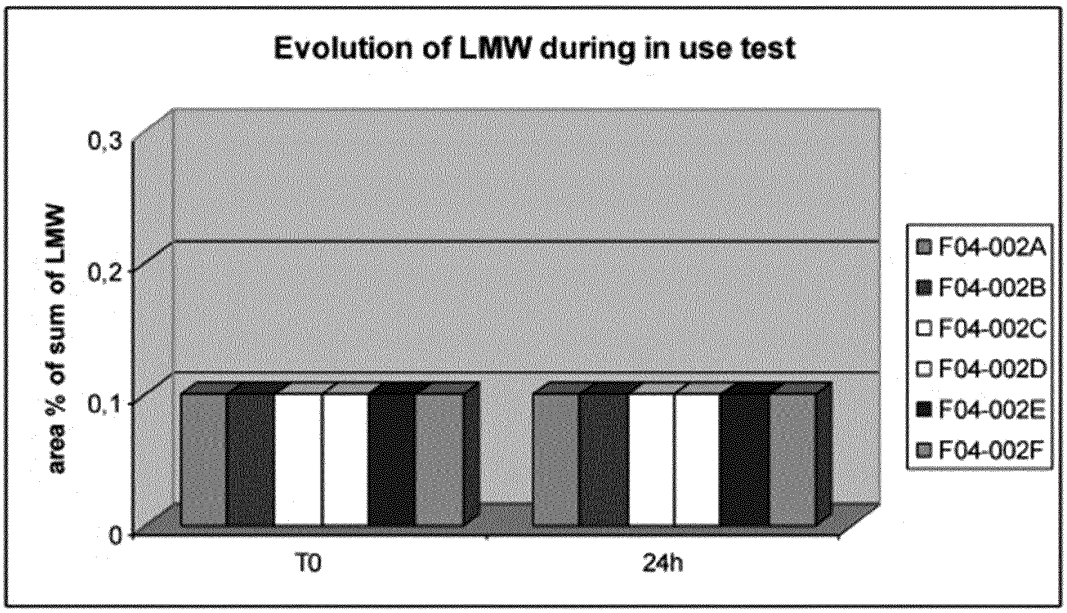

Evolution of LMW during in use test
area % of sum of LMW
0,3
0,2
0,1
0
T0
24h
F04-002A
F04-002B
F04-002C
F04-002D
F04-002E
F04-002F

FIG. 22

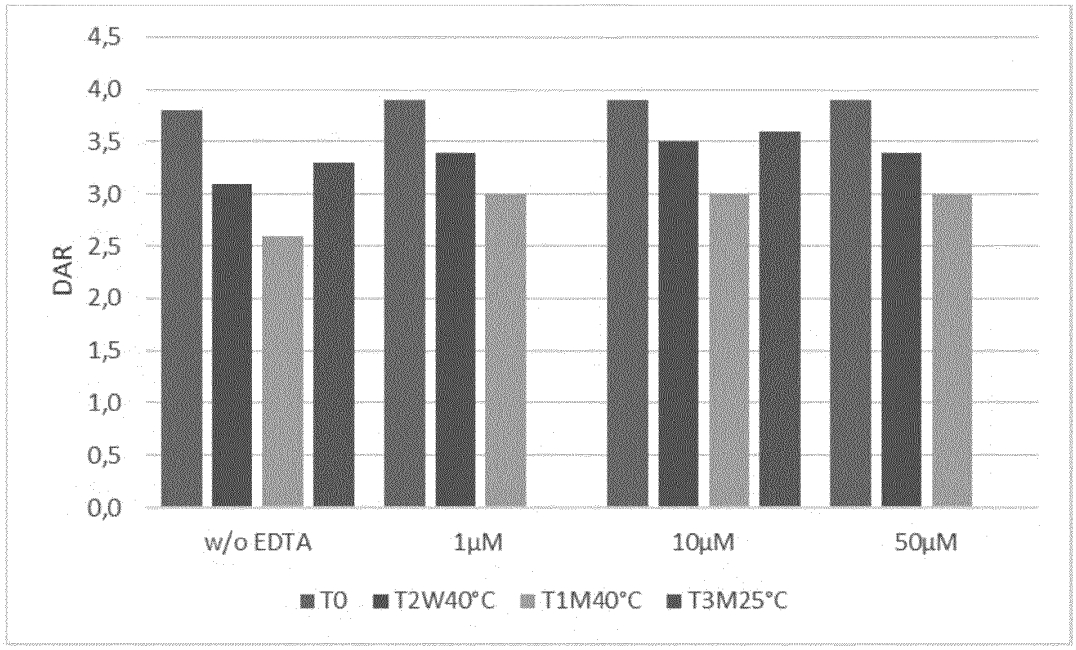

4,5
4,0
3,5
3,0
2,5
2,0
1,5
1,0
0,5
0,0
DAR
w/o EDTA
1µM
10µM
50µM
T0
T2W40°C
T1M40°C
T3M25°C

FIG. 23

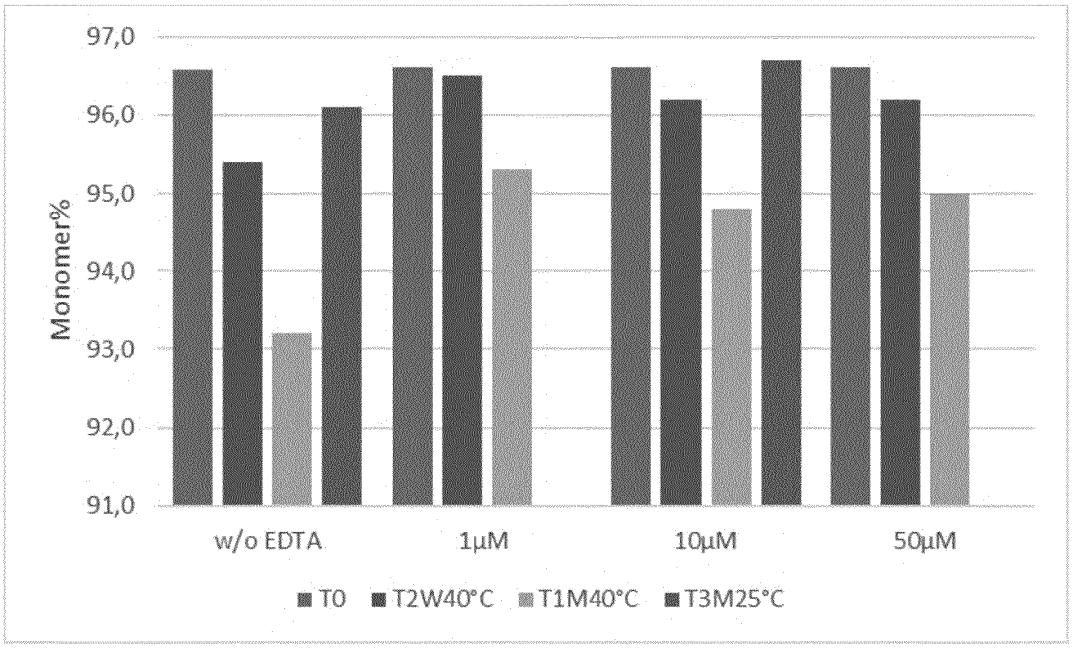

97,0
96,0
95,0
94,0
93,0
92,0
91,0
Monomer%
w/o EDTA
1µM
10µM
50µM
T0
T2W40°C
T1M40°C
T3M25°C

FIG. 24

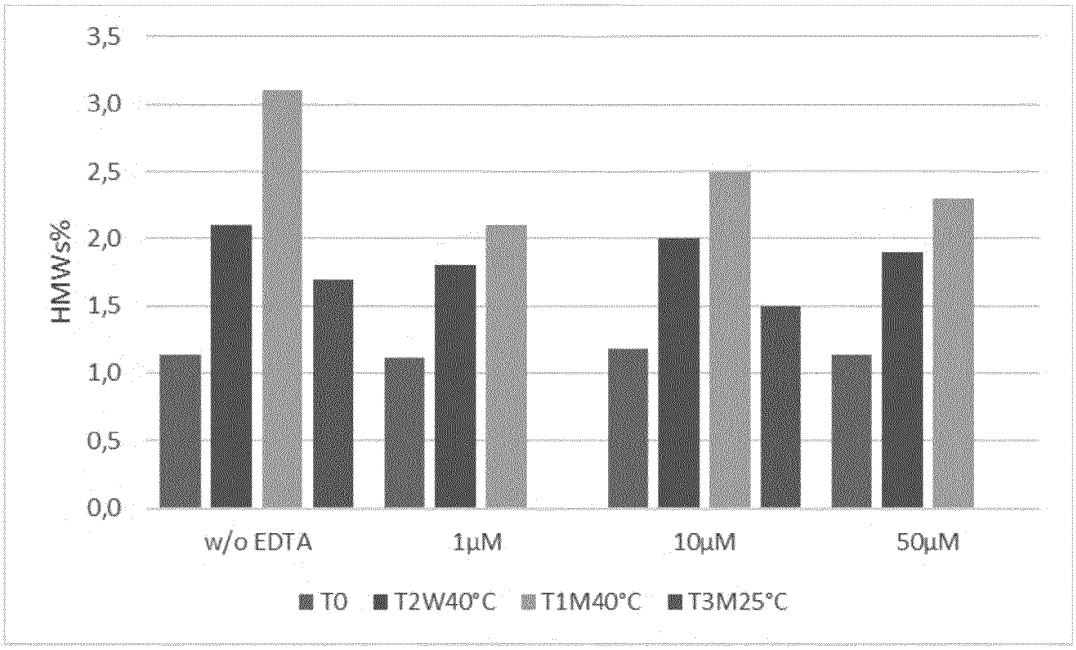

3,5
3,0
2,5
2,0
1,5
1,0
0,5
0,0
HMWs%
w/o EDTA
1µM
10µM
50µM
T0
T2W40°C
T1M40°C
T3M25°C

FIG. 25

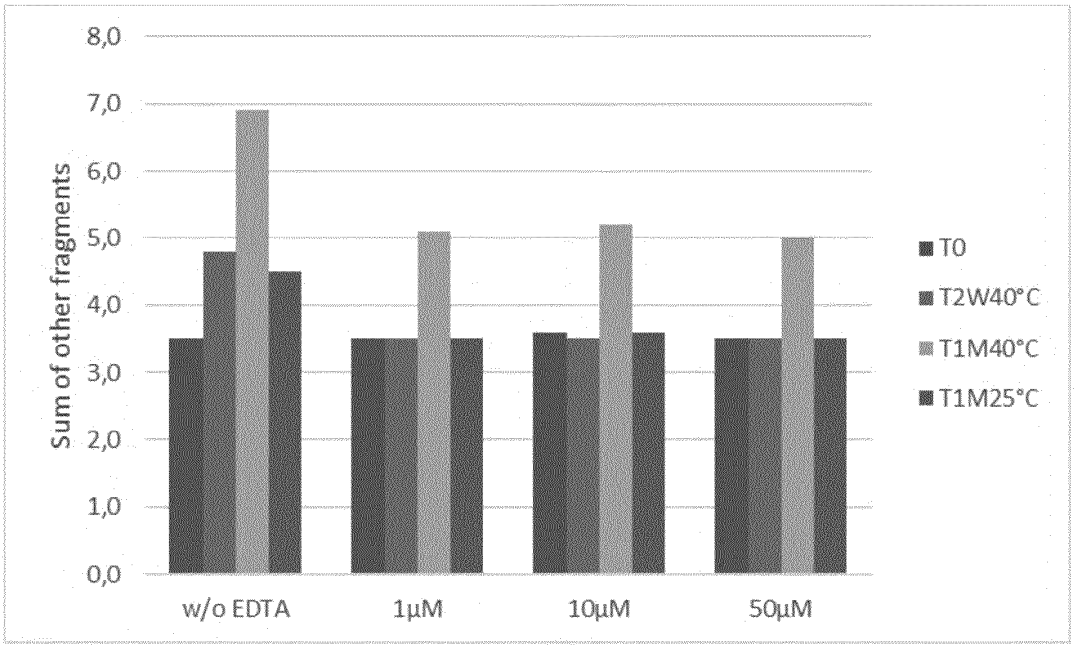

8,0
7,0
6,0
5,0
4,0
3,0
2,0
1,0
0,0
Sum of other fragments
w/o EDTA
1µM
10µM
50µM
T0
T2W40°C
T1M40°C
T1M25°C

FIG. 26

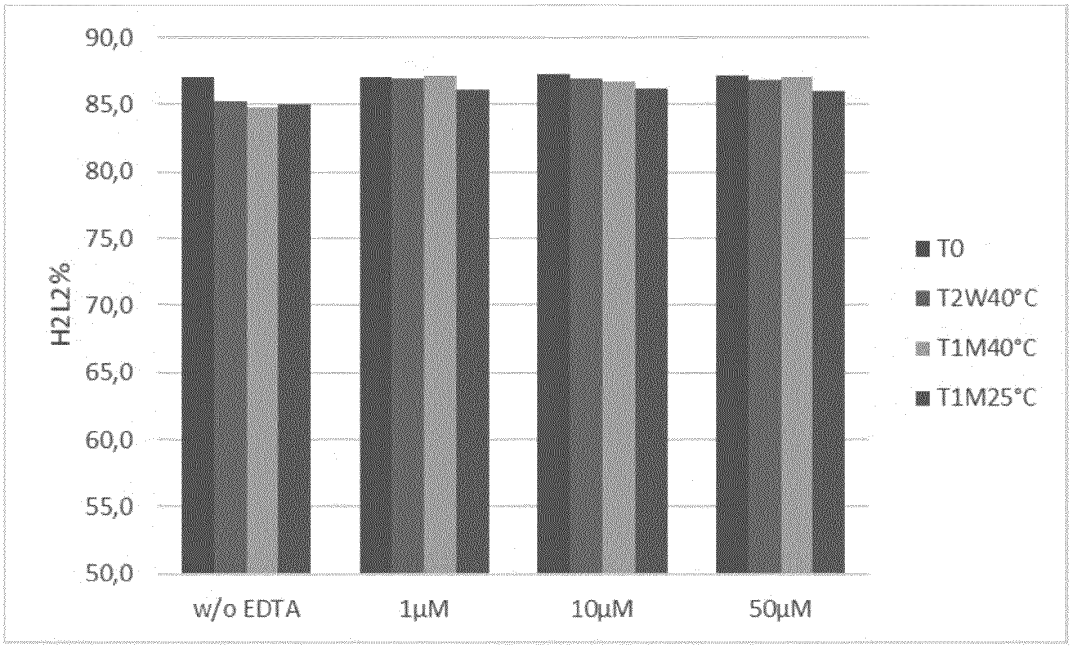

90,0
85,0
80,0
75,0
70,0
65,0
60,0
55,0
50,0
H2L2%
w/o EDTA
1µM
10µM
50µM
T0
T2W40°C
T1M40°C
T1M25°C

FIG. 27

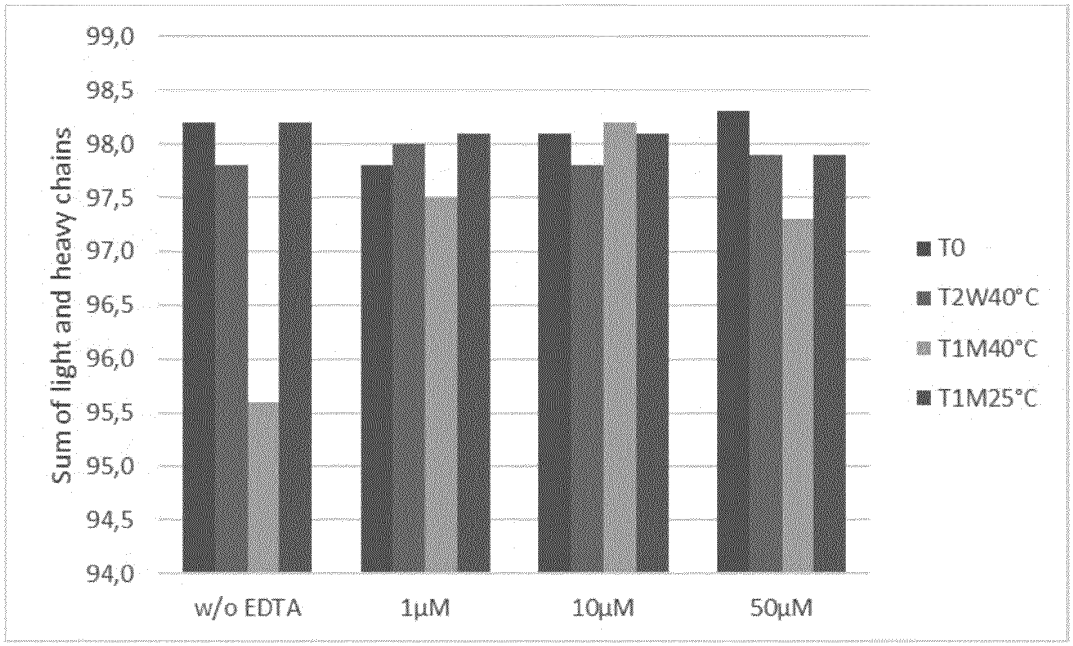

99,0
98,5
98,0
97,5
97,0
96,5
96,0
95,5
95,0
94,5
94,0
Sum of light and heavy chains
w/o EDTA
1µM
10µM
50µM
T0
T2W40°C
T1M40°C
T1M25°C

FIG. 28

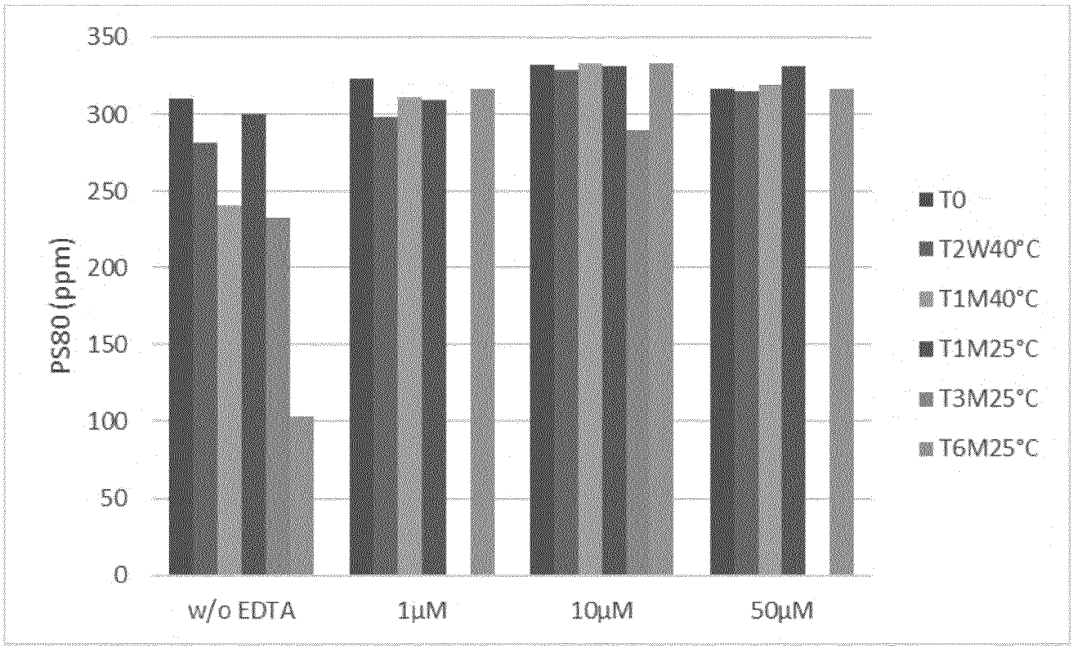

350
300
250
200
150
100
50
0
PS80 (ppm)
w/o EDTA
1µM
10µM
50µM
T0
T2W40°C
T1M40°C
T1M25°C
T3M25°C
T6M25°C

FIG. 29

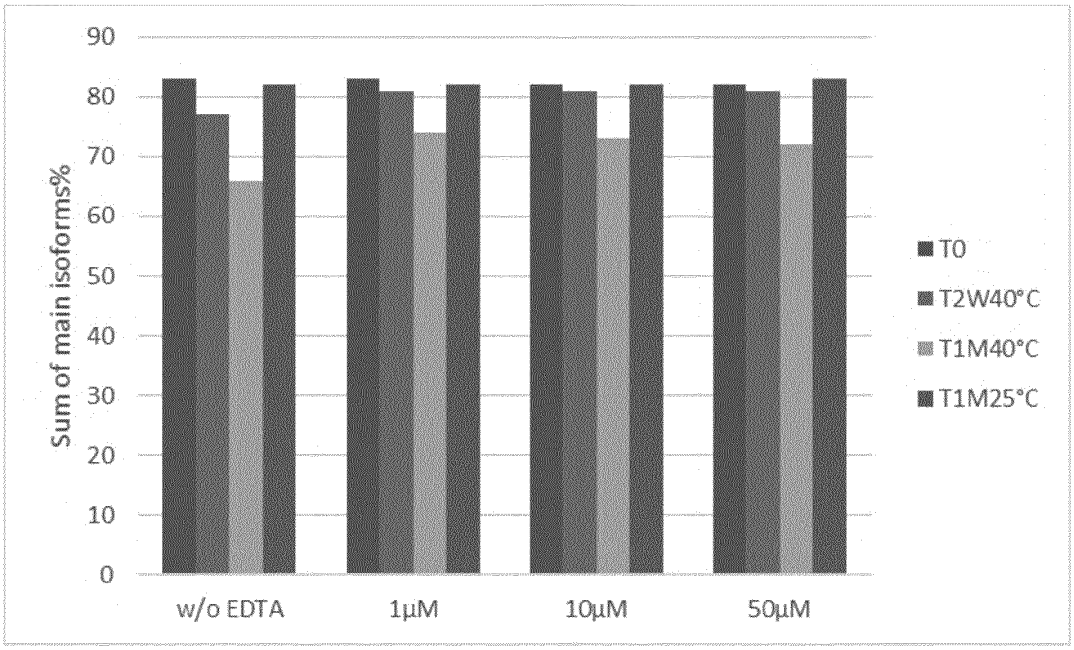

90
80
70
60
50
40
30
20
10
0
Sum of main isoforms%
w/o EDTA
1µM
10µM
50µM
T0
T2W40°C
T1M40°C
T1M25°C

FIG. 30

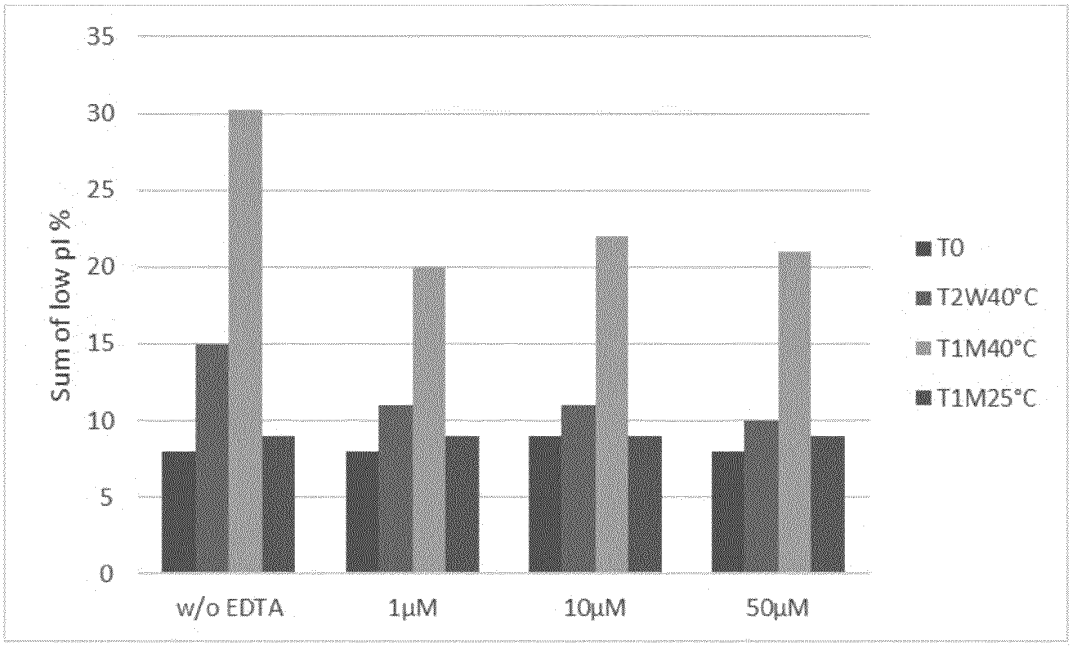

35
30
25
20
15
10
5
0
Sum of low pI %
w/o EDTA
1µM
10µM
50µM
T0
T2W40°C
T1M40°C
T1M25°C

FIG. 31