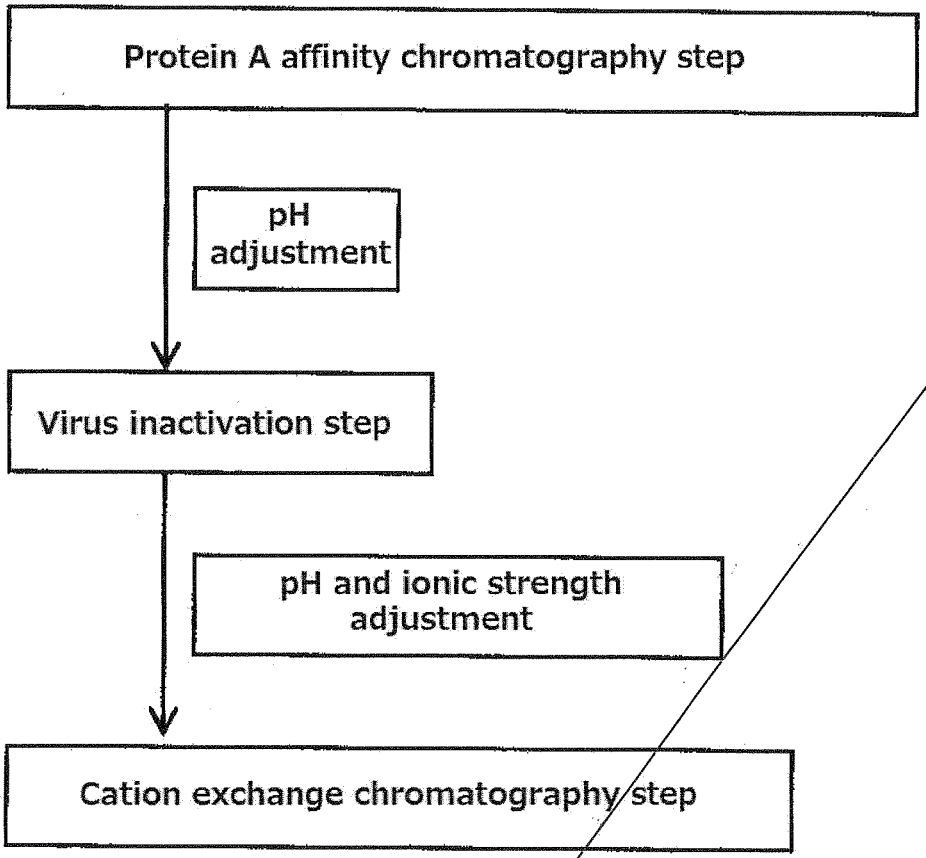
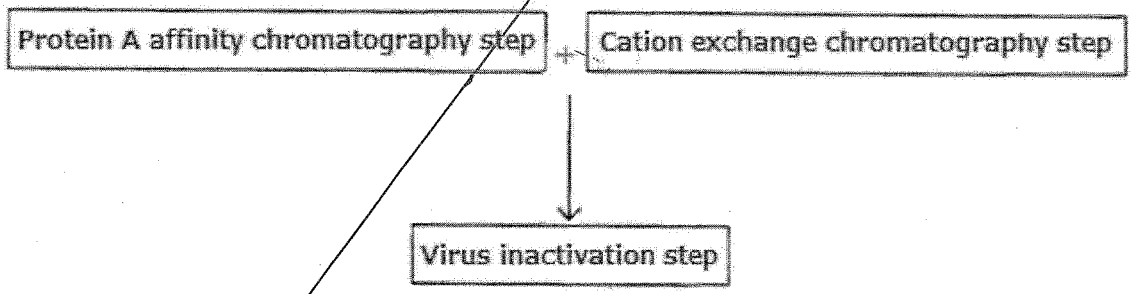
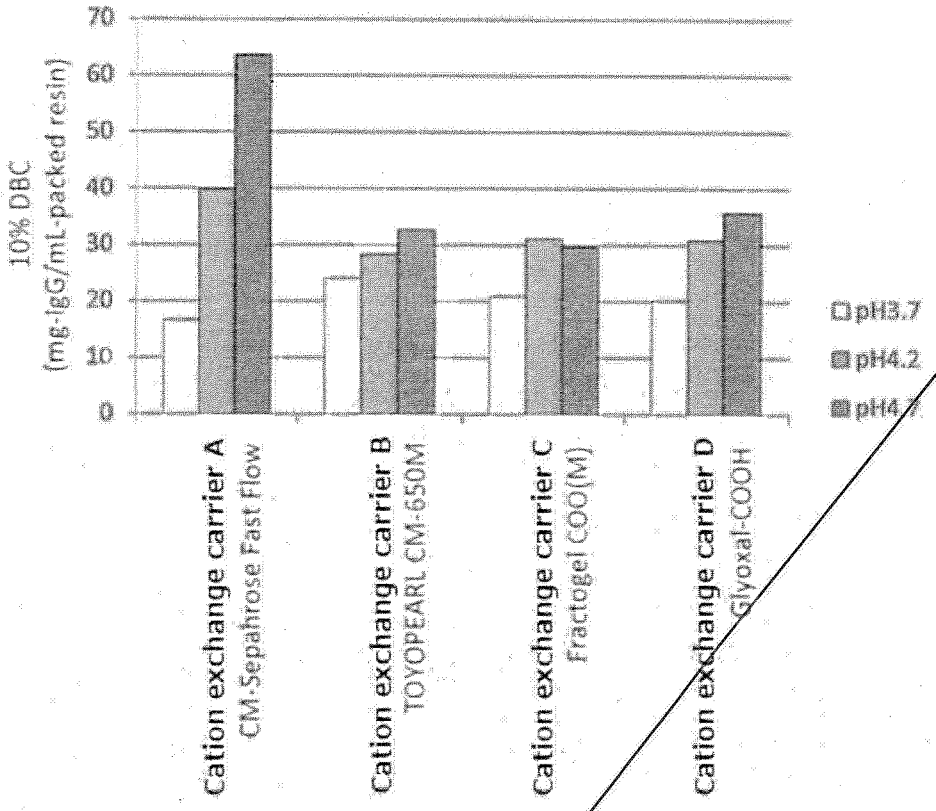
[Fig.1]



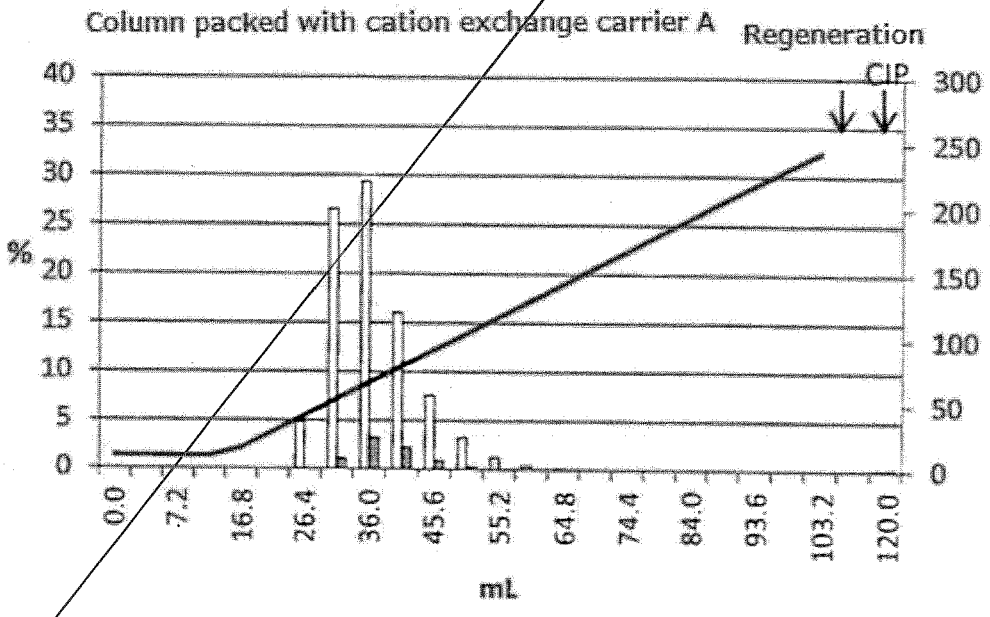
[Fig.2]



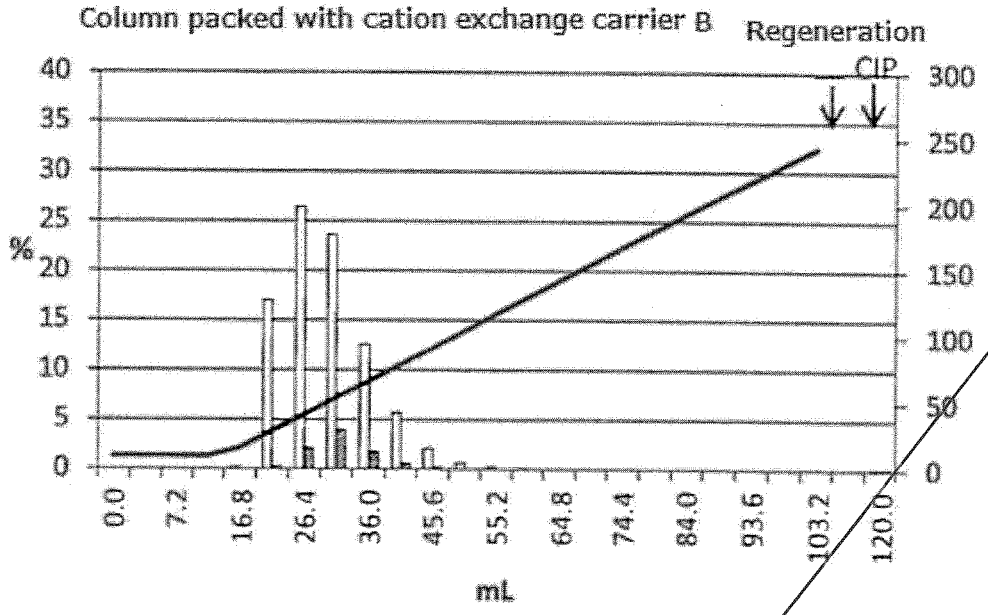
[Fig.3]


10% DBC
(mg-IgG/mL-packed resin)
70
60
50
40
30
20
10
0
pH3.7
pH4.2
pH4.7
Cation exchange carrier A
CM-Sepahrose Fast Flow
Cation exchange carrier B
TOYOPEARL CM-650M
Cation exchange carrier C
Fractogel COO(M)
Cation exchange carrier D
Glyoxal-COOH

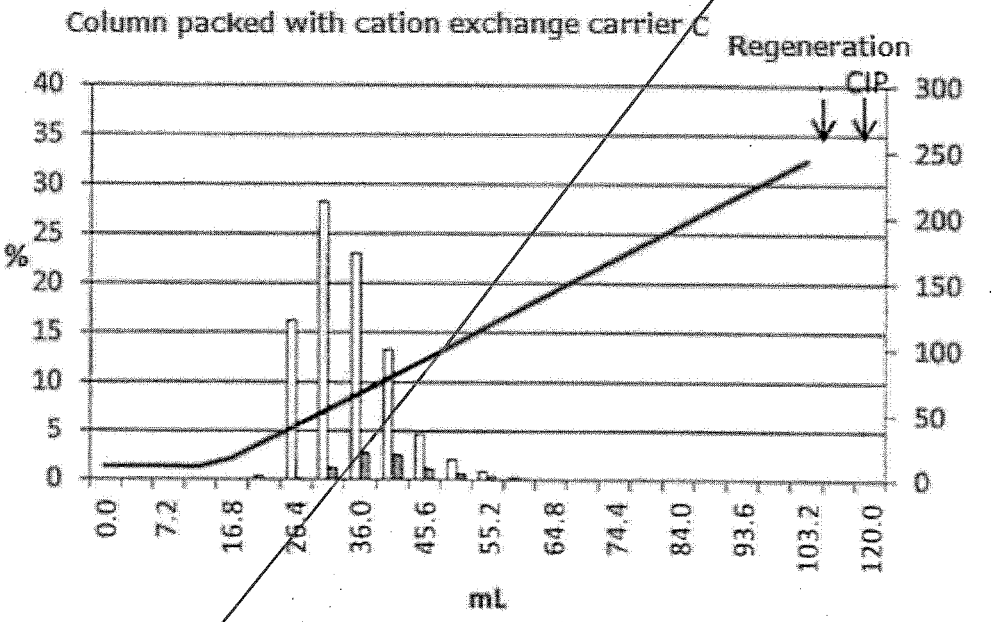
[Fig.4]


Column packed with cation exchange carrier A
Regeneration
CIP
%
mL
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
103.2
120.0

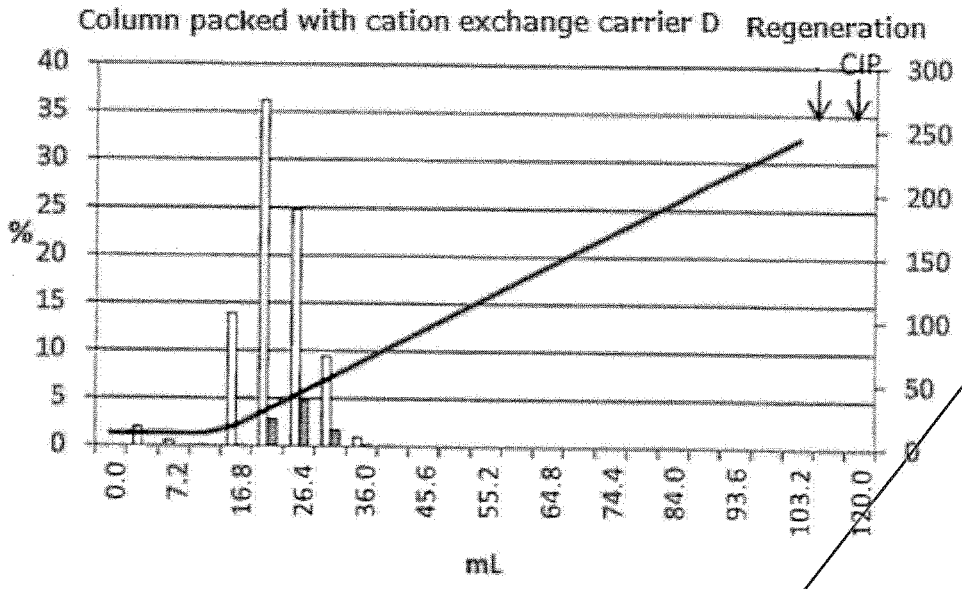
[Fig.5]


Column packed with cation exchange carrier B
Regeneration
CIP
%
mL
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
103.2
120.0

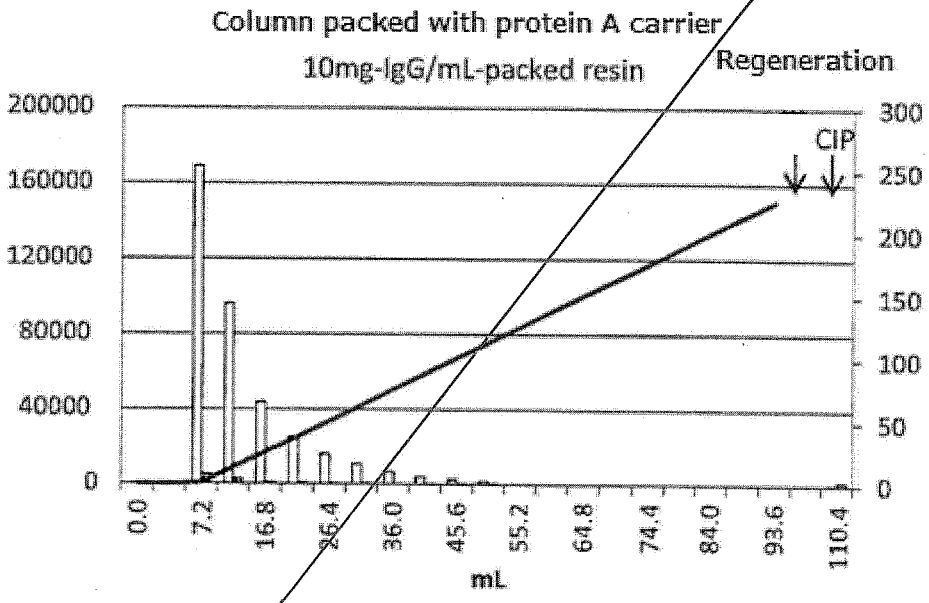
[Fig.6]


Column packed with cation exchange carrier C
Regeneration
CIP
%
mL
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
103.2
120.0

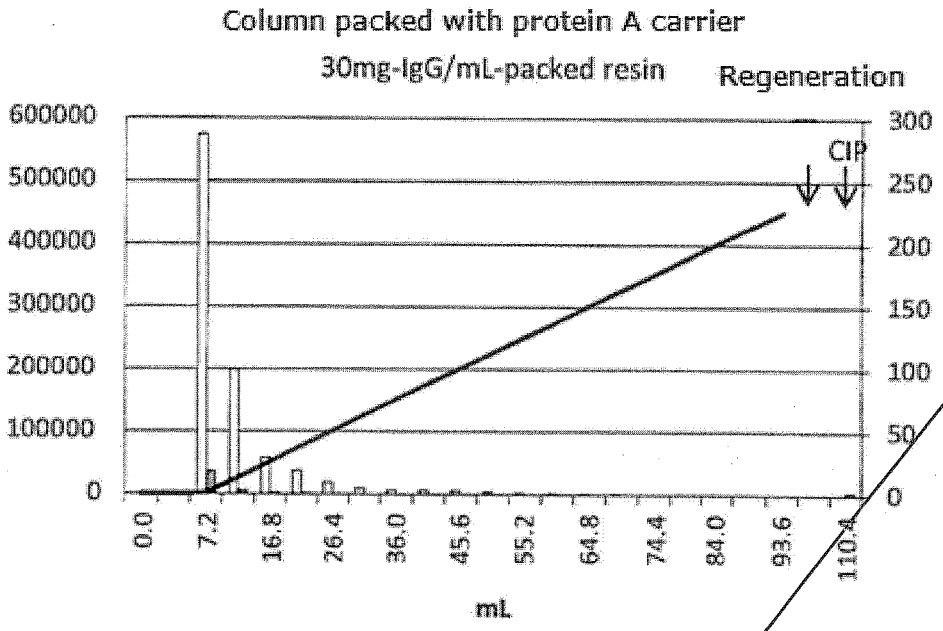
[Fig.7]


Column packed with cation exchange carrier D
Regeneration
CIP
%
mL
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
103.2
120.0

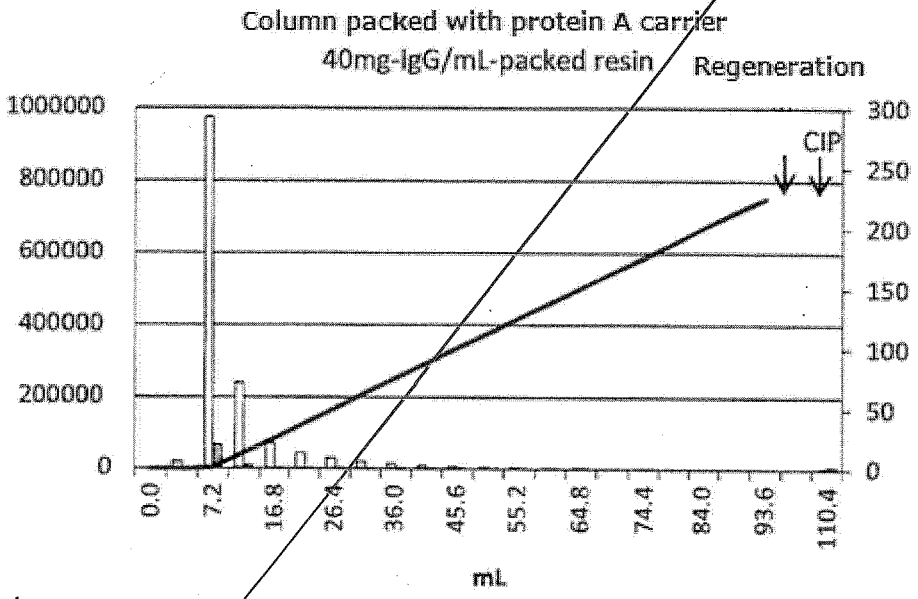
[Fig.8]


Column packed with protein A carrier
10mg-IgG/mL-packed resin
Regeneration
CIP
mL
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4

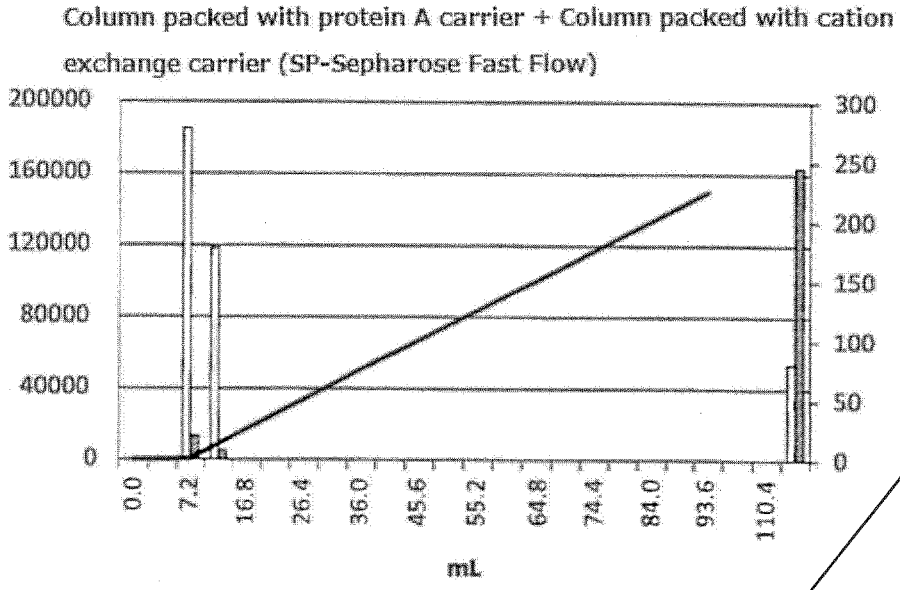
[Fig.9]


Column packed with protein A carrier
30mg-IgG/mL-packed resin
Regeneration
CIP
600000
500000
400000
300000
200000
100000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

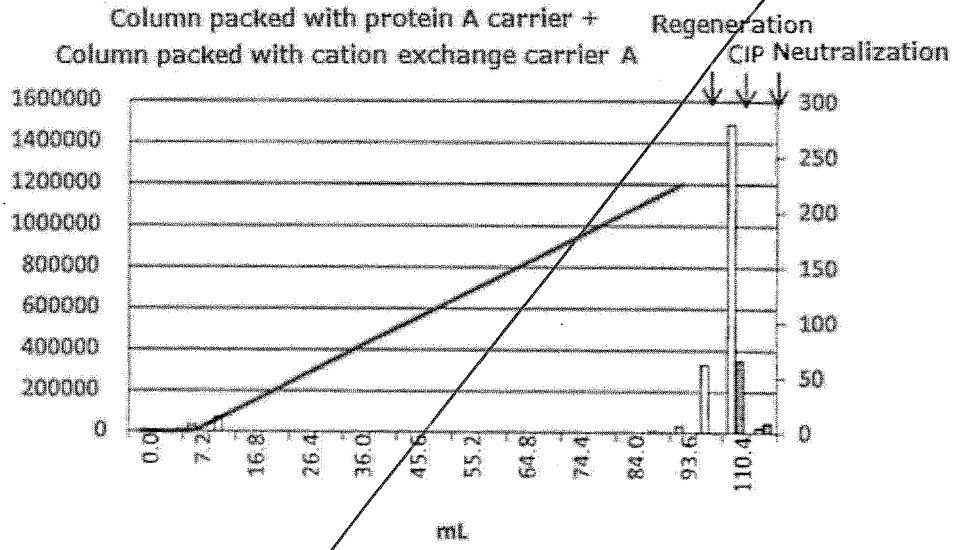
[Fig.10]


Column packed with protein A carrier
40mg-IgG/mL-packed resin
Regeneration
CIP
1000000
800000
600000
400000
200000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

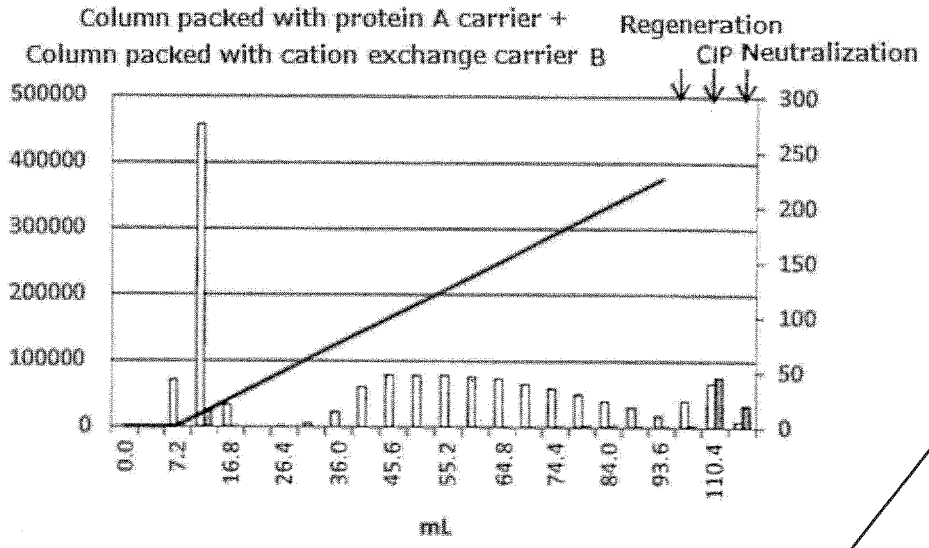
[Fig.11]


Column packed with protein A carrier + Column packed with cation exchange carrier (SP-Sepharose Fast Flow)
200000
160000
120000
80000
40000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

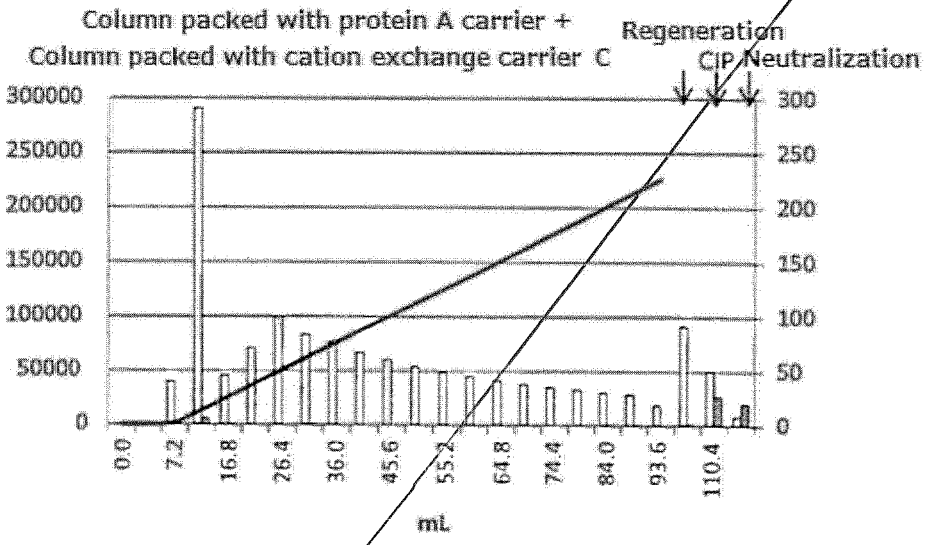
[Fig.12]


Column packed with protein A carrier +
Column packed with cation exchange carrier A
Regeneration
CIP Neutralization
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

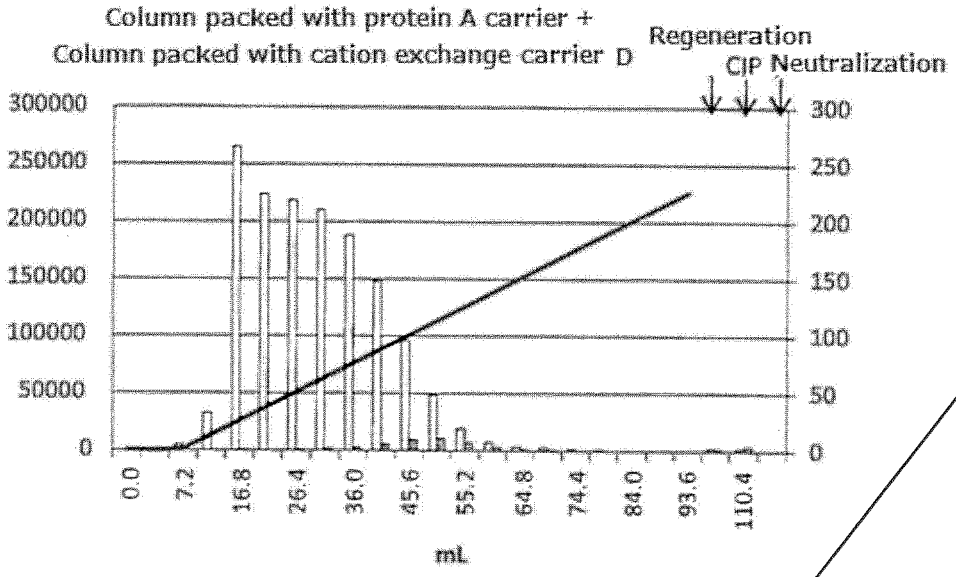
[Fig.13]


Column packed with protein A carrier +
Column packed with cation exchange carrier B
Regeneration
CIP Neutralization
500000
400000
300000
200000
100000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

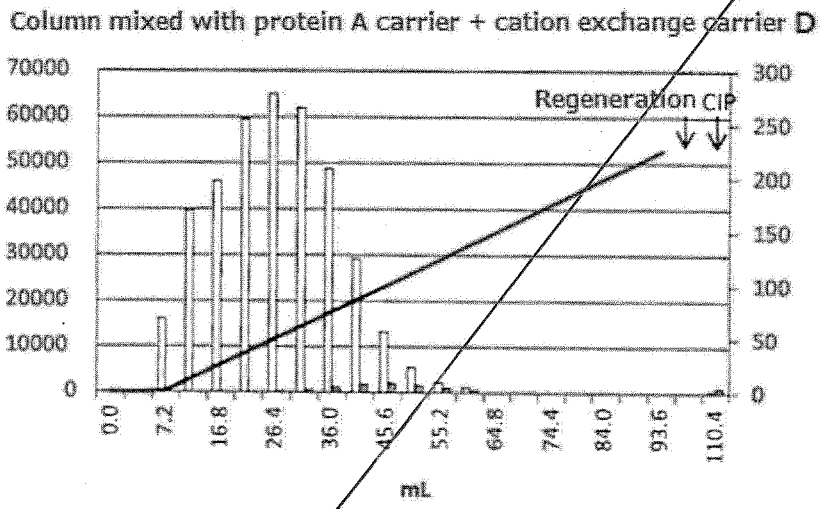
[Fig.14]


Column packed with protein A carrier +
Column packed with cation exchange carrier C
Regeneration
CIP Neutralization
300000
250000
200000
150000
100000
50000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

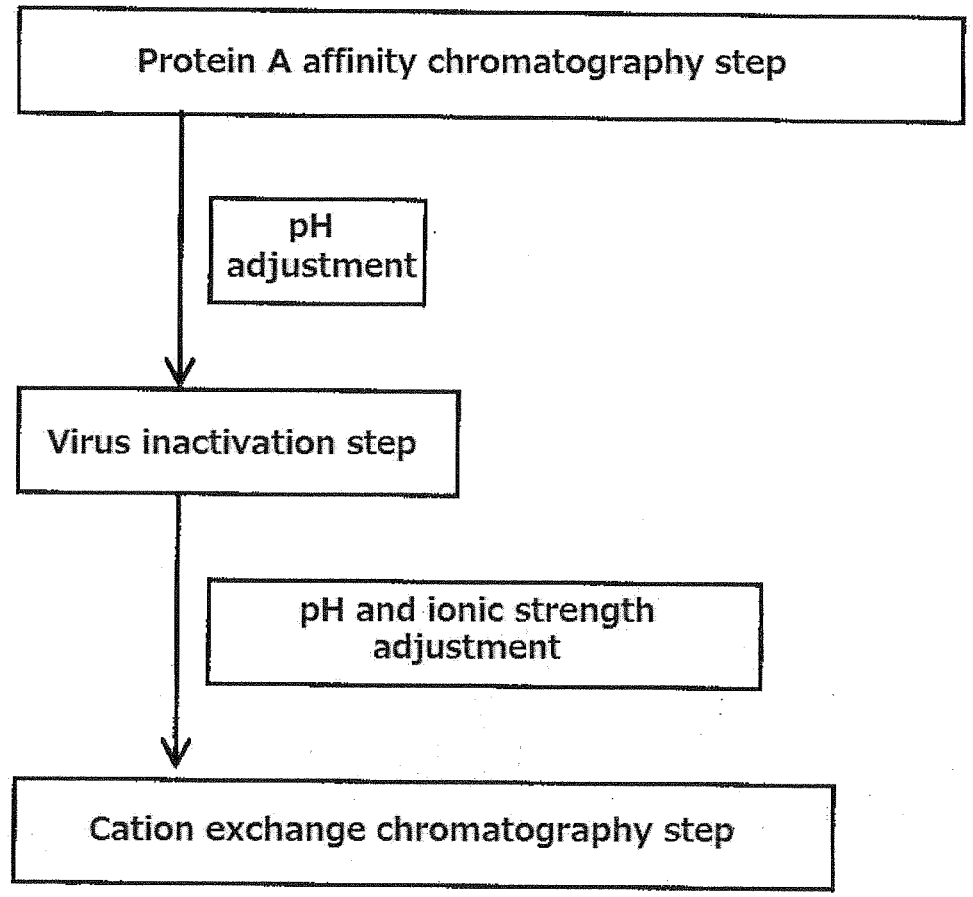
[Fig.15]


Column packed with protein A carrier +
Column packed with cation exchange carrier D
Regeneration
CIP
Neutralization
300000
250000
200000
150000
100000
50000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

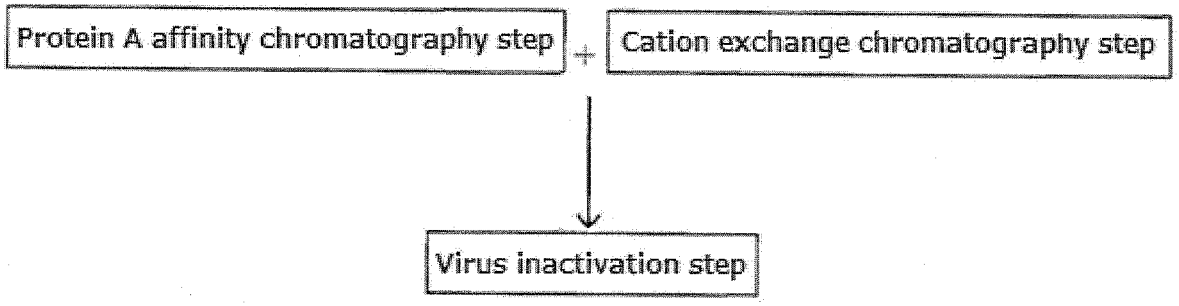
[Fig.16]


Column mixed with protein A carrier + cation exchange carrier D
70000
60000
50000
40000
30000
20000
10000
0
Regeneration
CIP
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

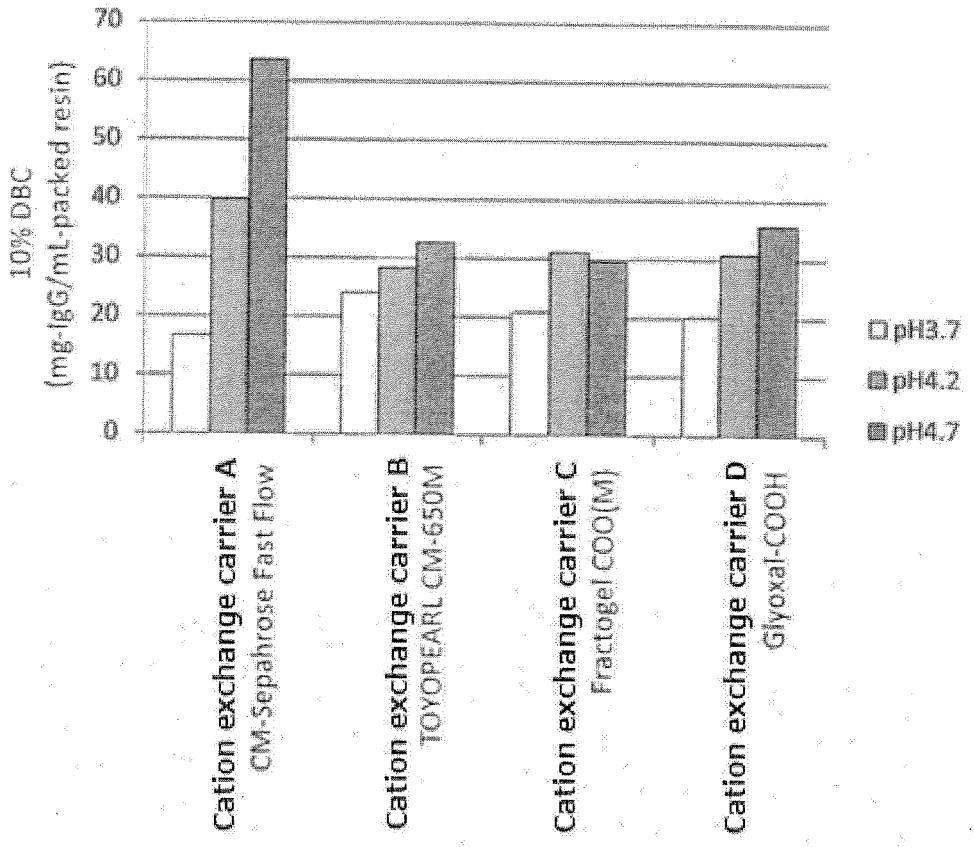
[Fig.1]


Protein A affinity chromatography step
pH adjustment
Virus inactivation step
pH and ionic strength adjustment
Cation exchange chromatography step

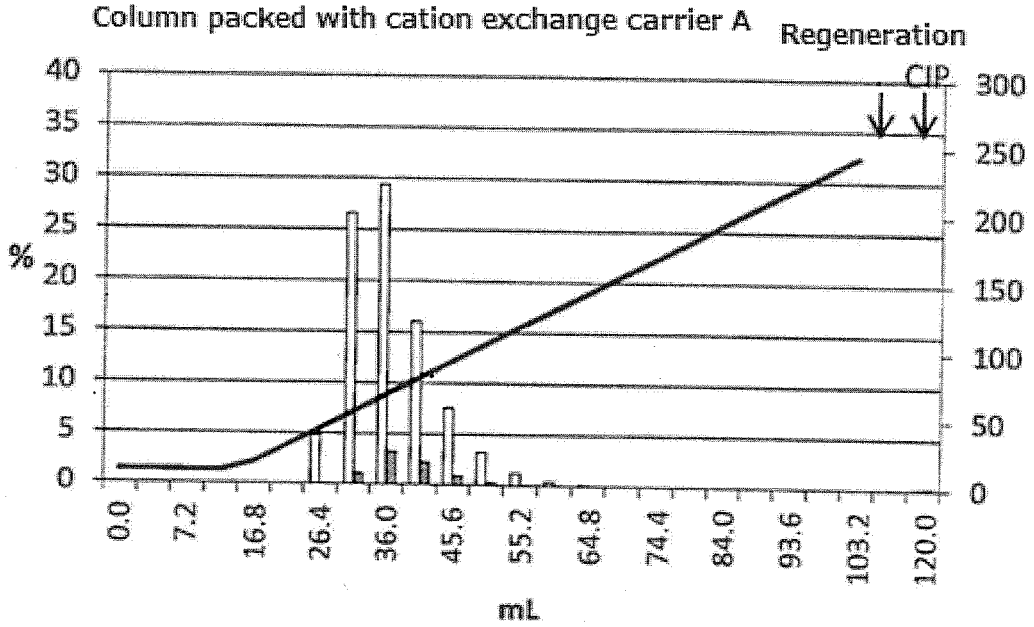
[Fig.2]


Protein A affinity chromatography step
+
Cation exchange chromatography step
Virus inactivation step

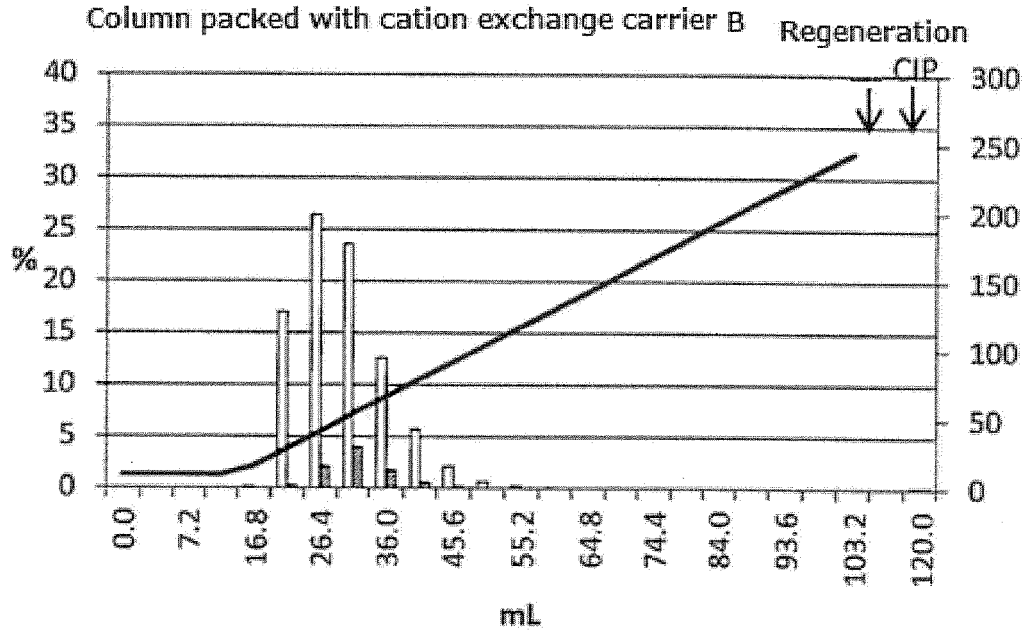
[Fig.3]


10% DBC
(mg-IgG/mL-packed resin)
70
60
50
40
30
20
10
0
pH3.7
pH4.2
pH4.7
Cation exchange carrier A
CM-Sepahrose Fast Flow
Cation exchange carrier B
TOYOPEARL CM-650M
Cation exchange carrier C
Fractogel COO(M)
Cation exchange carrier D
Glyoxal-COOH

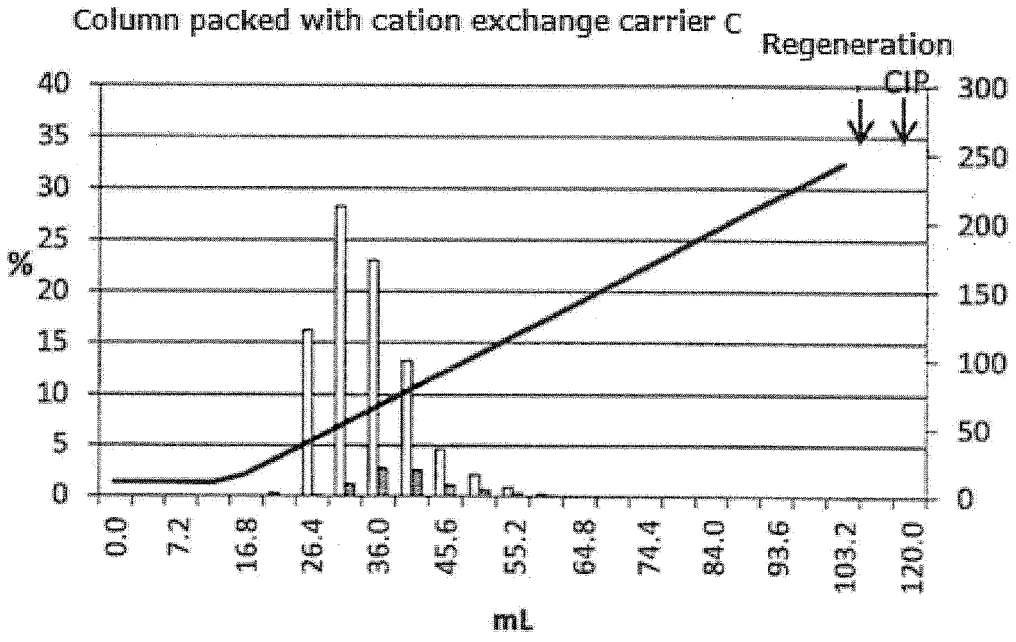
[Fig.4]


Column packed with cation exchange carrier A
Regeneration
CIP
%
40
35
30
25
20
15
10
5
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
103.2
120.0
mL

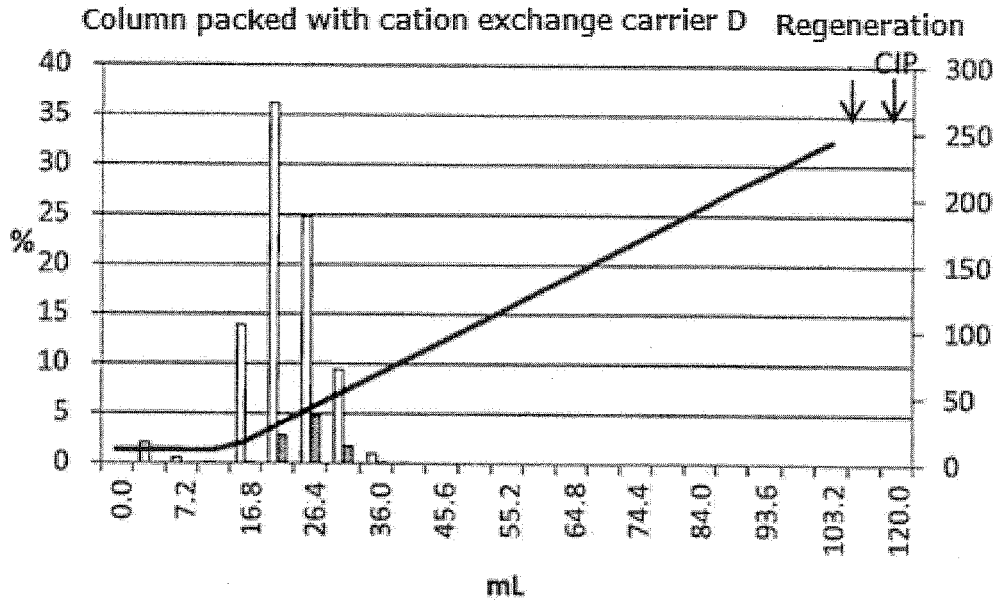
[Fig.5]


Column packed with cation exchange carrier B
Regeneration
CIP
%
mL
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
103.2
120.0

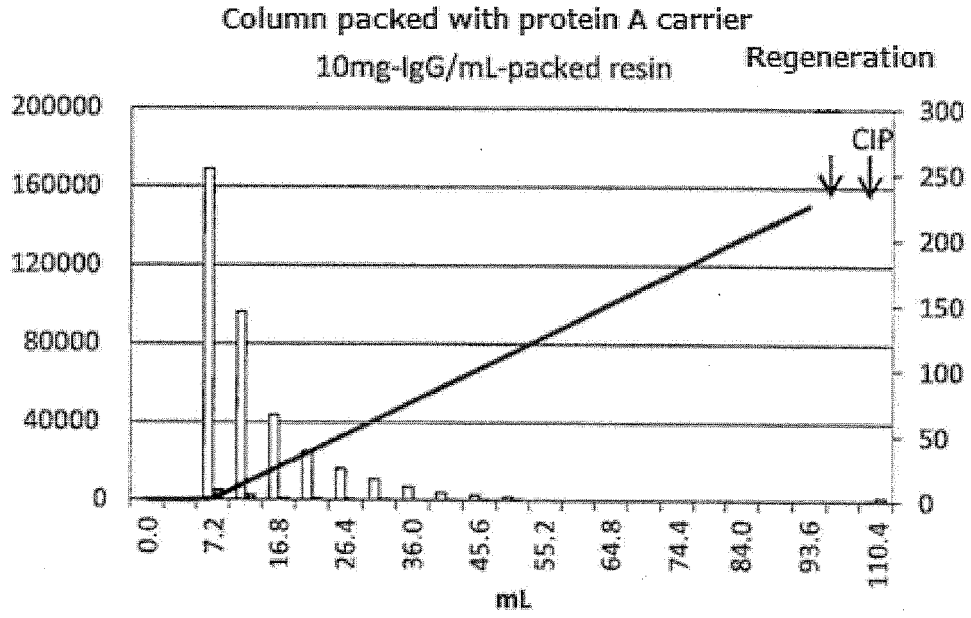
[Fig.6]


Column packed with cation exchange carrier C
Regeneration
CIP
%
mL
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
103.2
120.0

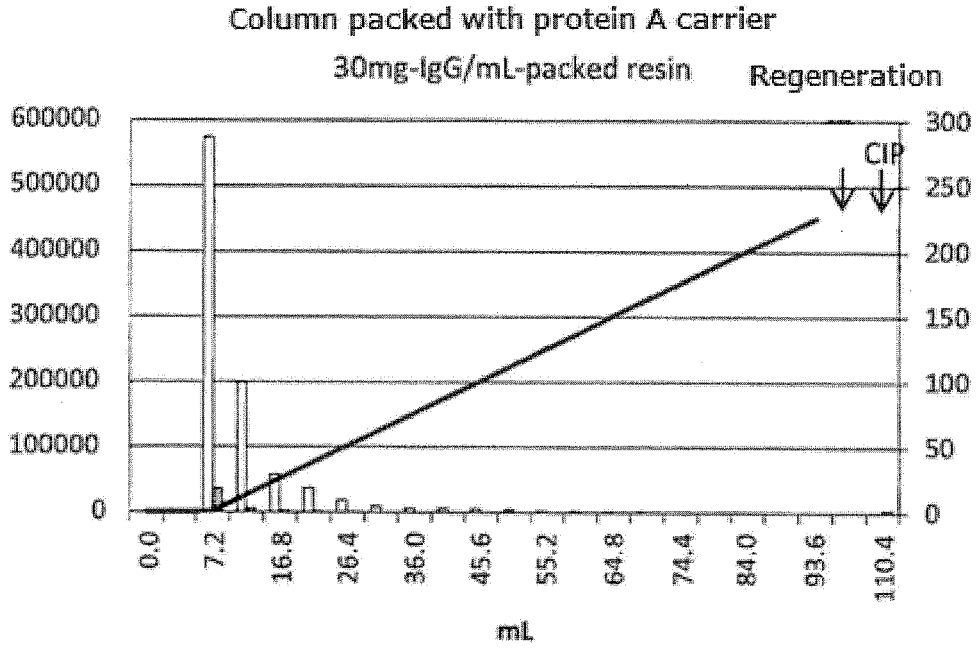
[Fig.7]


Column packed with cation exchange carrier D
Regeneration
CIP
%
mL
0
5
10
15
20
25
30
35
40
50
100
150
200
250
300
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
103.2
120.0

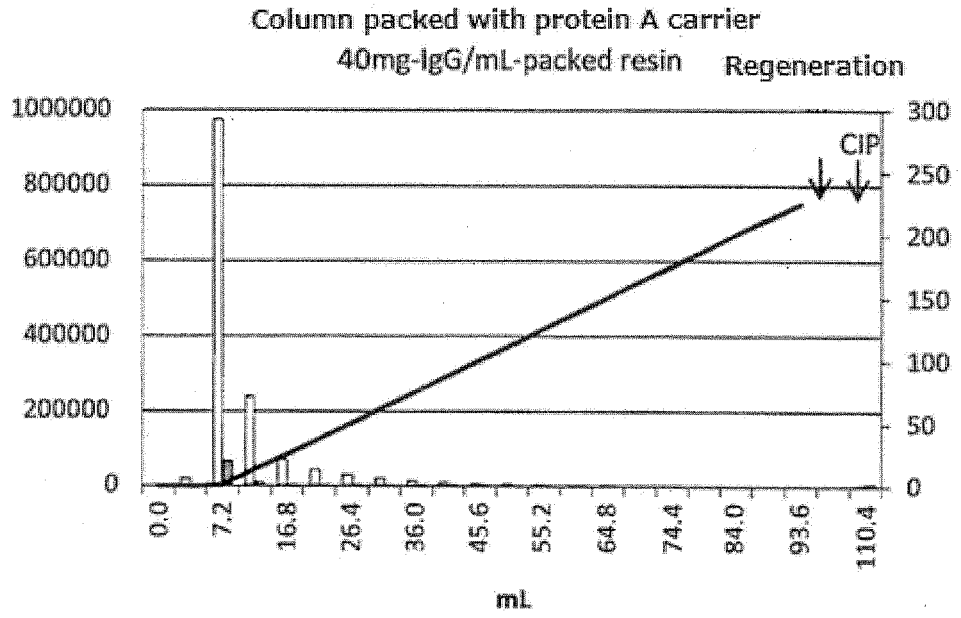
[Fig.8]


Column packed with protein A carrier
10mg-IgG/mL-packed resin
Regeneration
CIP
mL
0
40000
80000
120000
160000
200000
50
100
150
200
250
300
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4

[Fig.9]

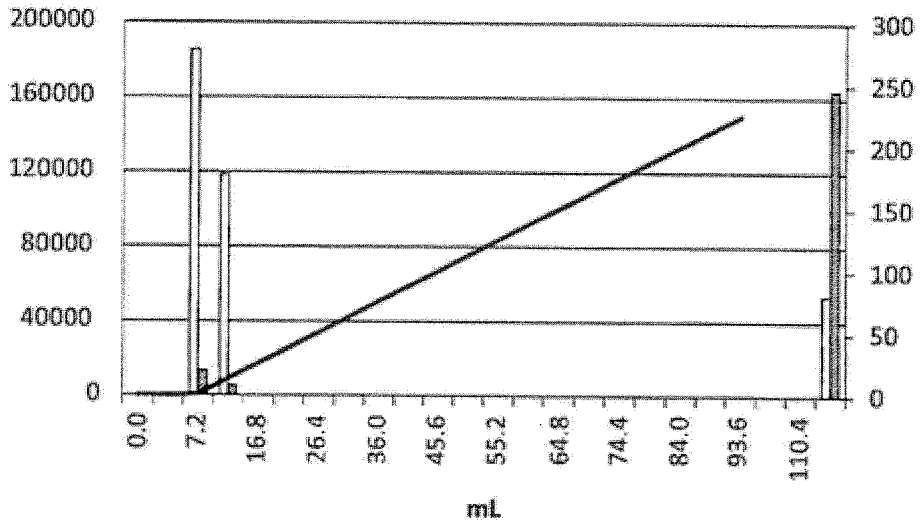

Column packed with protein A carrier
30mg-IgG/mL-packed resin
Regeneration
CIP
600000
500000
400000
300000
200000
100000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

[Fig.10]


Column packed with protein A carrier
40mg-IgG/mL-packed resin
Regeneration
CIP
1000000
800000
600000
400000
200000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

[Fig.11]

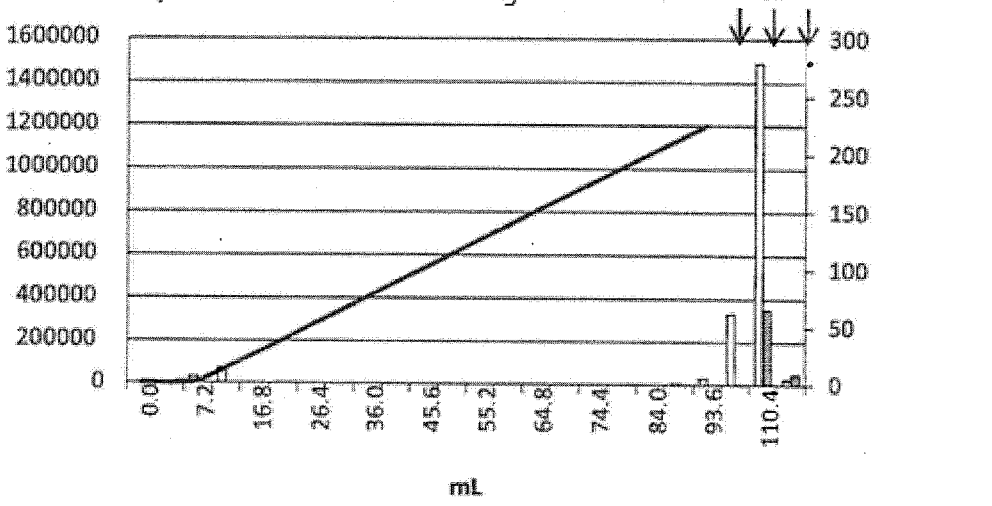
Column packed with protein A carrier + Column packed with cation exchange carrier (SP-Sepharose Fast Flow)



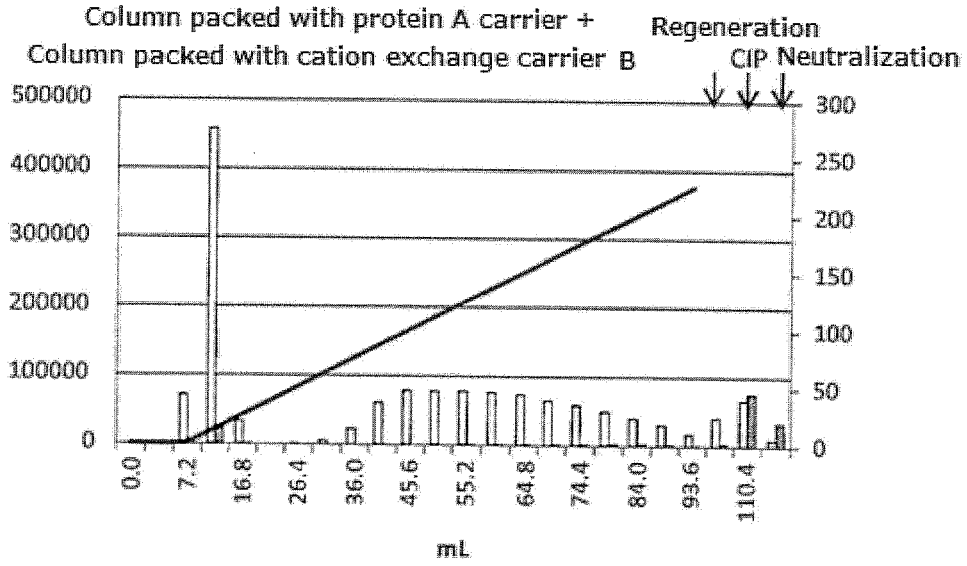
[Fig.12]

Column packed with protein A carrier + Column packed with cation exchange carrier A

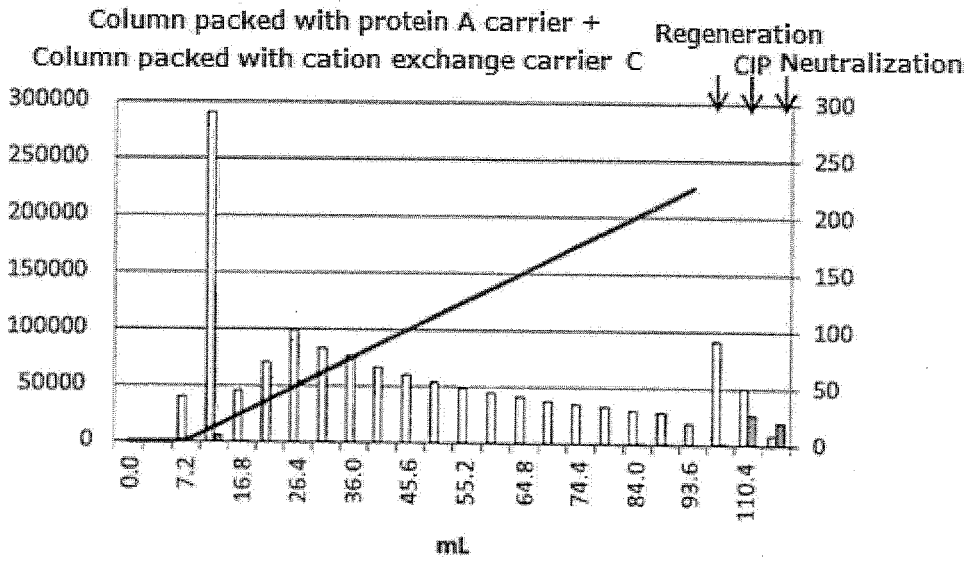
Regeneration CIP Neutralization



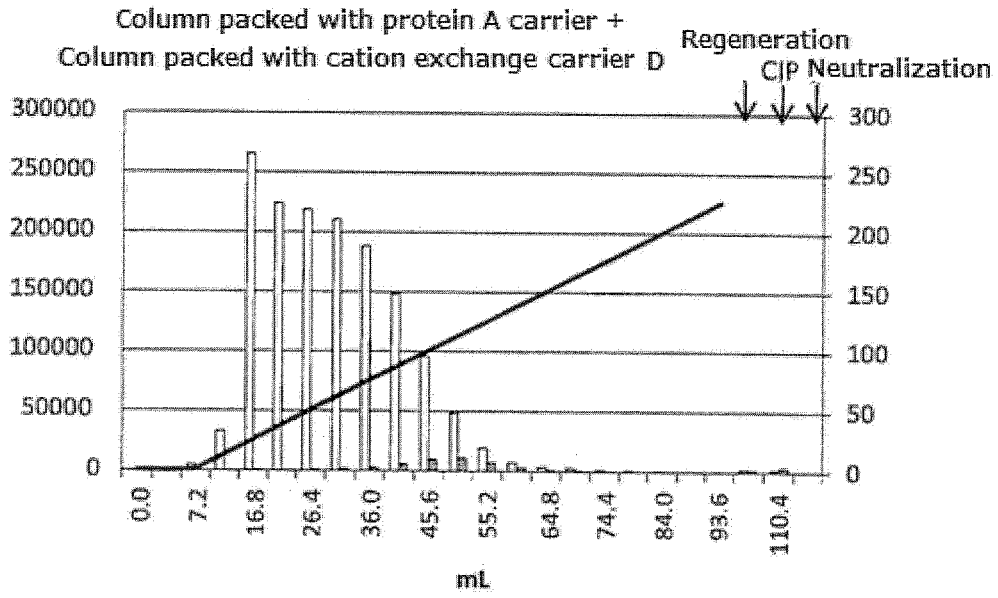
[Fig.13]


Column packed with protein A carrier +
Column packed with cation exchange carrier B
Regeneration
CIP Neutralization
500000
400000
300000
200000
100000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

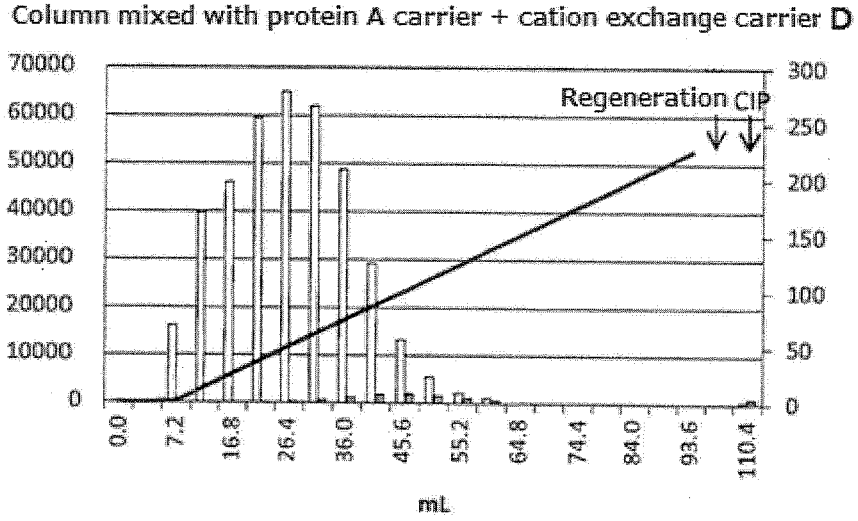
[Fig.14]


Column packed with protein A carrier +
Column packed with cation exchange carrier C
Regeneration
CIP Neutralization
300000
250000
200000
150000
100000
50000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

[Fig.15]


Column packed with protein A carrier +
Column packed with cation exchange carrier D
Regeneration
CIP Neutralization
300000
250000
200000
150000
100000
50000
0
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL

[Fig.16]


Column mixed with protein A carrier + cation exchange carrier D
70000
60000
50000
40000
30000
20000
10000
0
Regeneration
CIP
300
250
200
150
100
50
0
0.0
7.2
16.8
26.4
36.0
45.6
55.2
64.8
74.4
84.0
93.6
110.4
mL