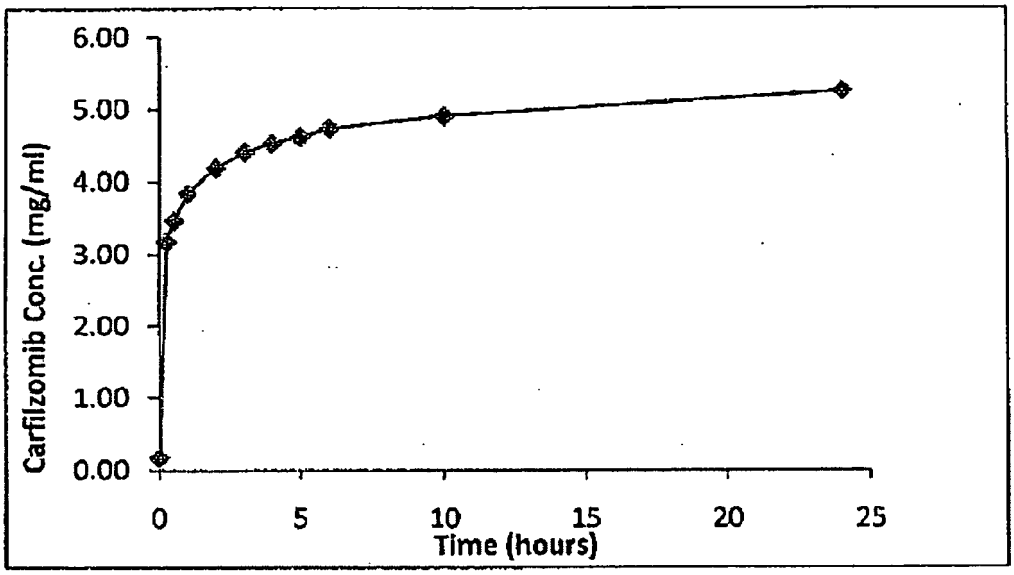

6.00
5.00
4.00
3.00
2.00
1.00
0.00
Carfilzomib Conc. (mg/ml)
0
5
10
15
20
25
Time (hours)

FIG. 1

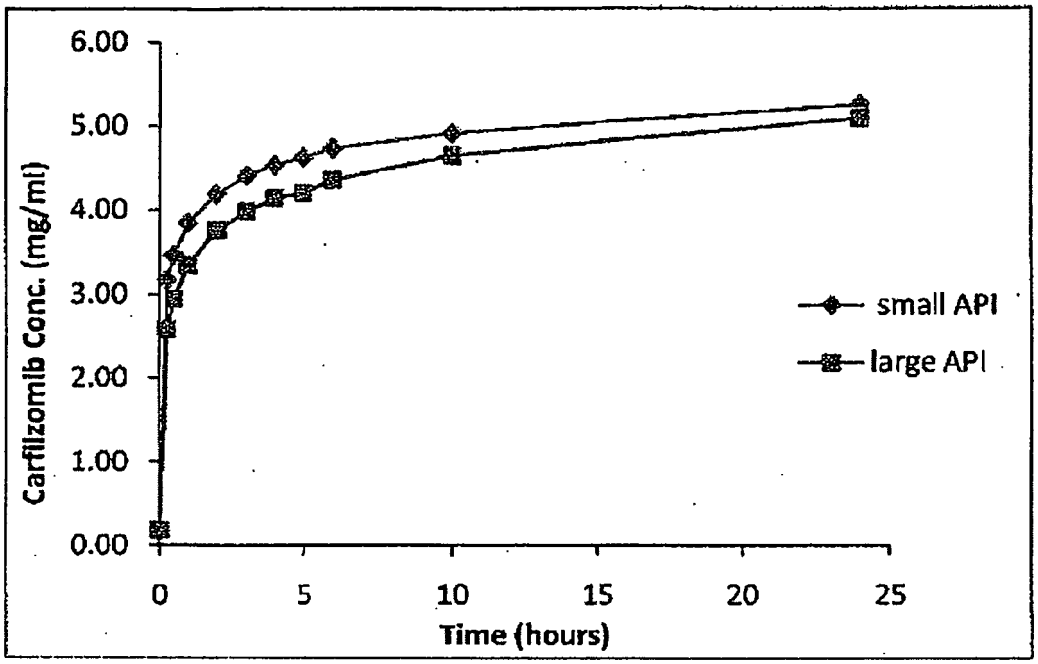

6.00
5.00
4.00
3.00
2.00
1.00
0.00
Carfilzomib Conc. (mg/ml)
0
5
10
15
20
25
Time (hours)
small API
large API

FIG. 2

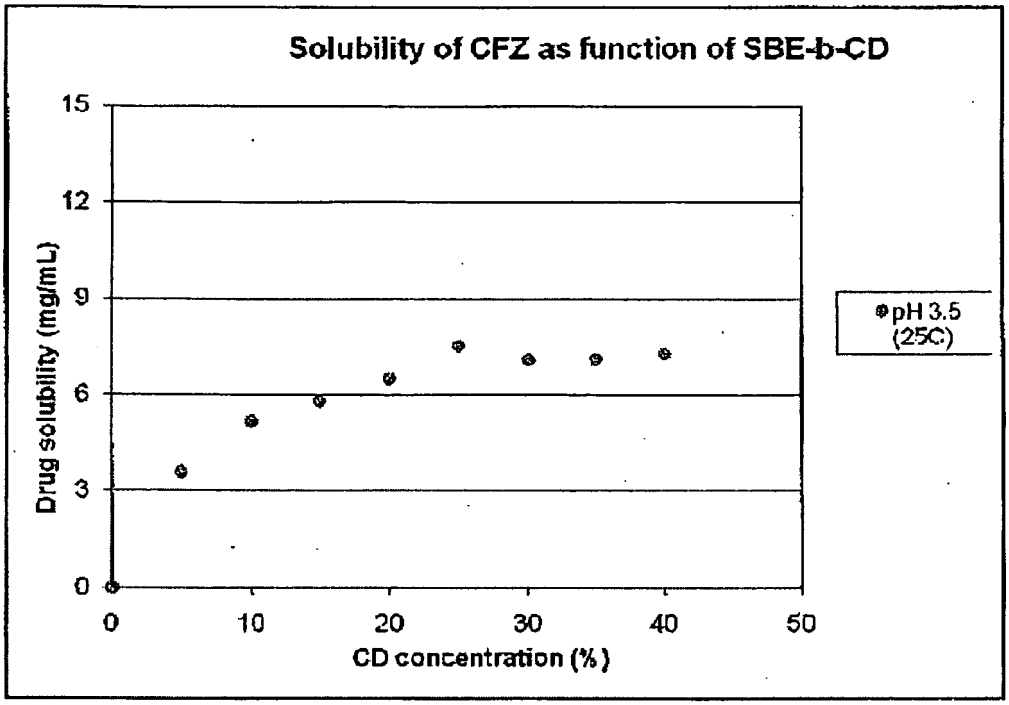

Solubility of CFZ as function of SBE-b-CD
Drug solubility (mg/mL)
15
12
9
6
3
0
0
10
20
30
40
50
CD concentration (%)
pH 3.5 (25C)

FIG. 3

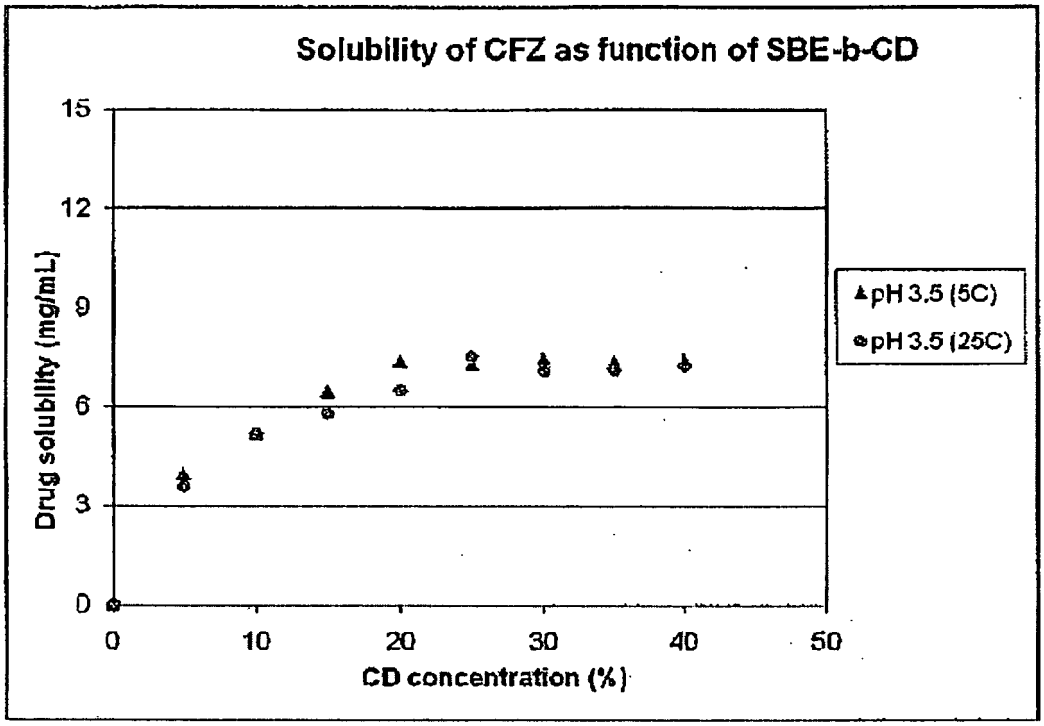

Solubility of CFZ as function of SBE-b-CD
Drug solubility (mg/mL)
15
12
9
6
3
0
0
10
20
30
40
50
CD concentration (%)
pH 3.5 (5C)
pH 3.5 (25C)

FIG. 4

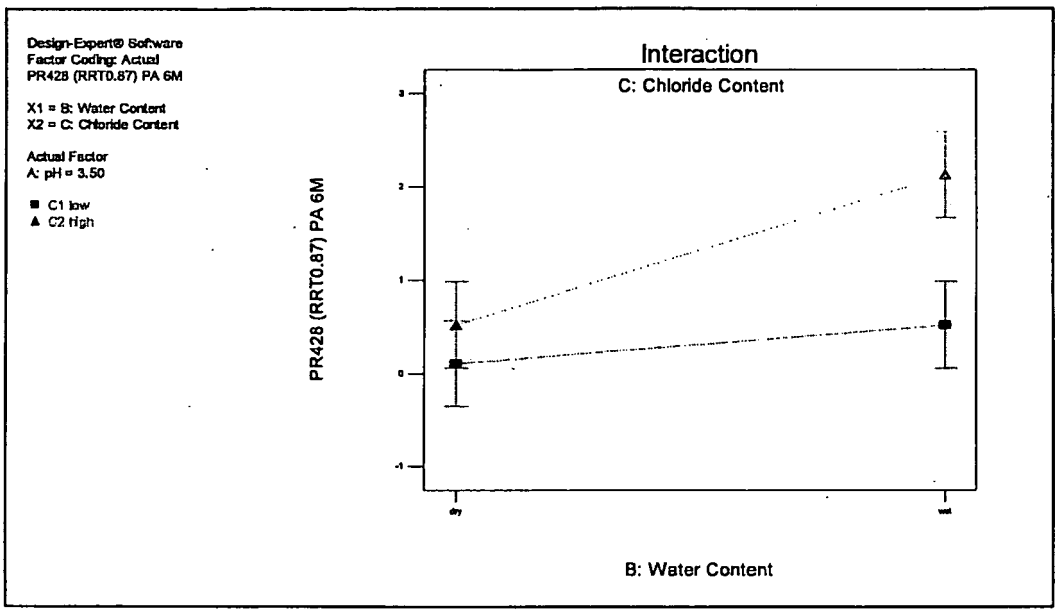

Design-Expert® Software
Factor Coding: Actual
PR428 (RRT0.87) PA 6M
X1 = B: Water Content
X2 = C: Chloride Content
Actual Factor
A: pH = 3.50
C1 low
C2 High
Interaction
C: Chloride Content
PR428 (RRT0.87) PA 6M
B: Water Content

FIG. 5

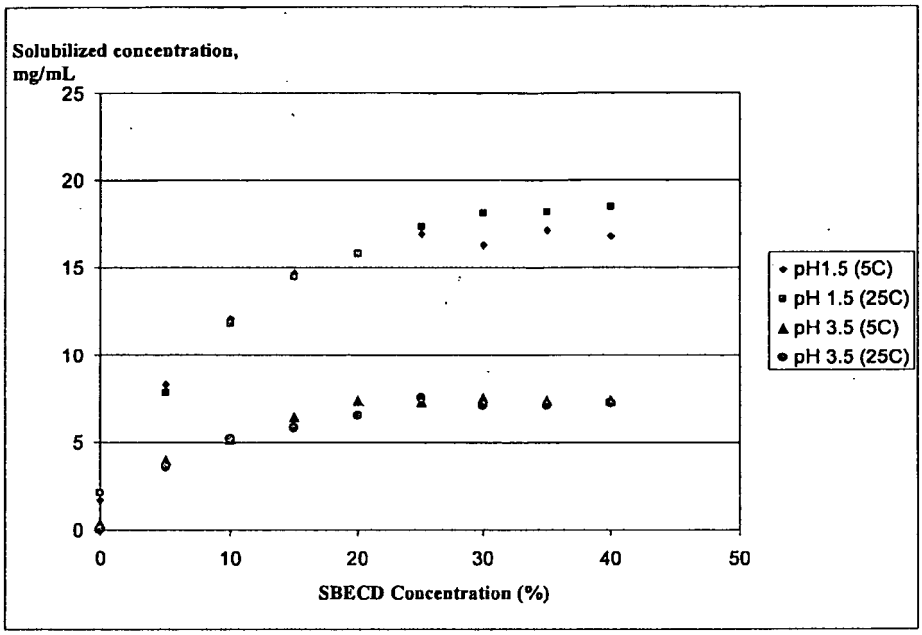

Solubilized concentration, mg/mL
25
20
15
10
5
0
0
10
20
30
40
50
SBECD Concentration (%)
pH1.5 (5C)
pH 1.5 (25C)
pH 3.5 (5C)
pH 3.5 (25C)

FIG. 6

FIG. 7

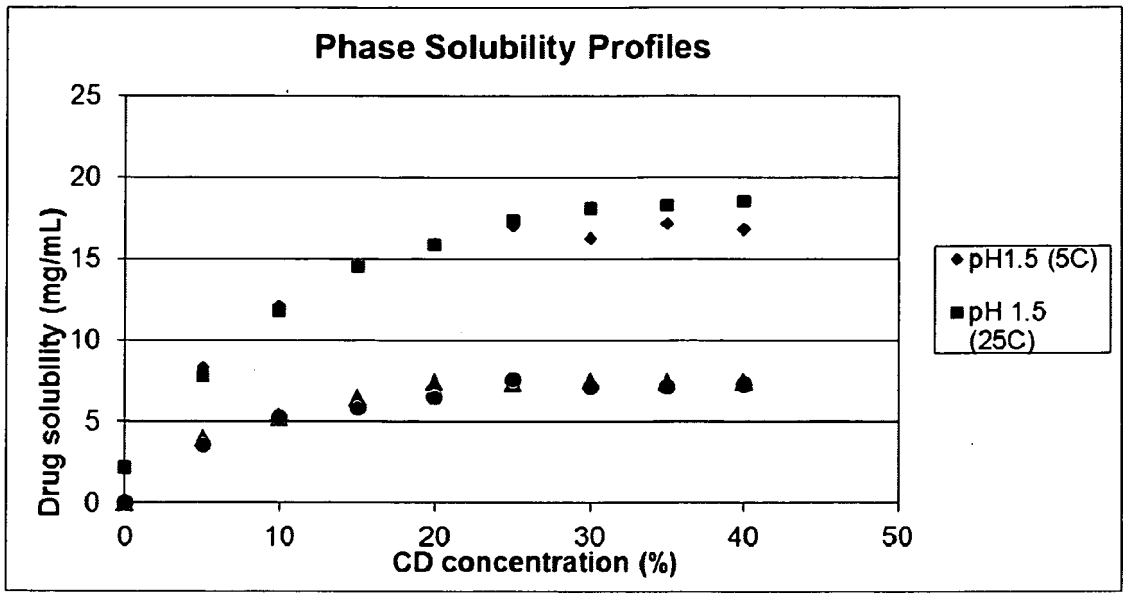

Phase Solubility Profiles
Drug solubility (mg/mL)
25
20
15
10
5
0
0
10
20
30
40
50
CD concentration (%)
pH1.5 (5C)
pH 1.5 (25C)

FIG. 8

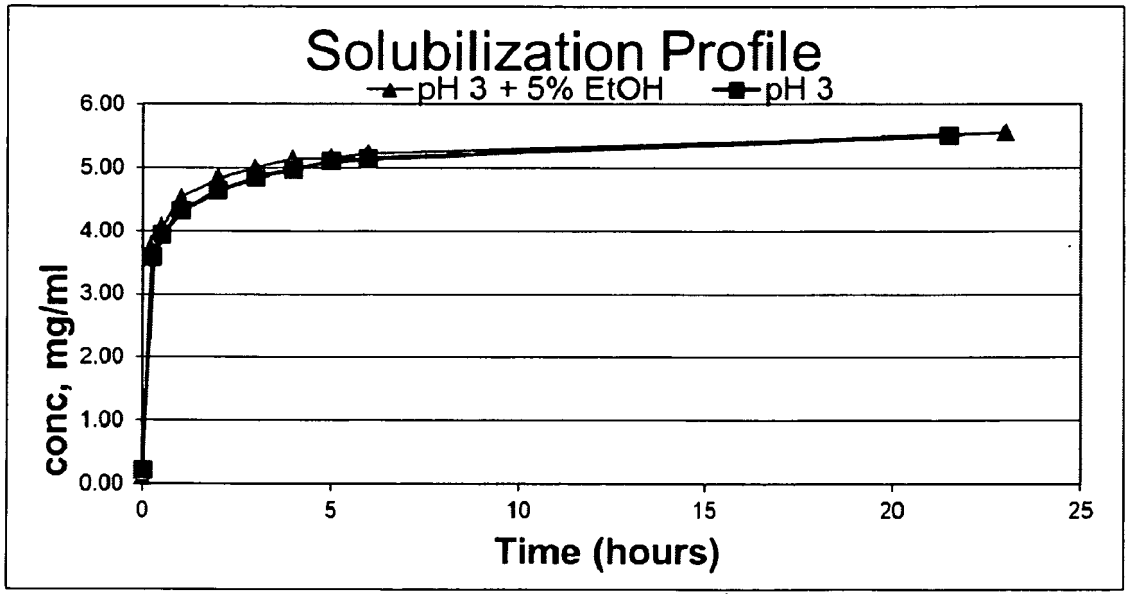
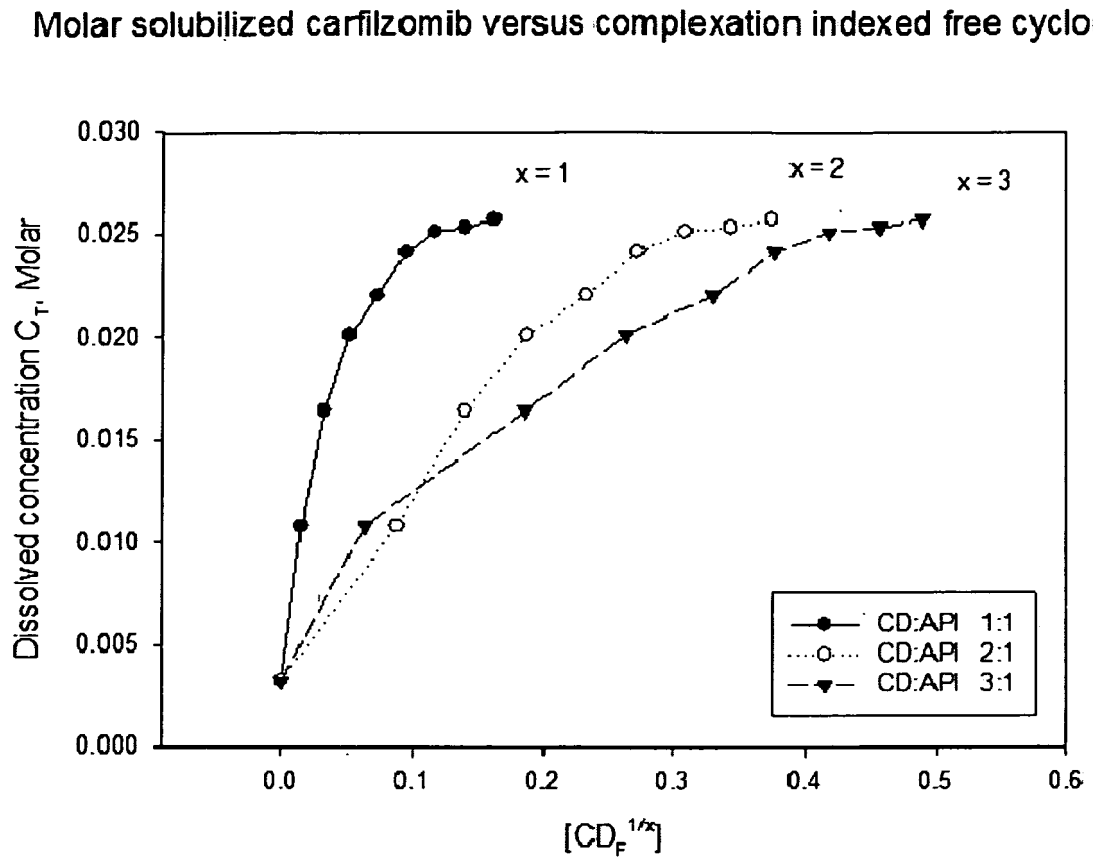

Solubilization Profile
pH 3 + 5% EtOH
pH 3
conc, mg/ml
6.00
5.00
4.00
3.00
2.00
1.00
0.00
0
5
10
15
20
25
Time (hours)

FIG. 9


Molar solubilized carfilzomib versus complexation indexed free cyclodextrin
Dissolved concentration C_T, Molar
0.030
0.025
0.020
0.015
0.010
0.005
0.000
x = 1
x = 2
x = 3
CD:API 1:1
CD:API 2:1
CD:API 3:1
0.0
0.1
0.2
0.3
0.4
0.5
0.6
$[CD_F^{1/x}]$