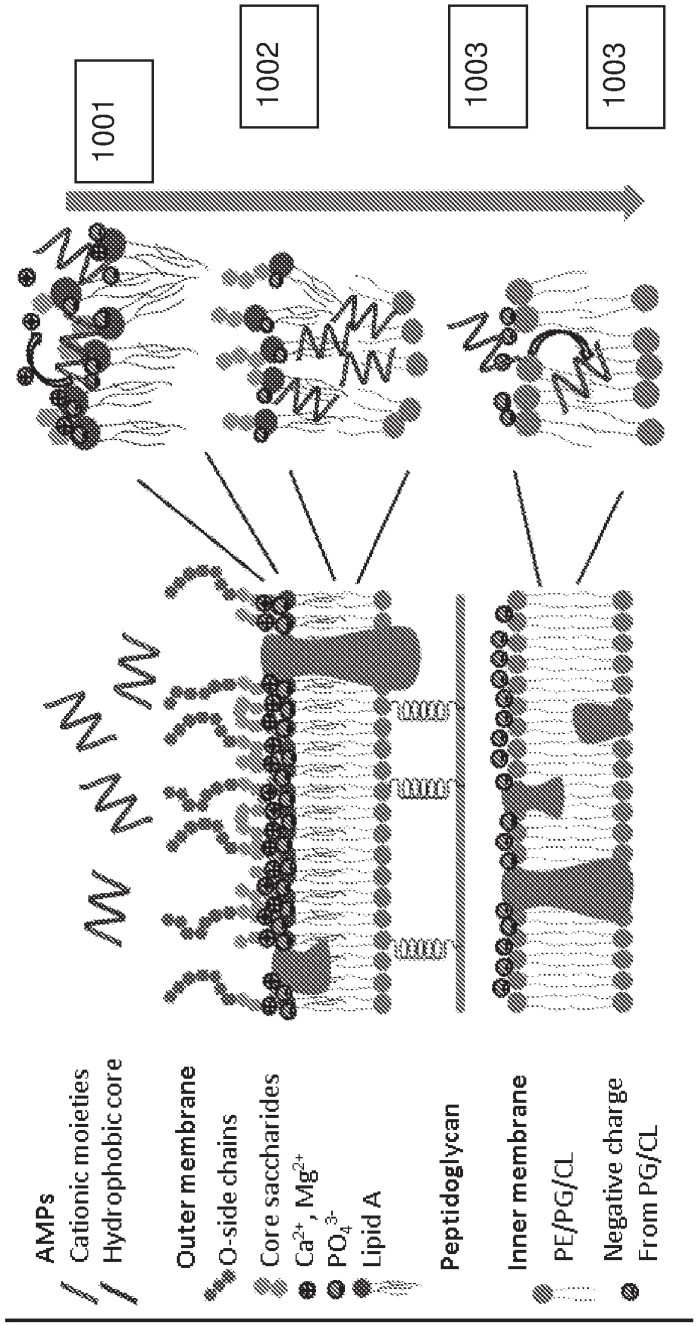
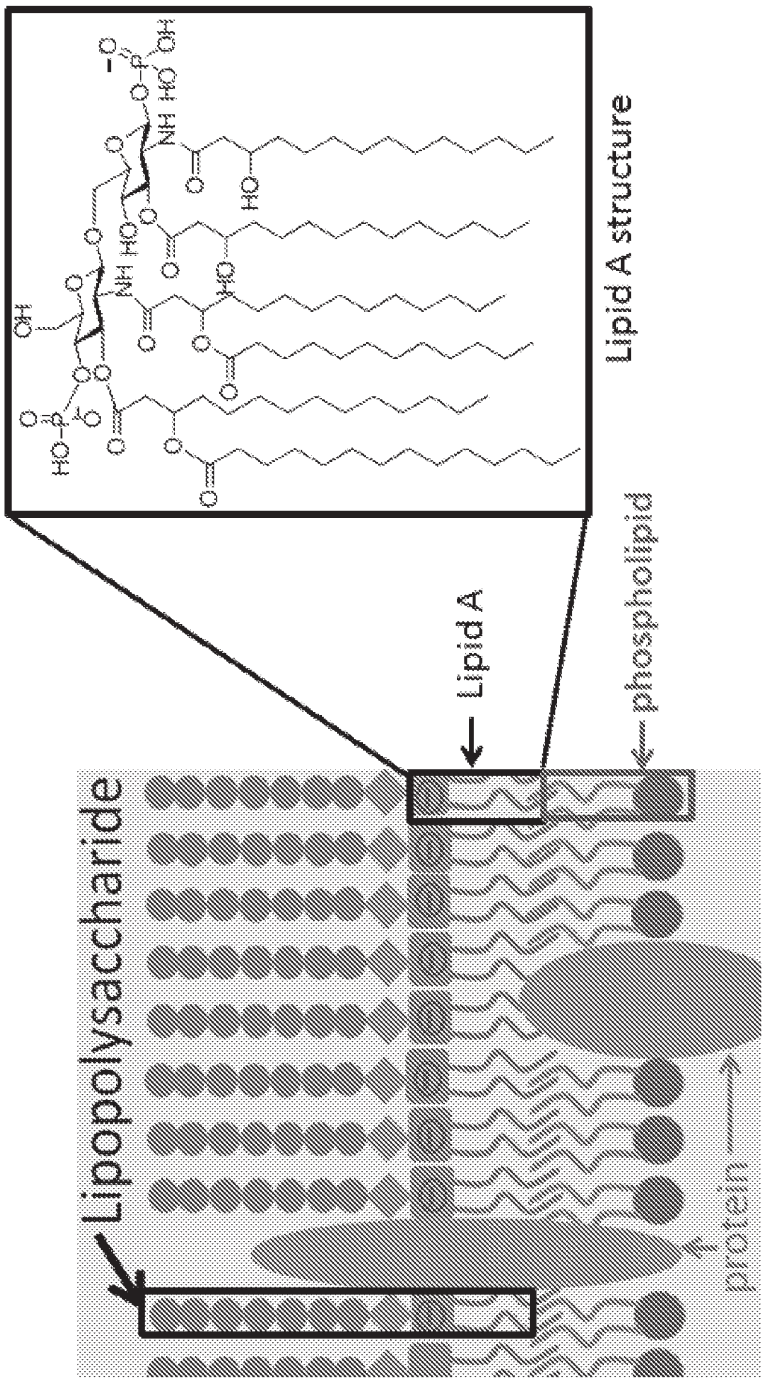
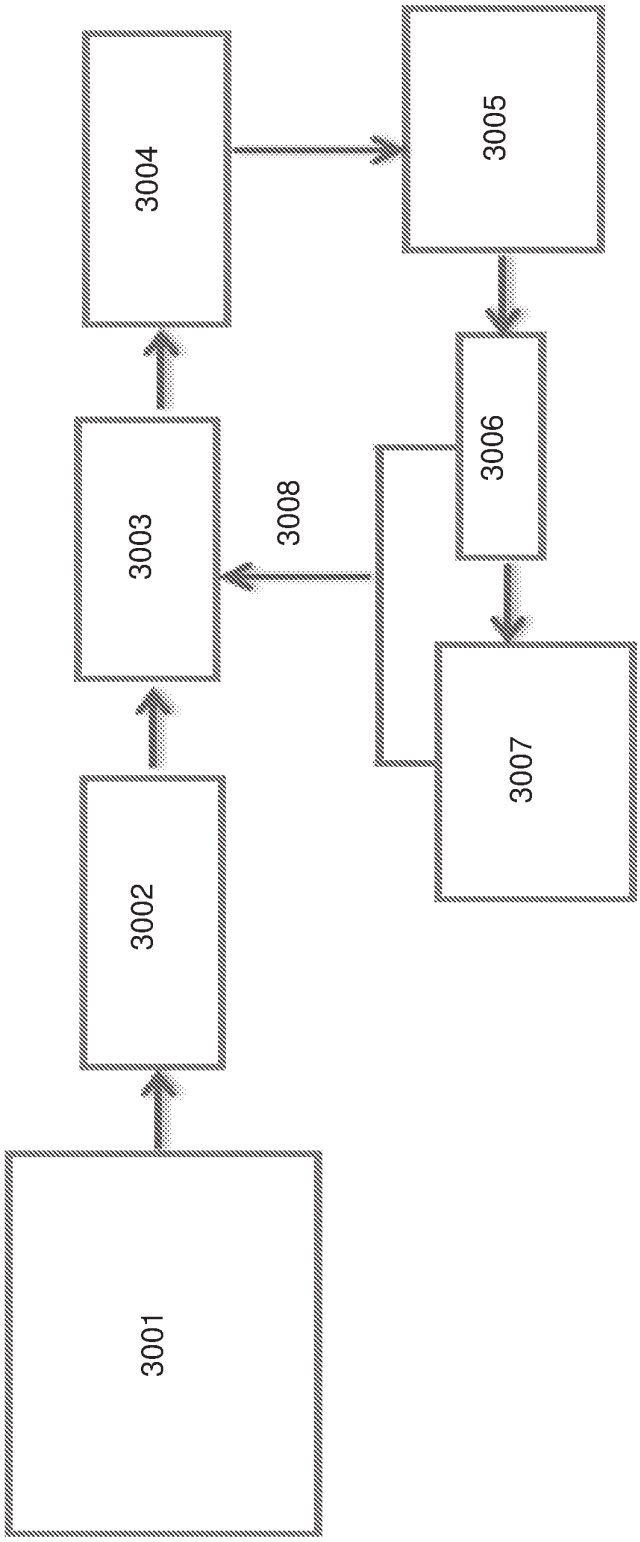
[Fig. 1]


1001
1002
1003
1003
AMPs
Cationic moieties
Hydrophobic core
Outer membrane
O-side chains
Core saccharides
Ca^{2+}, Mg^{2+}
PO_4^{3-}
Lipid A
Peptidoglycan
Inner membrane
PE/PG/CL
Negative charge
From PG/CL

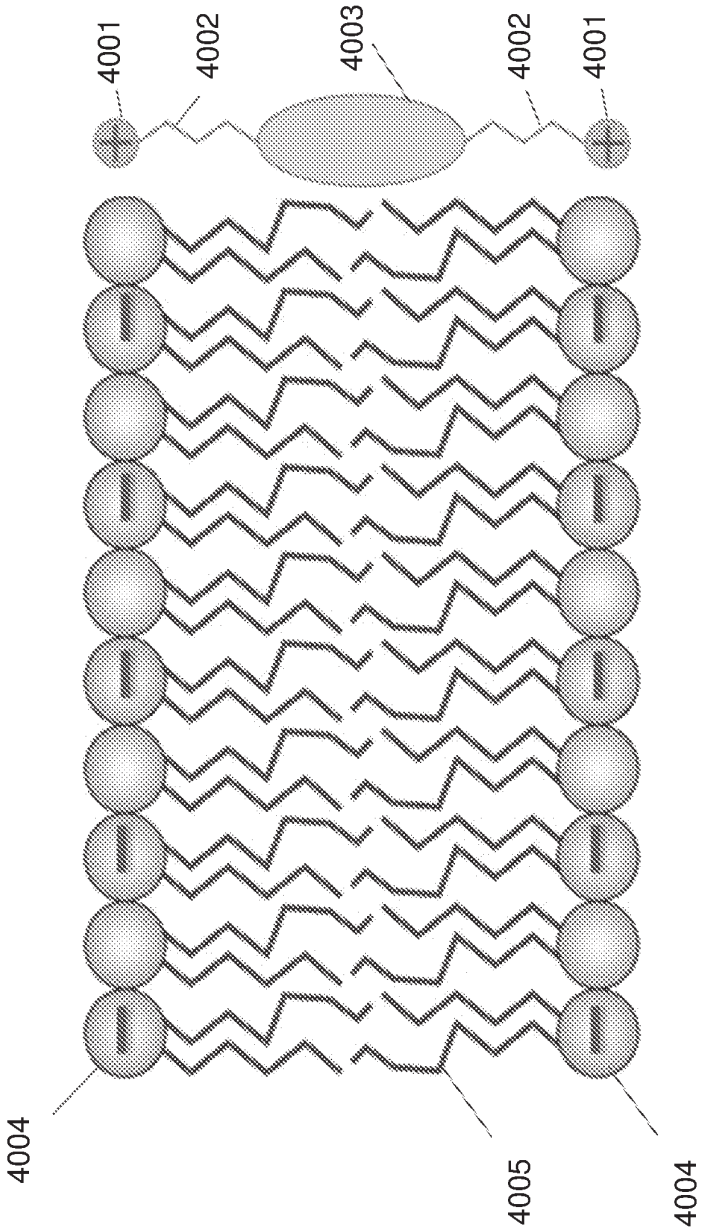
[Fig. 2]


Lipopolysaccharide
Lipid A
phospholipid
protein
Lipid A structure

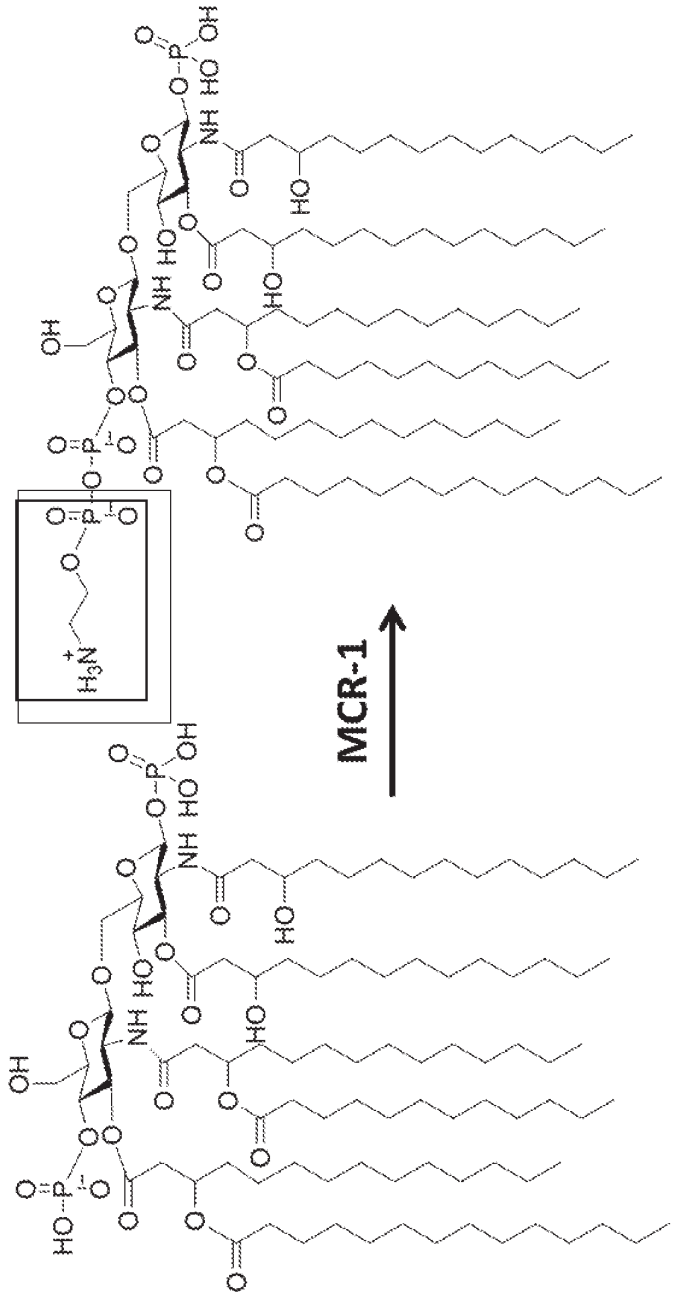
[Fig. 3]



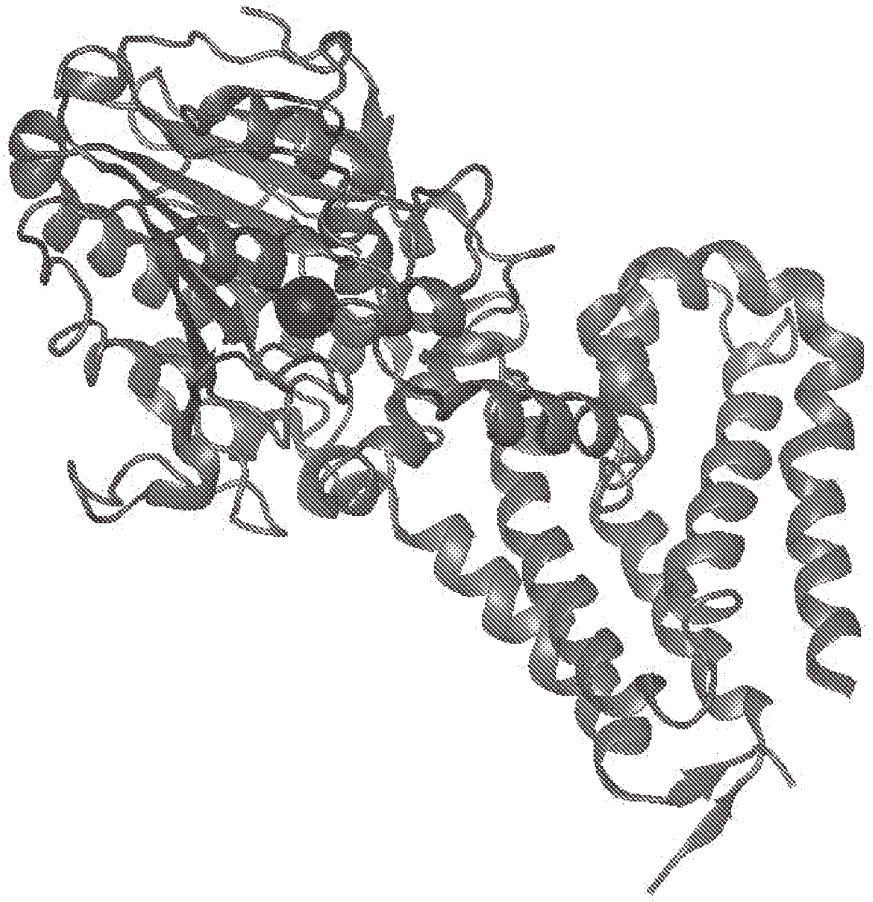
[Fig. 4]



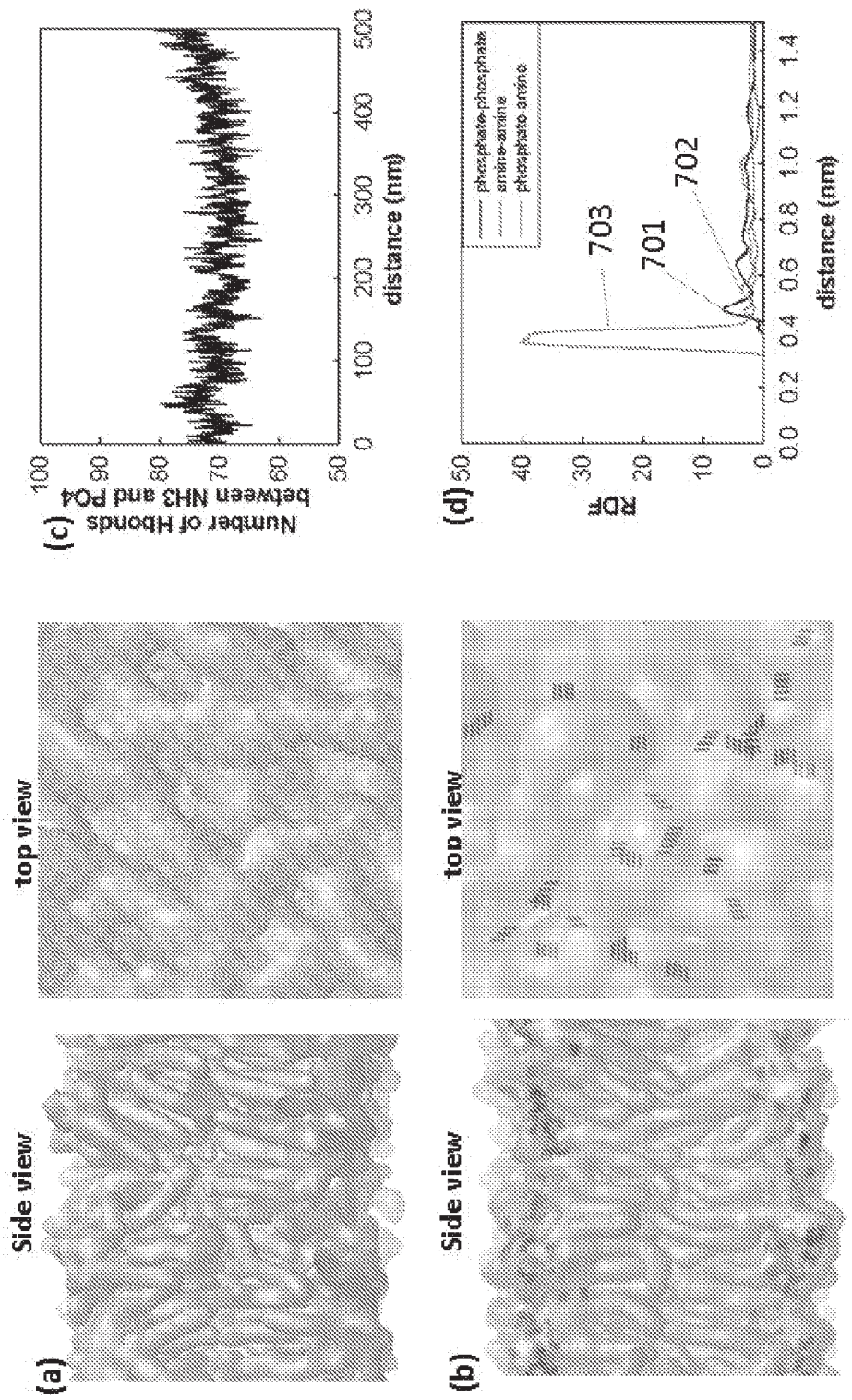
[Fig. 5]



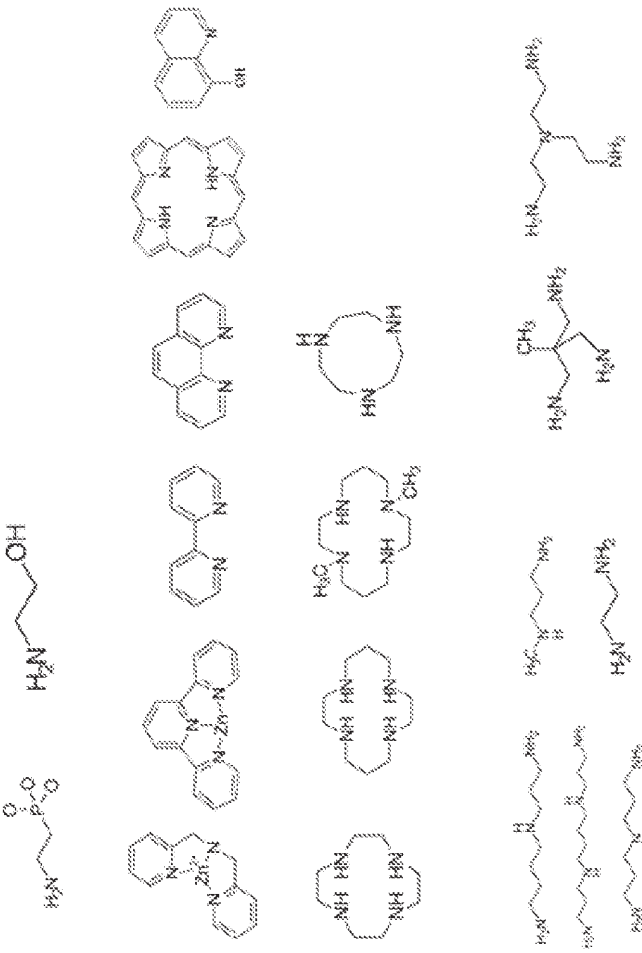
[Fig. 6]



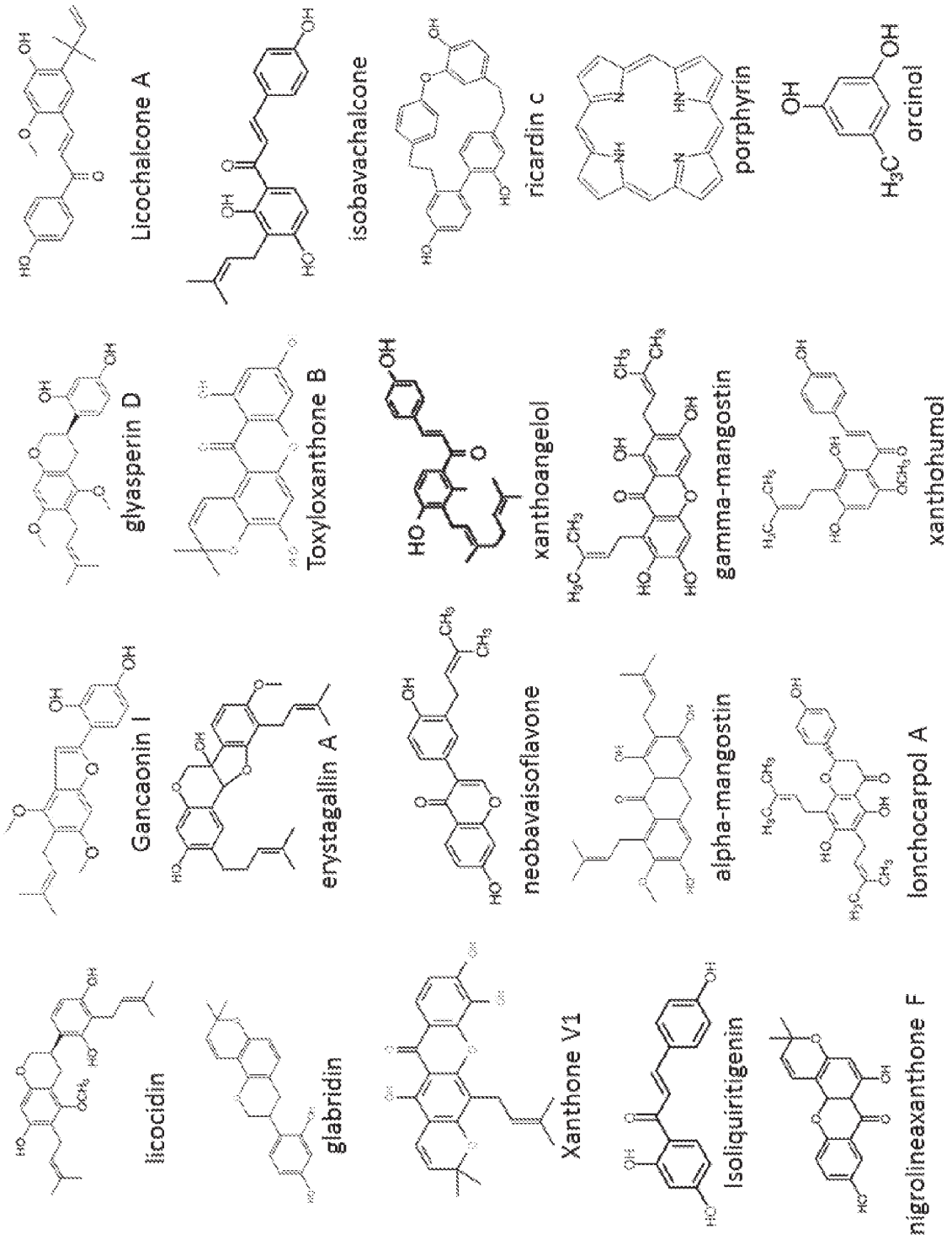
[Fig. 7]


(a)
Side view
top view
(b)
Side view
top view
(c)
Number of Hbonds between NH3 and PO4
distance (nm)
(d)
RDF
distance (nm)
phosphate-phosphate
amine-amine
phosphate-amine
703
701
702

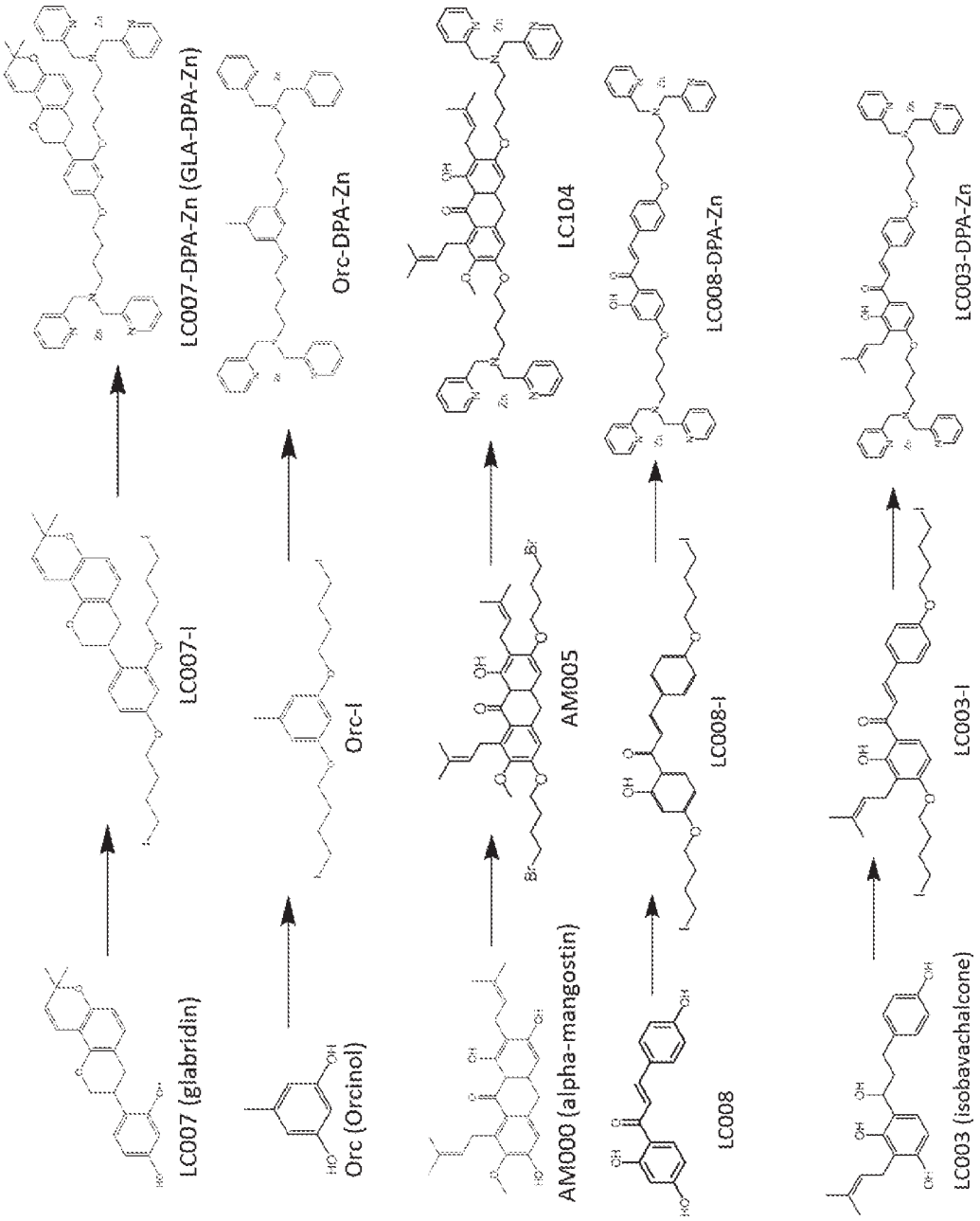
[Fig. 8]


(1) PE and analogues
(2) Zinc chelating groups
(3) Cyclic polyamines
(4) Amine and linear or branched polyamines
(5) Guanidine and poly-guanidine derivatives
(6) Basic amine acid and the derivatives
Arg, (Arg)n, Lys, (Lys)n, poly epsilon-lysine

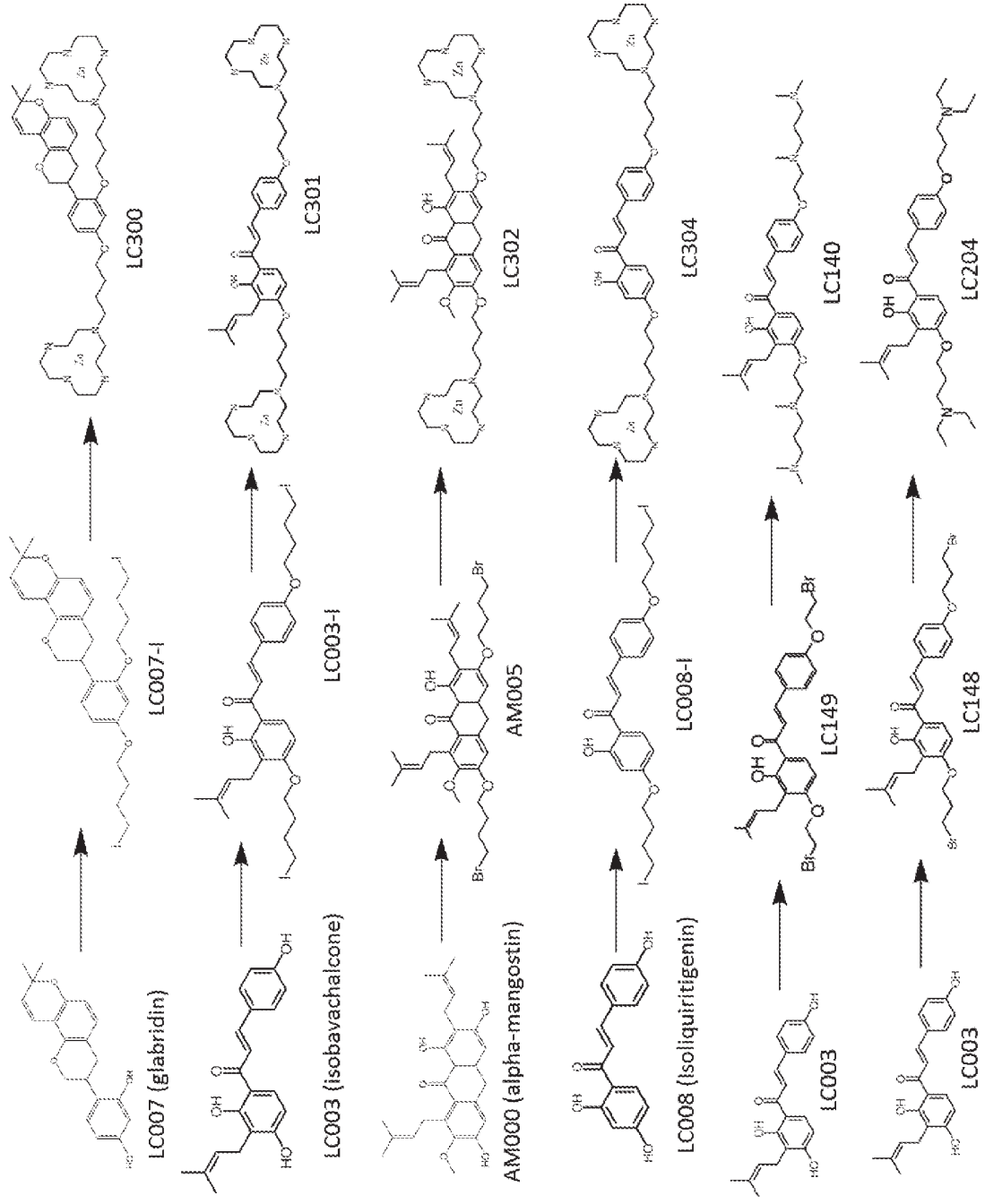
[Fig. 9]


licocidin
Gancaonin I
glyasperin D
Licochalcone A
glabridin
erystagallin A
Toxyloxanthone B
isobavachalcone
Xanthone V1
neobavaisoflavone
xanthoangelol
ricardin c
Isoliquiritigenin
alpha-mangostin
gamma-mangostin
porphyrin
nigrolineaxanthone F
lonchocarpol A
xanthohumol
orcinol

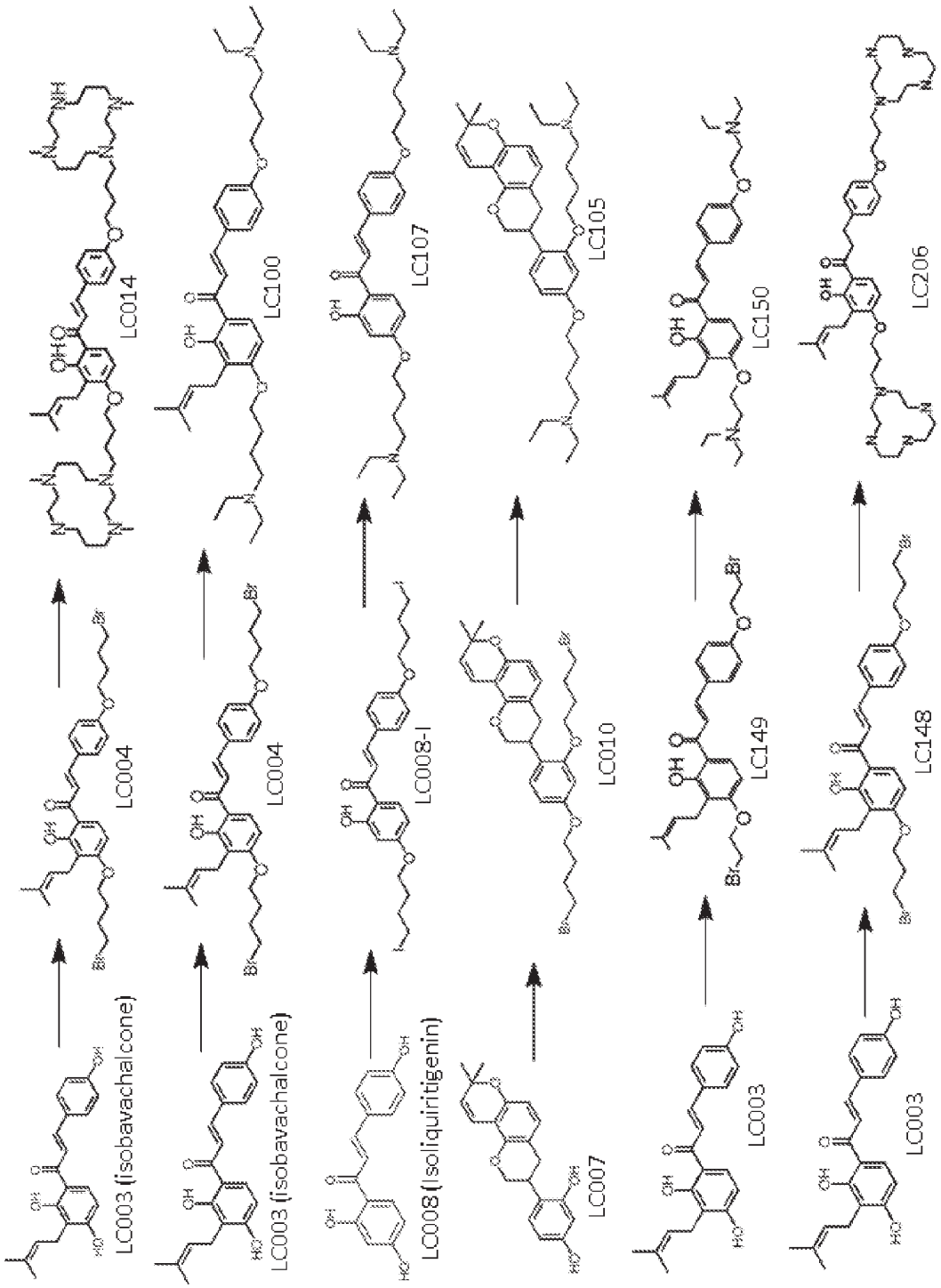
[Fig. 10]


LC007 (glabridin)
LC007-I
LC007-DPA-Zn (GLA-DPA-Zn)
Orc (Orcinol)
Orc-I
Orc-DPA-Zn
AM000 (alpha-mangostin)
AM005
LC104
LC008
LC008-I
LC008-DPA-Zn
LC003 (isobavachalcone)
LC003-I
LC003-DPA-Zn

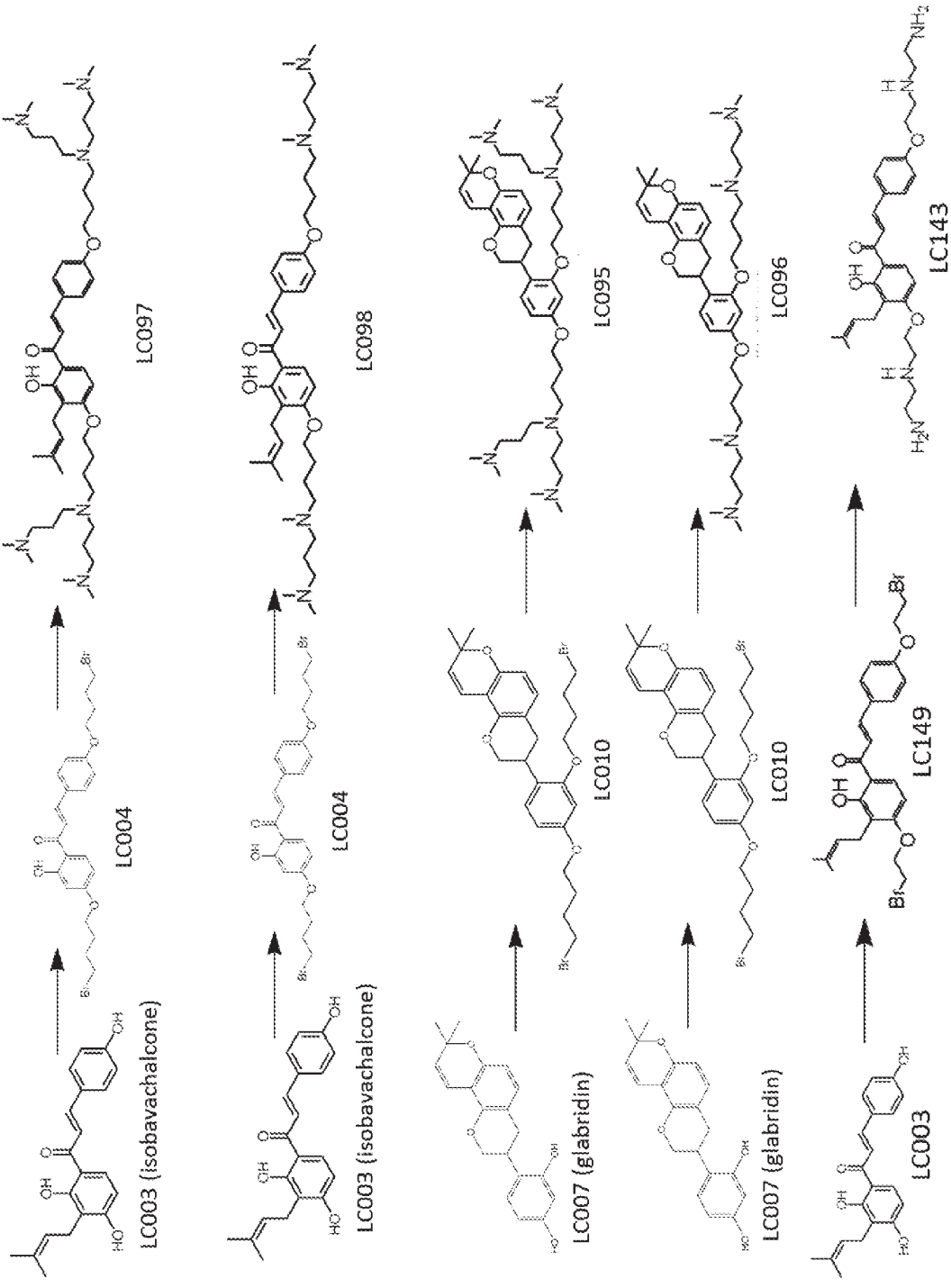
[Fig. 11]


LC007 (glabridin)
LC007-I
LC300
LC003 (isobavachalcone)
LC003-I
LC301
AM000 (alpha-mangostin)
AM005
LC302
LC008 (isoliquiritigenin)
LC008-I
LC304
LC003
LC149
LC140
LC003
LC148
LC204

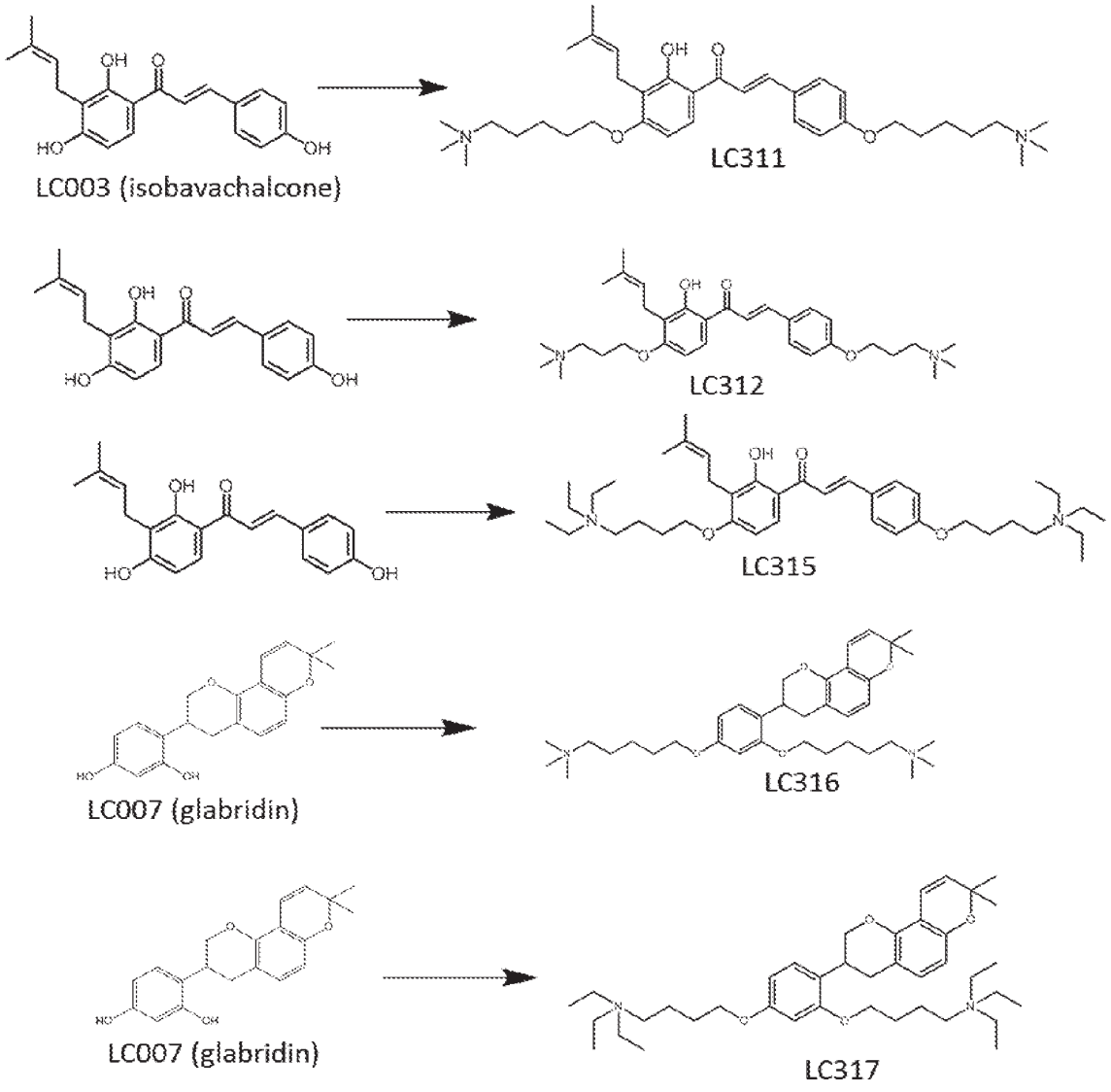
[Fig. 11 cont.]


LC003 (isobavachalcone)
LC004
LC014
LC003 (isobavachalcone)
LC004
LC100
LC008 (Isoliquiritigenin)
LC008-I
LC107
LC007
LC010
LC105
LC003
LC149
LC150
LC003
LC148
LC206

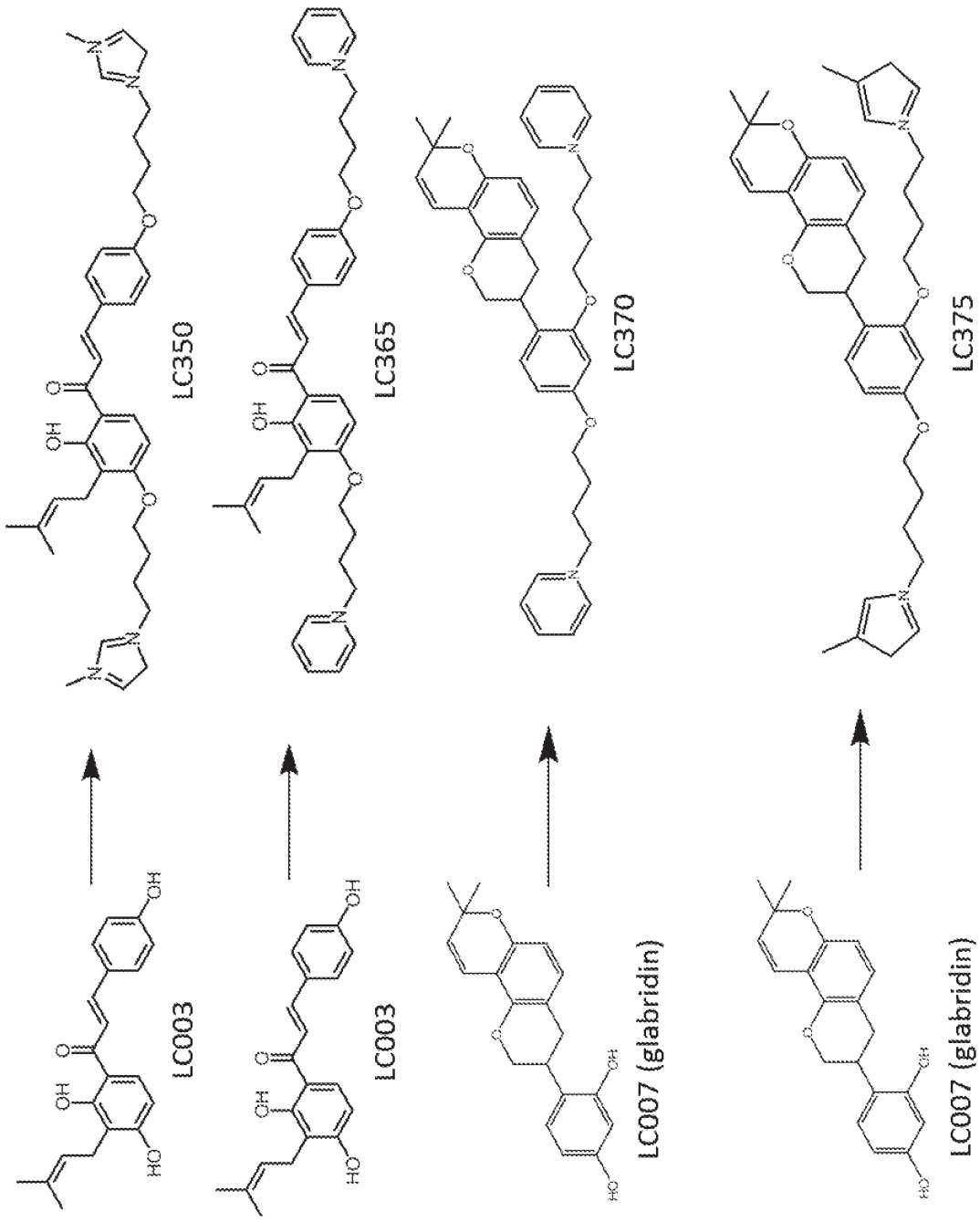
[Fig. 11 cont.]


LC003 (isobavachalcone)
LC004
LC097
LC003 (isobavachalcone)
LC004
LC098
LC007 (glabridin)
LC010
LC095
LC007 (glabridin)
LC010
LC096
LC003
LC149
LC143

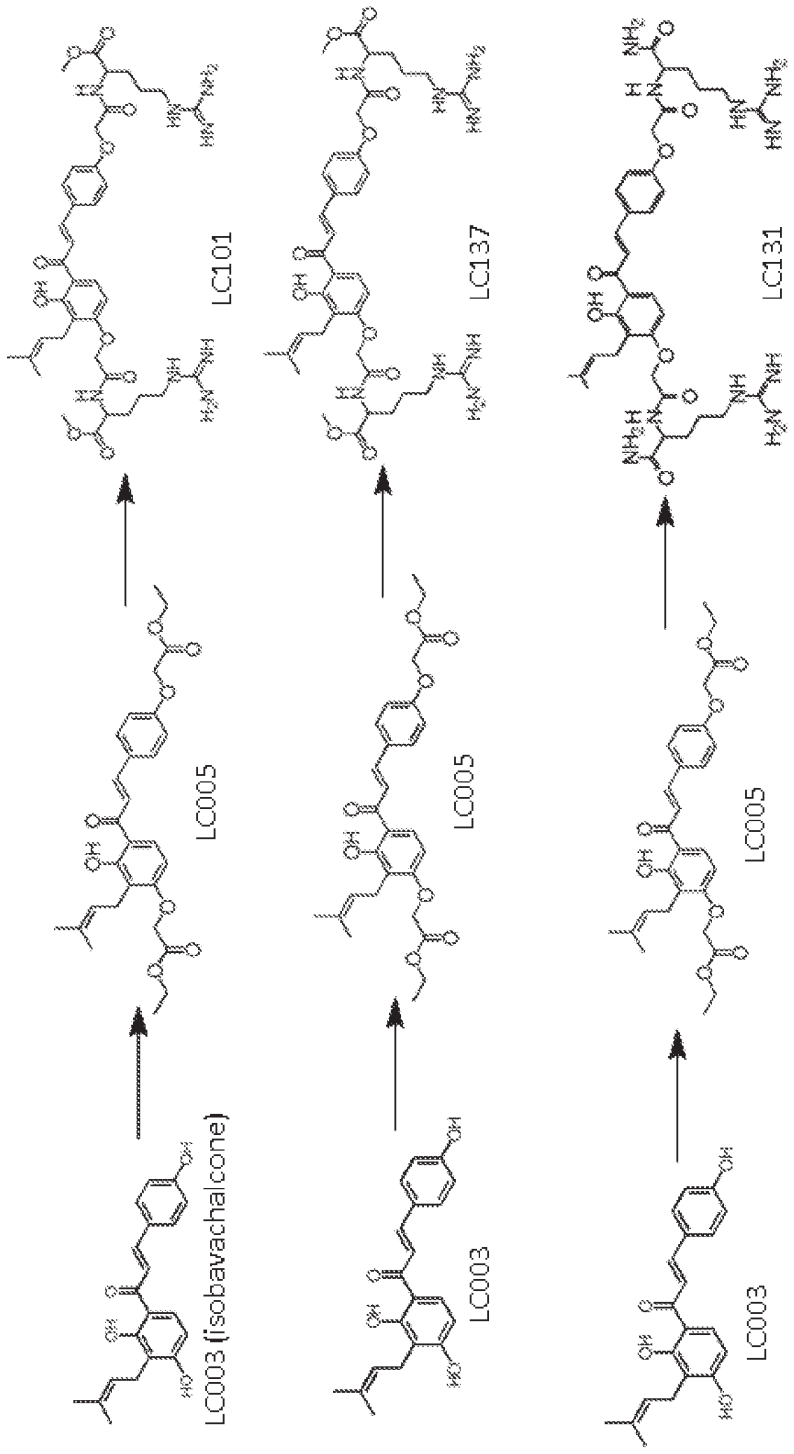
[Fig. 11 cont.]


LC003 (isobavachalcone)
LC311
LC312
LC315
LC007 (glabridin)
LC316
LC007 (glabridin)
LC317

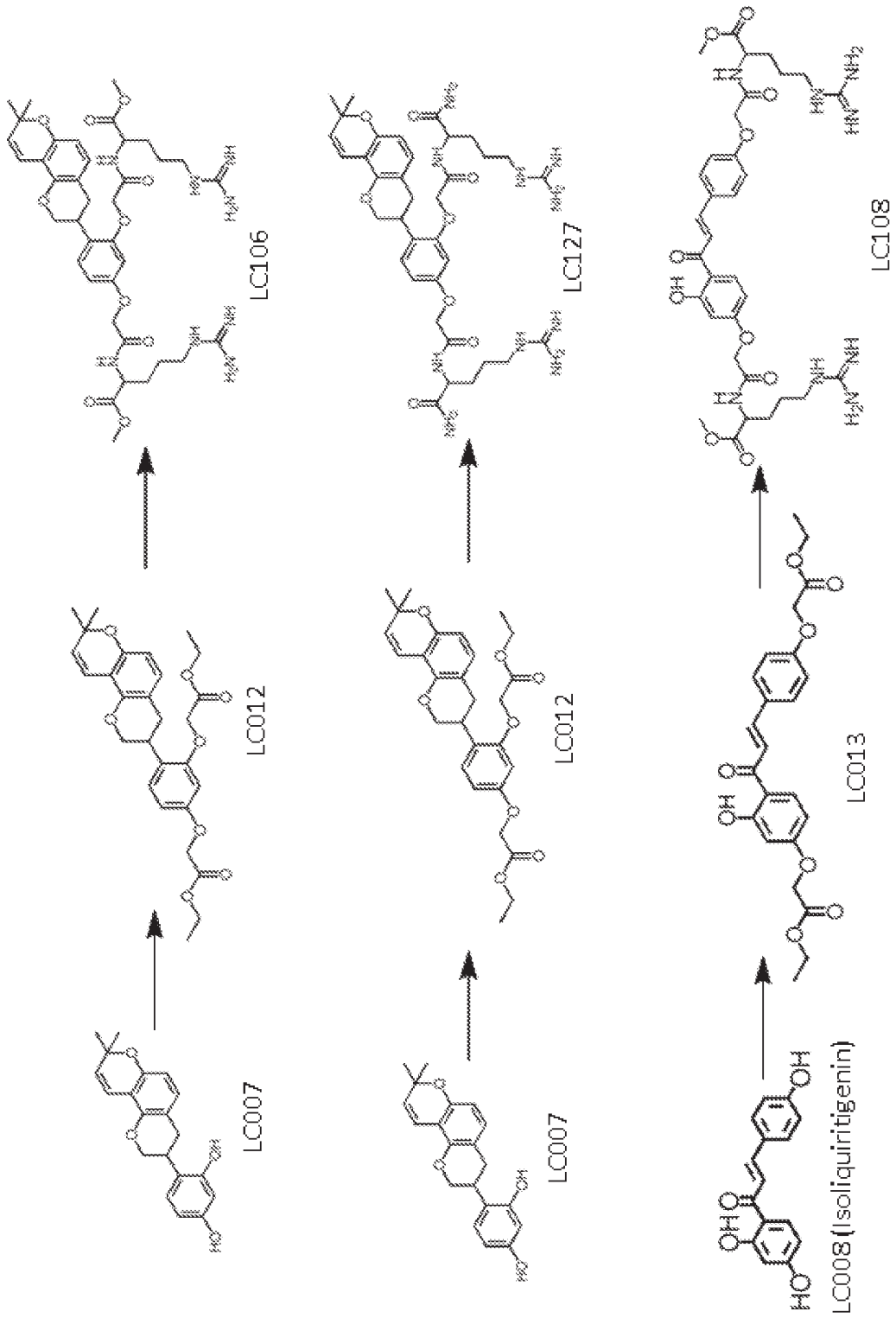
[Fig. 11 cont.]


LC003
LC350
LC003
LC365
LC007 (glabridin)
LC370
LC007 (glabridin)
LC375

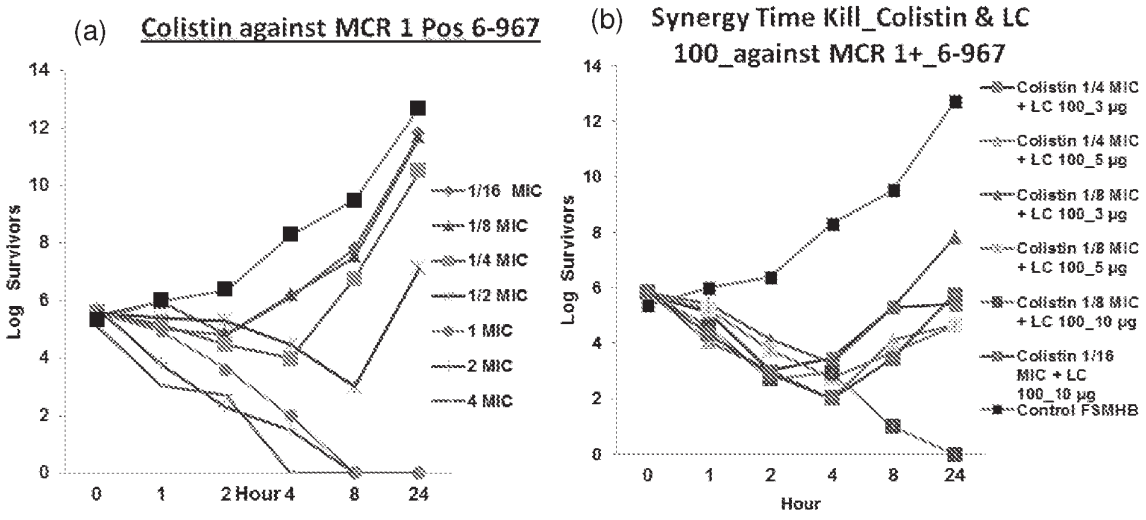
[Fig. 12]


LC003 (isobavachalcone)
LC005
LC101
LC003
LC005
LC137
LC003
LC005
LC131

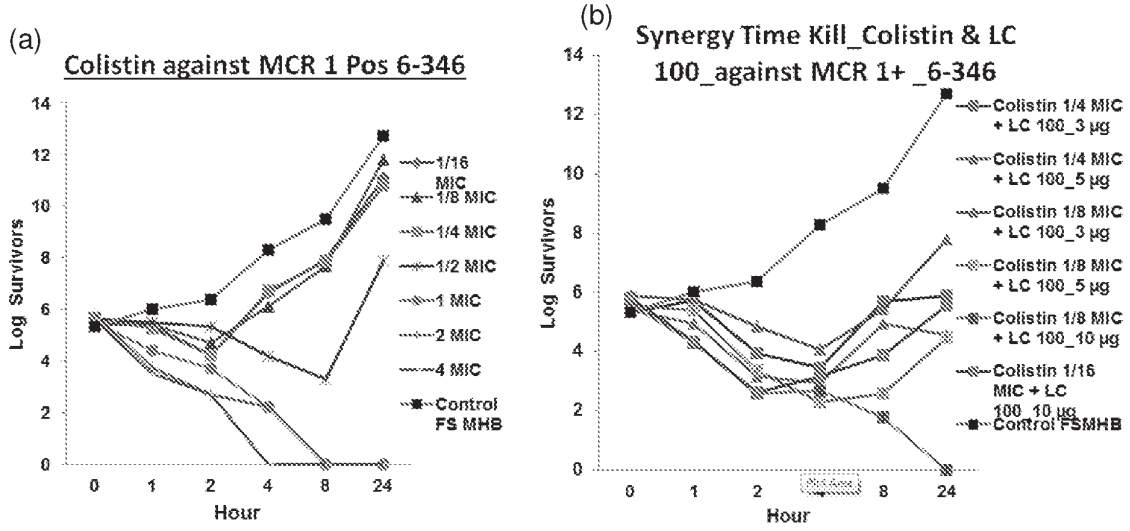
[Fig. 12 cont.]


LC007
LC012
LC106
LC007
LC012
LC127
LC008 (Isoliquiritigenin)
LC013
LC108

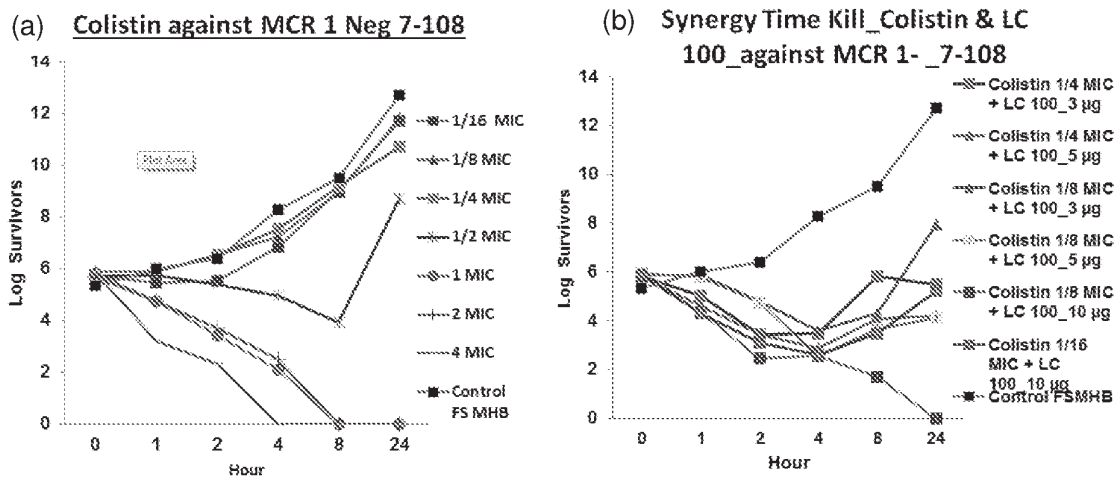
[Fig. 13]


(a)
Colistin against MCR 1 Pos 6-967
Log Survivors
Hour
1/16 MIC
1/8 MIC
1/4 MIC
1/2 MIC
1 MIC
2 MIC
4 MIC
(b)
Synergy Time Kill_Colistin & LC 100_against MCR 1+_6-967
Colistin 1/4 MIC + LC 100_3 µg
Colistin 1/4 MIC + LC 100_5 µg
Colistin 1/8 MIC + LC 100_3 µg
Colistin 1/8 MIC + LC 100_5 µg
Colistin 1/8 MIC + LC 100_10 µg
Colistin 1/16 MIC + LC 100_10 µg
Control FSMHB

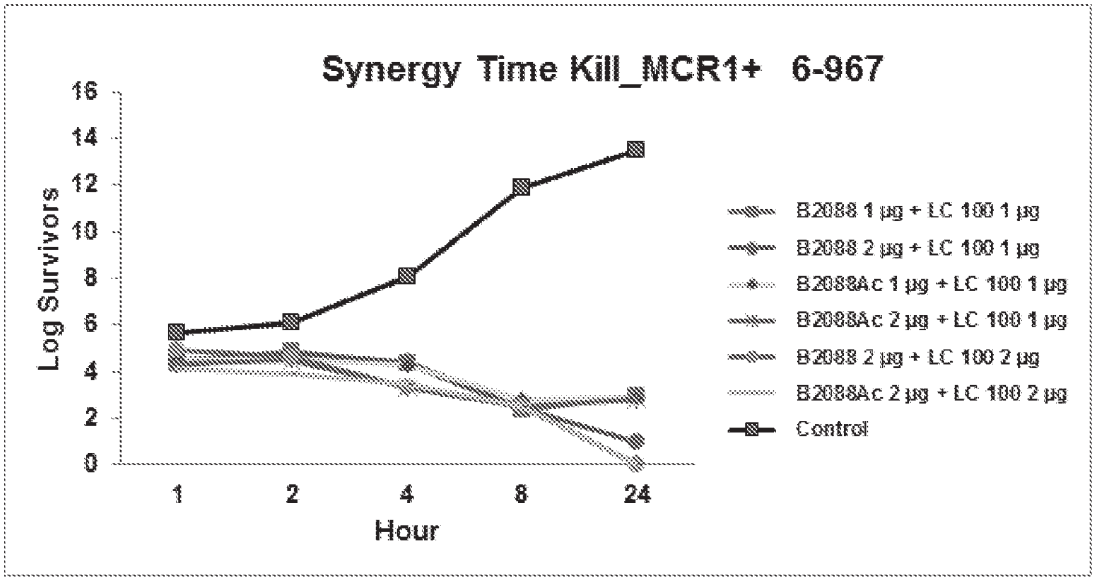
[Fig. 14]


(a)
Colistin against MCR 1 Pos 6-346
Log Survivors
Hour
1/16 MIC
1/8 MIC
1/4 MIC
1/2 MIC
1 MIC
2 MIC
4 MIC
Control FS MHB
(b)
Synergy Time Kill_Colistin & LC 100_against MCR 1+ _6-346
Colistin 1/4 MIC + LC 100_3 µg
Colistin 1/4 MIC + LC 100_5 µg
Colistin 1/8 MIC + LC 100_3 µg
Colistin 1/8 MIC + LC 100_5 µg
Colistin 1/8 MIC + LC 100_10 µg
Colistin 1/16 MIC + LC 100_10 µg
Control FSMHB

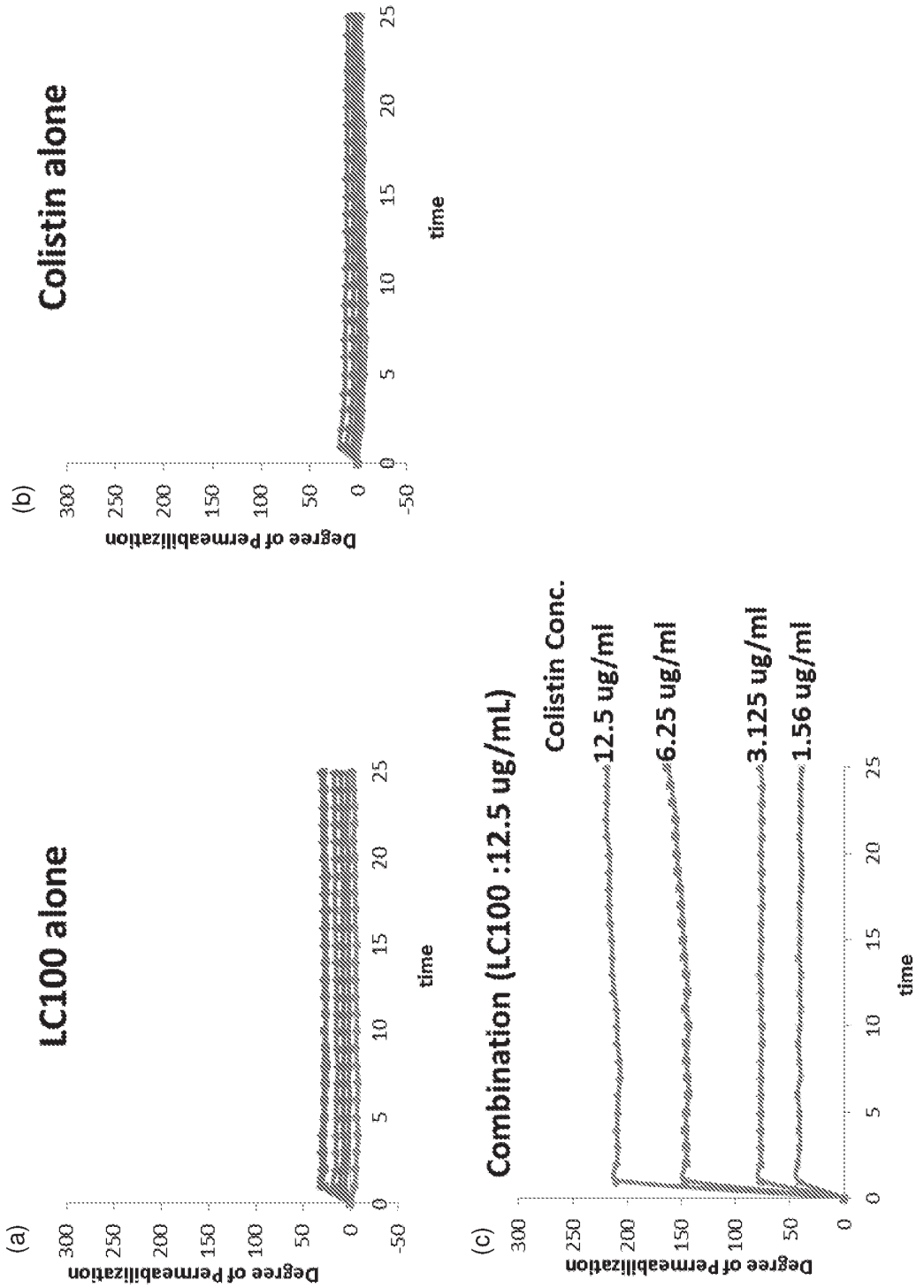
[Fig. 15]


(a) Colistin against MCR 1 Neg 7-108
Log Survivors
Hour
1/16 MIC
1/8 MIC
1/4 MIC
1/2 MIC
1 MIC
2 MIC
4 MIC
Control FS MHB
(b) Synergy Time Kill_Colistin & LC 100_against MCR 1- _7-108
Log Survivors
Hour
Colistin 1/4 MIC + LC 100_3 µg
Colistin 1/4 MIC + LC 100_5 µg
Colistin 1/8 MIC + LC 100_3 µg
Colistin 1/8 MIC + LC 100_5 µg
Colistin 1/8 MIC + LC 100_10 µg
Colistin 1/16 MIC + LC 100_10 µg
Control FSMHB

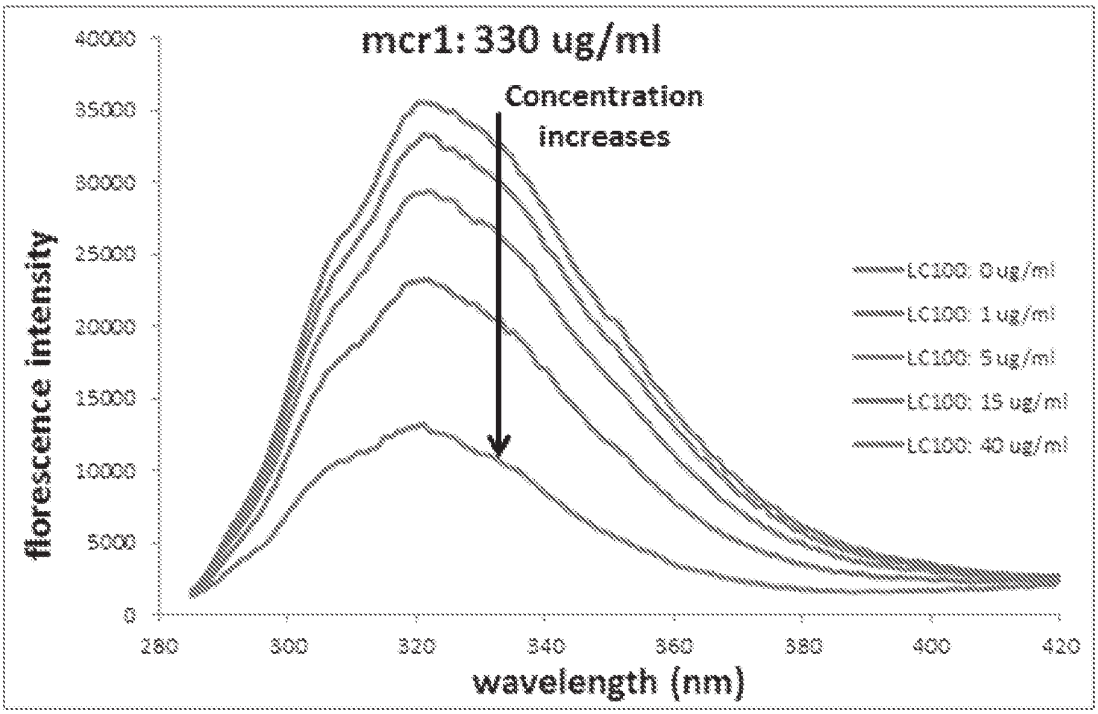
[Fig. 16]


Synergy Time Kill_MCR1+ 6-967
Log Survivors
16
14
12
10
8
6
4
2
0
1
2
4
8
24
Hour
B2088 1 μg + LC 100 1 μg
B2088 2 μg + LC 100 1 μg
B2088Ac 1 μg + LC 100 1 μg
B2088Ac 2 μg + LC 100 1 μg
B2088 2 μg + LC 100 2 μg
B2088Ac 2 μg + LC 100 2 μg
Control

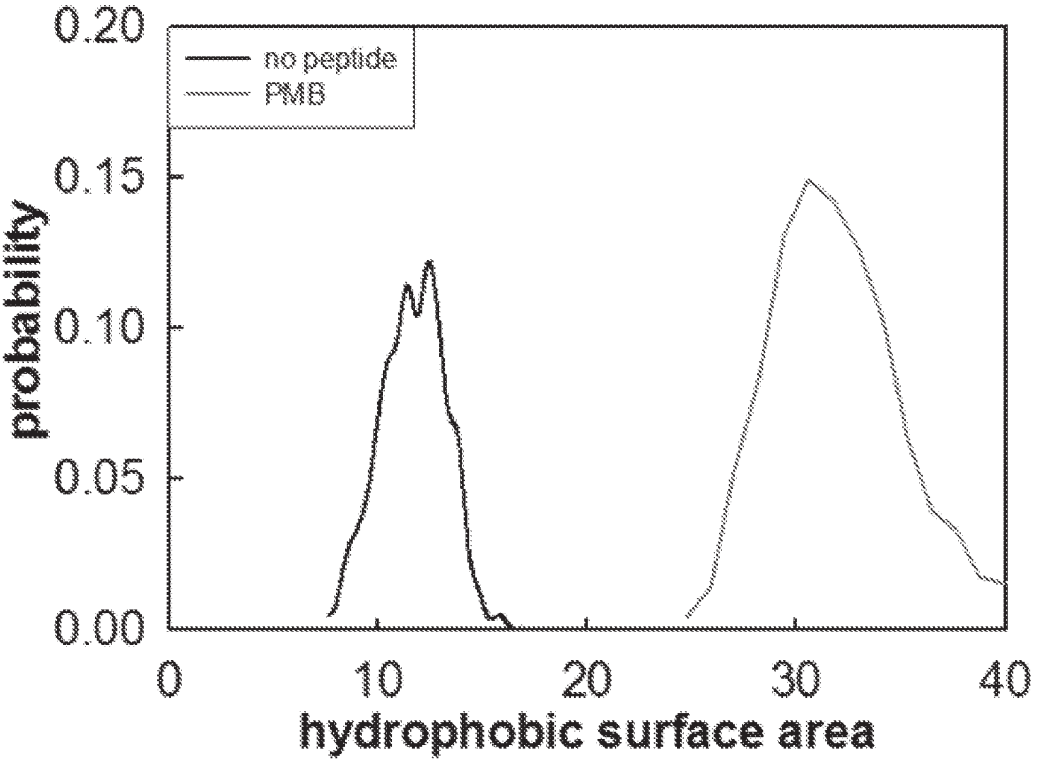
[Fig. 17]


(a)
LC100 alone
Degree of Permeabilization
time
(b)
Colistin alone
Degree of Permeabilization
time
(c)
Combination (LC100 :12.5 ug/mL)
Colistin Conc.
12.5 ug/ml
6.25 ug/ml
3.125 ug/ml
1.56 ug/ml
Degree of Permeabilization
time

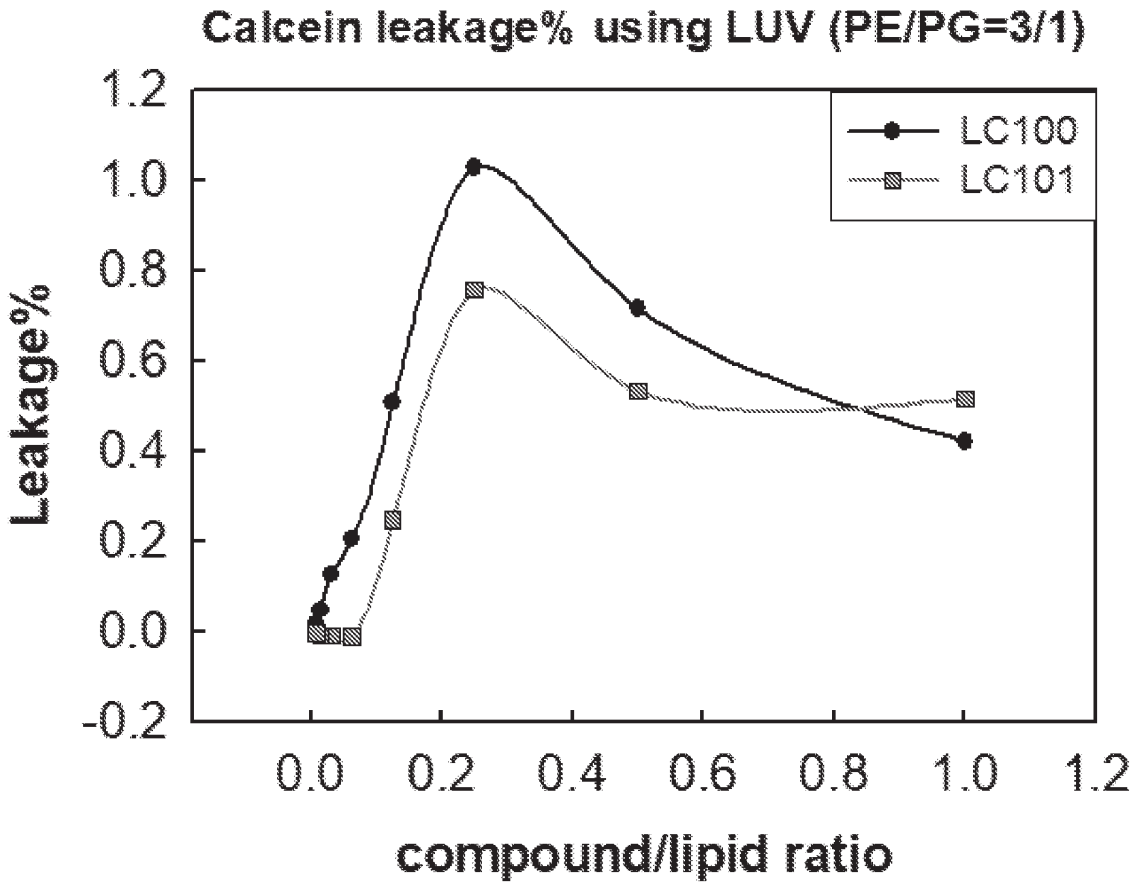
[Fig. 18]


mcr1: 330 ug/ml
Concentration increases
florescence intensity
wavelength (nm)
LC100: 0 ug/ml
LC100: 1 ug/ml
LC100: 5 ug/ml
LC100: 15 ug/ml
LC100: 40 ug/ml
40000
35000
30000
25000
20000
15000
10000
5000
0
280
300
320
340
360
380
400
420

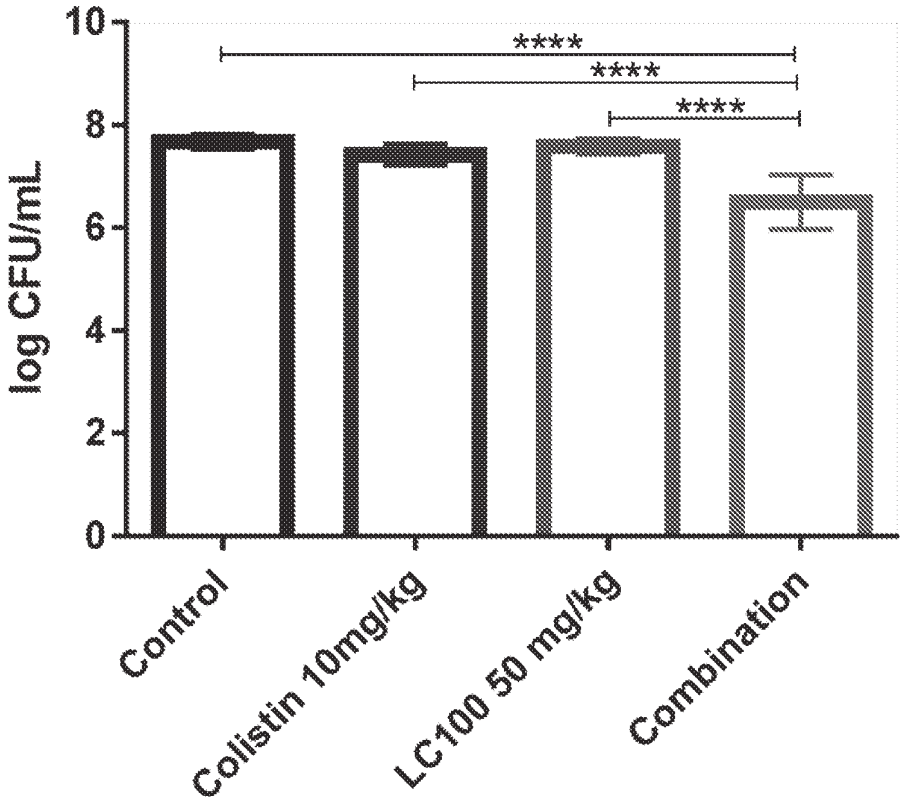
[Fig. 19]


0.20
0.15
0.10
0.05
0.00
probability
no peptide
PMB
0
10
20
30
40
hydrophobic surface area

[Fig. 20]


Calcein leakage% using LUV (PE/PG=3/1)
LC100
LC101
Leakage%
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
0.0
0.2
0.4
0.6
0.8
1.0
1.2
compound/lipid ratio

[Fig. 21]


10
8
6
4
2
0
log CFU/mL
****
****
****
Control
Colistin 10mg/kg
LC100 50 mg/kg
Combination