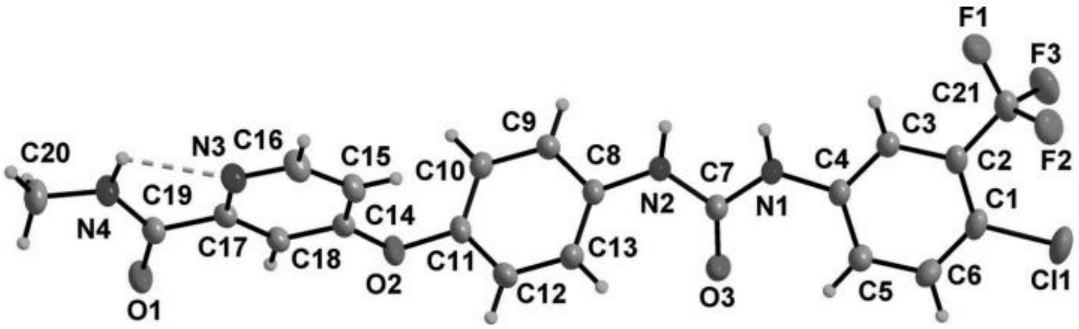

F1
F3
C21
C3
C9
C8
C7
C4
C2
F2
C1
C20
N3
C16
C15
C10
N2
N1
C19
C14
N4
C17
C18
O2
C11
C13
Cl1
C6
O1
C12
O3
C5

FIG. 1

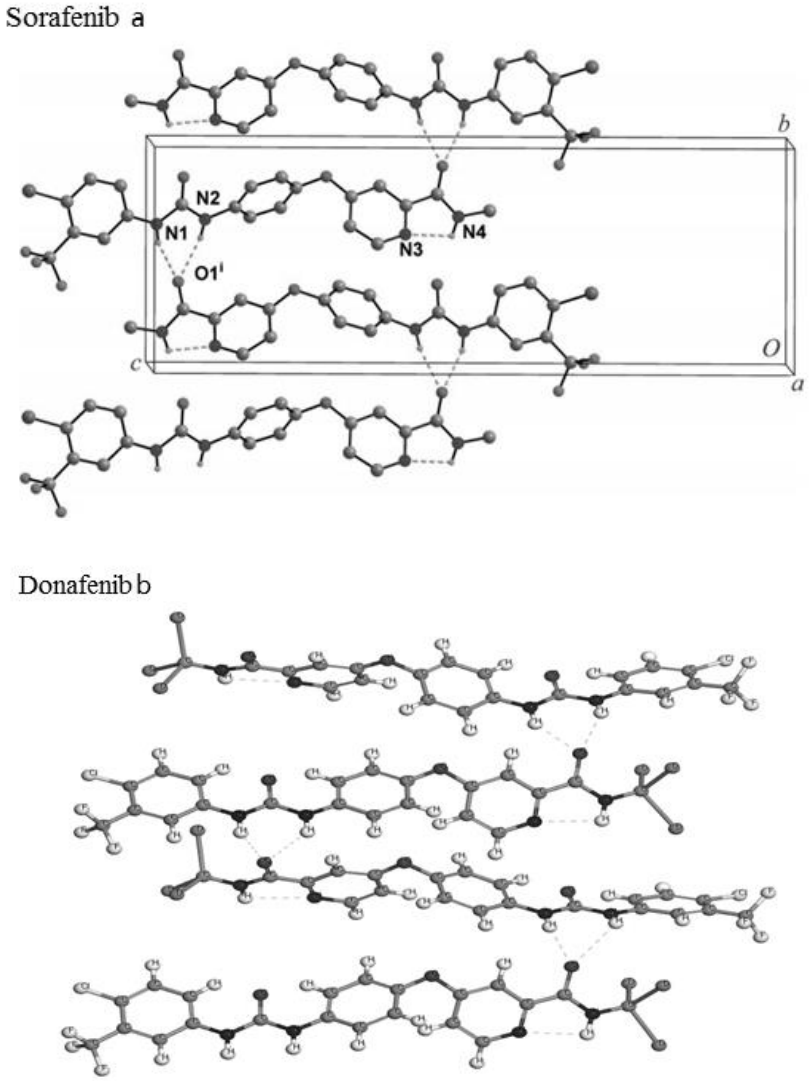

Sorafenib a
b
N2
N1
N3
N4
O1'
c
O
a
Donafenib b

FIG. 2

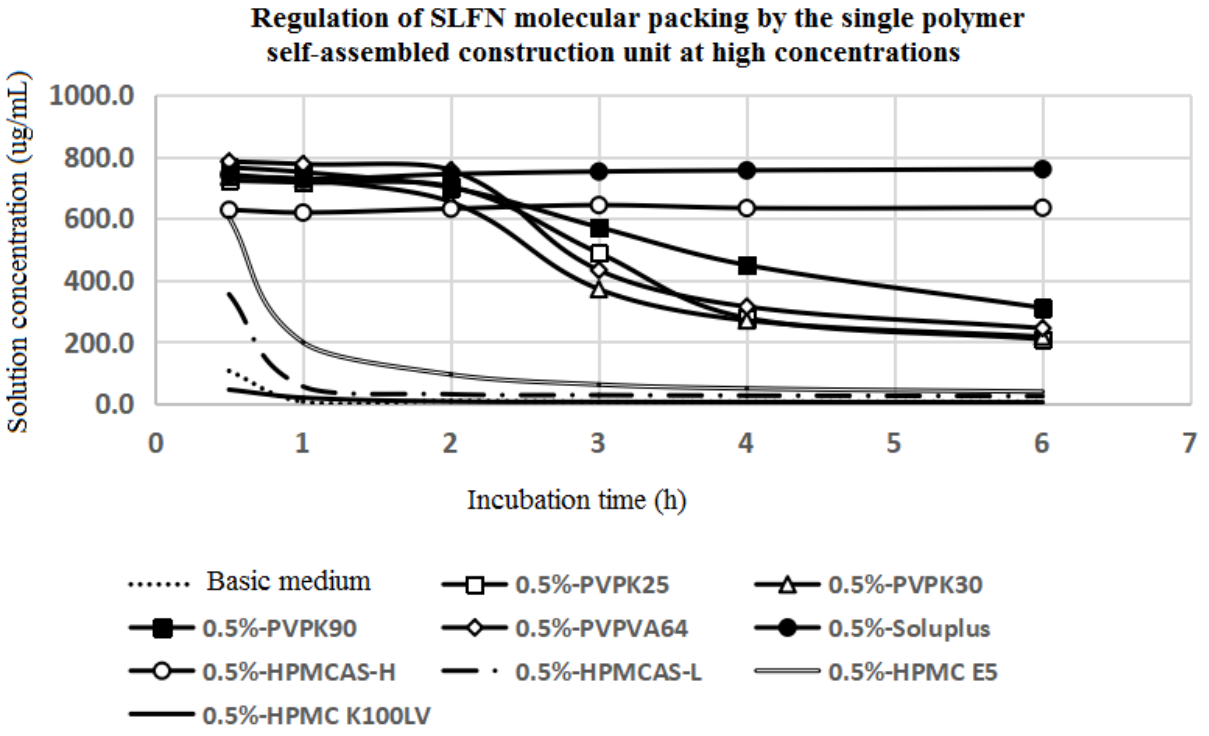

Regulation of SLFN molecular packing by the single polymer self-assembled construction unit at high concentrations
Solution concentration (ug/mL)
1000.0
800.0
600.0
400.0
200.0
0.0
0
1
2
3
4
5
6
7
Incubation time (h)
Basic medium
0.5%-PVPK25
0.5%-PVPK30
0.5%-PVPK90
0.5%-PVPVA64
0.5%-Soluplus
0.5%-HPMCAS-H
0.5%-HPMCAS-L
0.5%-HPMC E5
0.5%-HPMC K100LV

FIG. 3

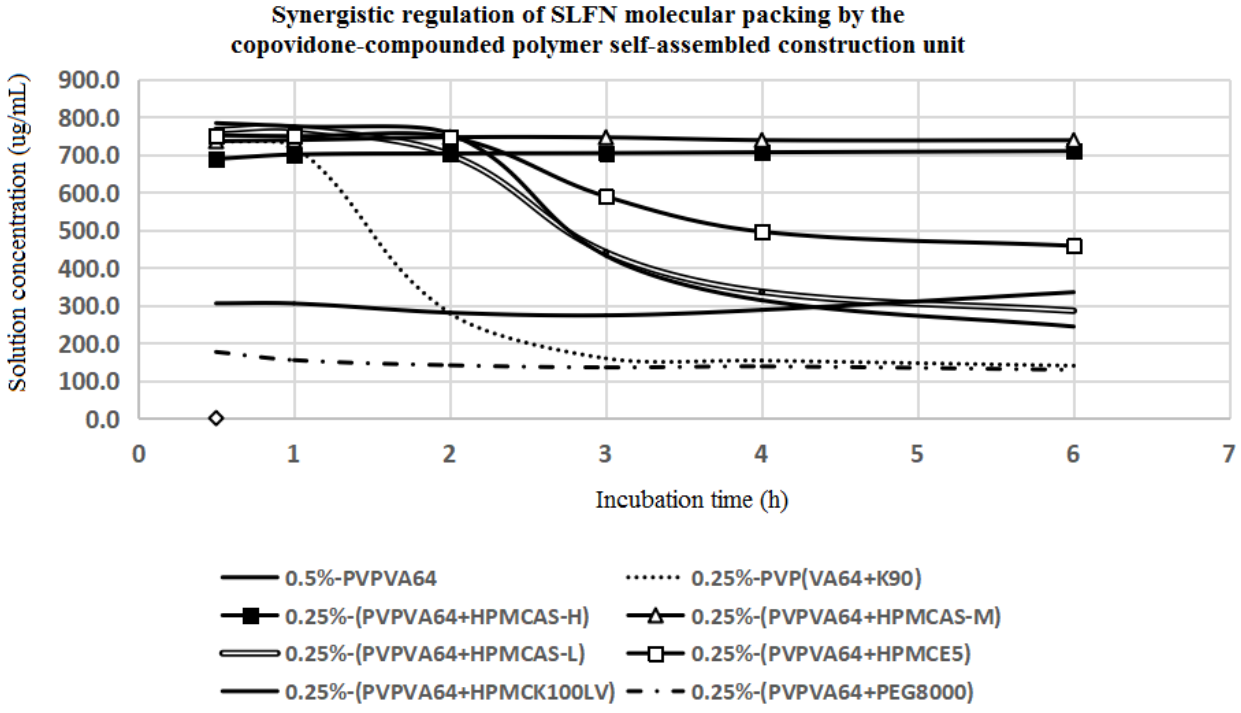

Synergistic regulation of SLFN molecular packing by the copovidone-compounded polymer self-assembled construction unit
Solution concentration (ug/mL)
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
0
1
2
3
4
5
6
7
Incubation time (h)
0.5%-PVPVA64
0.25%-PVP(VA64+K90)
0.25%-(PVPVA64+HPMCAS-H)
0.25%-(PVPVA64+HPMCAS-M)
0.25%-(PVPVA64+HPMCAS-L)
0.25%-(PVPVA64+HPMCE5)
0.25%-(PVPVA64+HPMCK100LV)
0.25%-(PVPVA64+PEG8000)

FIG. 4

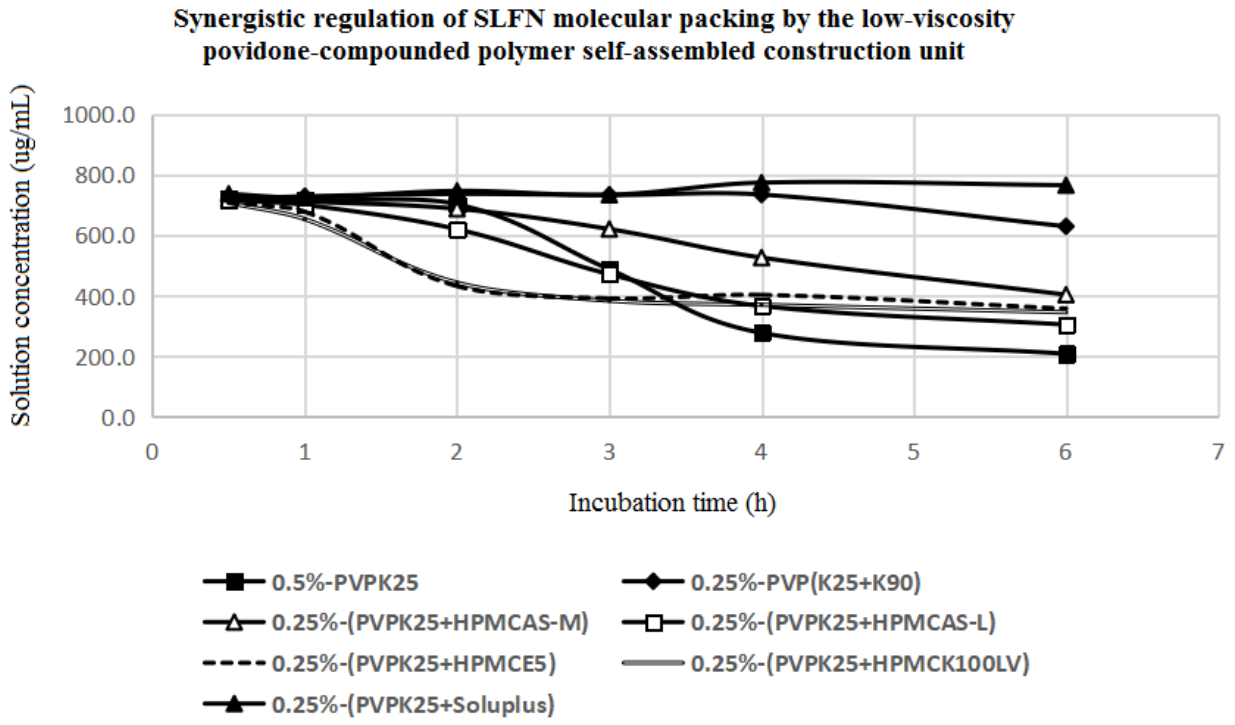

Synergistic regulation of SLFN molecular packing by the low-viscosity povidone-compounded polymer self-assembled construction unit
Solution concentration (ug/mL)
1000.0
800.0
600.0
400.0
200.0
0.0
0
1
2
3
4
5
6
7
Incubation time (h)
0.5%-PVPK25
0.25%-PVP(K25+K90)
0.25%-(PVPK25+HPMCAS-M)
0.25%-(PVPK25+HPMCAS-L)
0.25%-(PVPK25+HPMCE5)
0.25%-(PVPK25+HPMCK100LV)
0.25%-(PVPK25+Soluplus)

FIG. 5

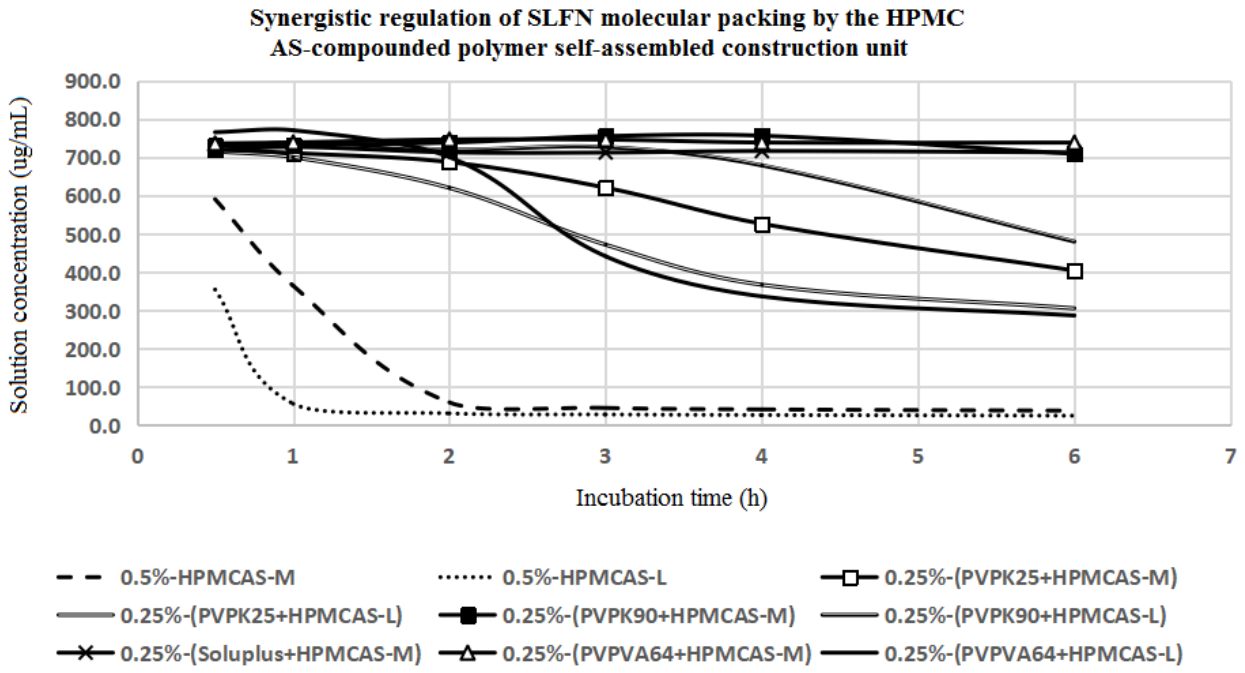

Synergistic regulation of SLFN molecular packing by the HPMC AS-compounded polymer self-assembled construction unit
Solution concentration (ug/mL)
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
0
1
2
3
4
5
6
7
Incubation time (h)
0.5%-HPMCAS-M
0.5%-HPMCAS-L
0.25%-(PVPK25+HPMCAS-M)
0.25%-(PVPK25+HPMCAS-L)
0.25%-(PVPK90+HPMCAS-M)
0.25%-(PVPK90+HPMCAS-L)
0.25%-(Soluplus+HPMCAS-M)
0.25%-(PVPVA64+HPMCAS-M)
0.25%-(PVPVA64+HPMCAS-L)

FIG. 6

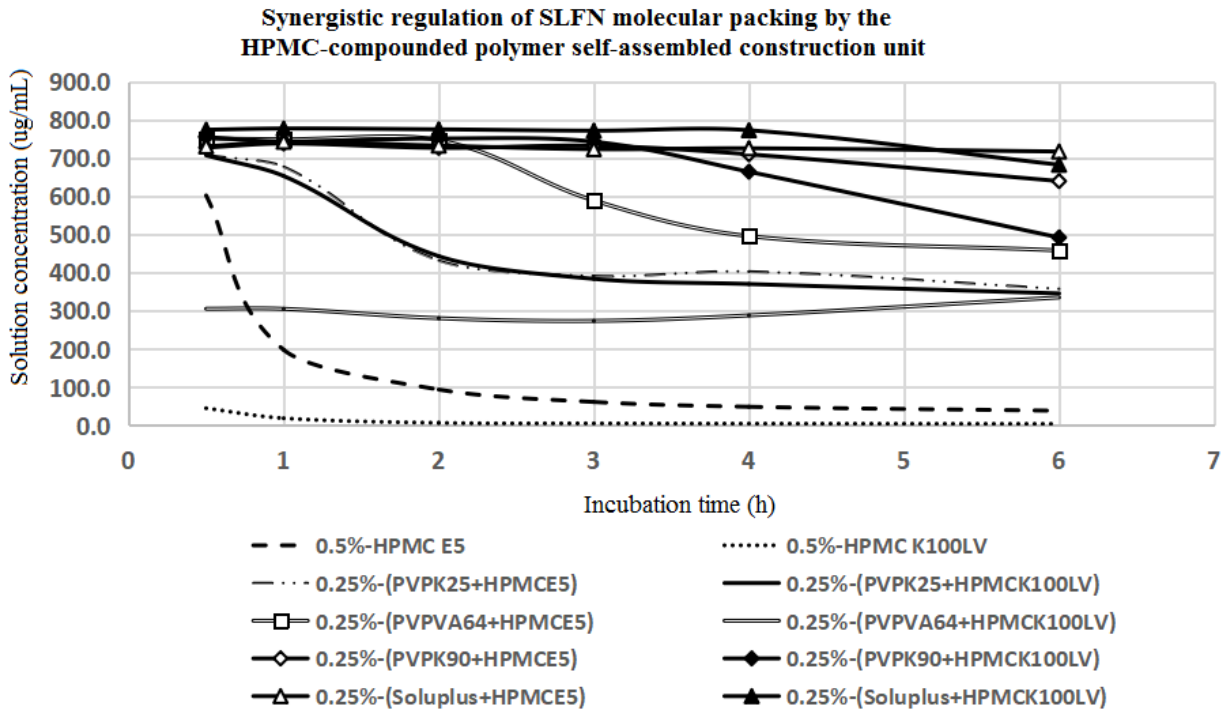

Synergistic regulation of SLFN molecular packing by the
HPMC-compounded polymer self-assembled construction unit
Solution concentration (ug/mL)
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
0
1
2
3
4
5
6
7
Incubation time (h)
0.5%-HPMC E5
0.5%-HPMC K100LV
0.25%-(PVPK25+HPMCE5)
0.25%-(PVPK25+HPMCK100LV)
0.25%-(PVPVA64+HPMCE5)
0.25%-(PVPVA64+HPMCK100LV)
0.25%-(PVPK90+HPMCE5)
0.25%-(PVPK90+HPMCK100LV)
0.25%-(Soluplus+HPMCE5)
0.25%-(Soluplus+HPMCK100LV)

FIG. 7

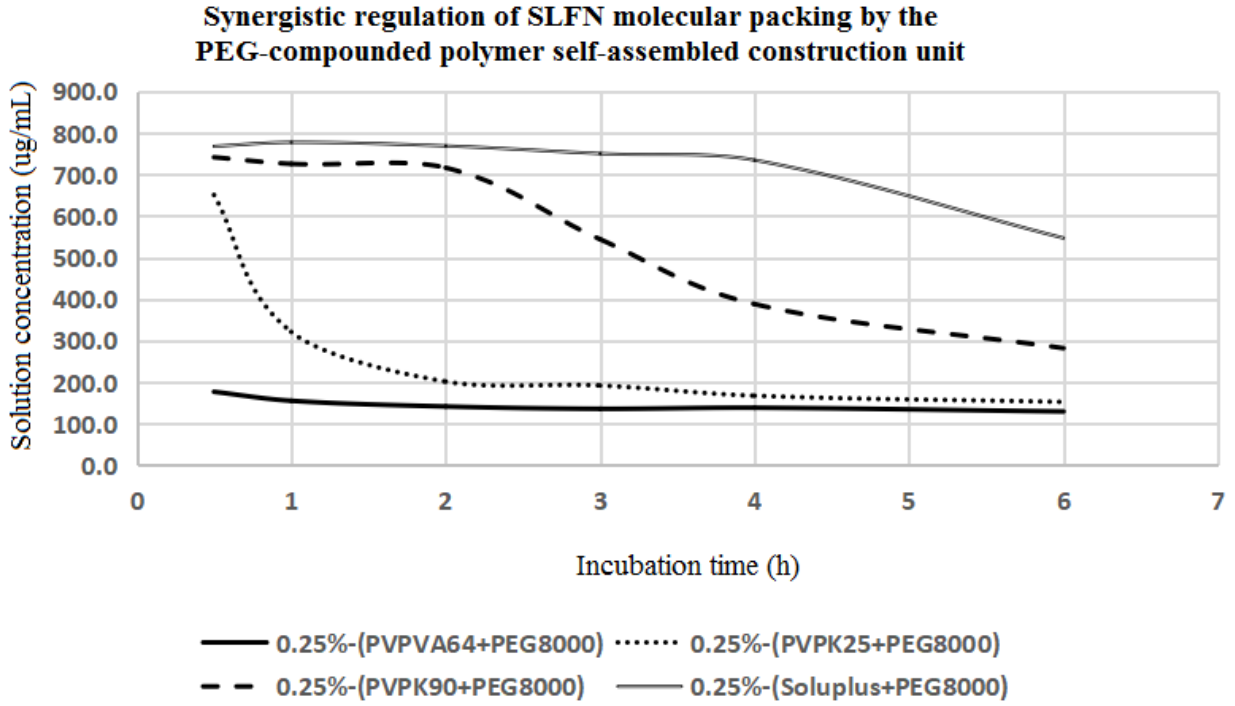

Synergistic regulation of SLFN molecular packing by the
PEG-compounded polymer self-assembled construction unit
Solution concentration (ug/mL)
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
0
1
2
3
4
5
6
7
Incubation time (h)
0.25%-(PVPVA64+PEG8000)
0.25%-(PVPK25+PEG8000)
0.25%-(PVPK90+PEG8000)
0.25%-(Soluplus+PEG8000)

FIG. 8

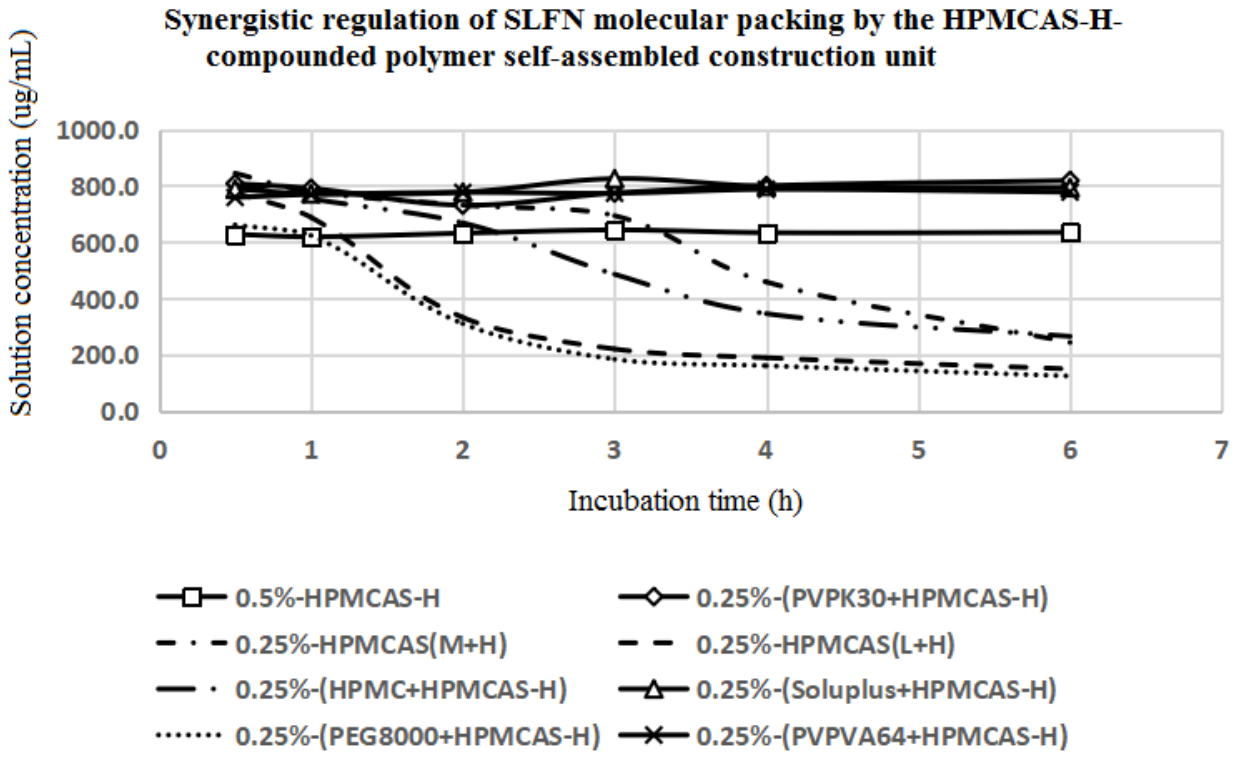

Synergistic regulation of SLFN molecular packing by the HPMCAS-H-compounded polymer self-assembled construction unit
Solution concentration (ug/mL)
1000.0
800.0
600.0
400.0
200.0
0.0
0
1
2
3
4
5
6
7
Incubation time (h)
0.5%-HPMCAS-H
0.25%-(PVPK30+HPMCAS-H)
0.25%-HPMCAS(M+H)
0.25%-HPMCAS(L+H)
0.25%-(HPMC+HPMCAS-H)
0.25%-(Soluplus+HPMCAS-H)
0.25%-(PEG8000+HPMCAS-H)
0.25%-(PVPVA64+HPMCAS-H)

FIG. 9

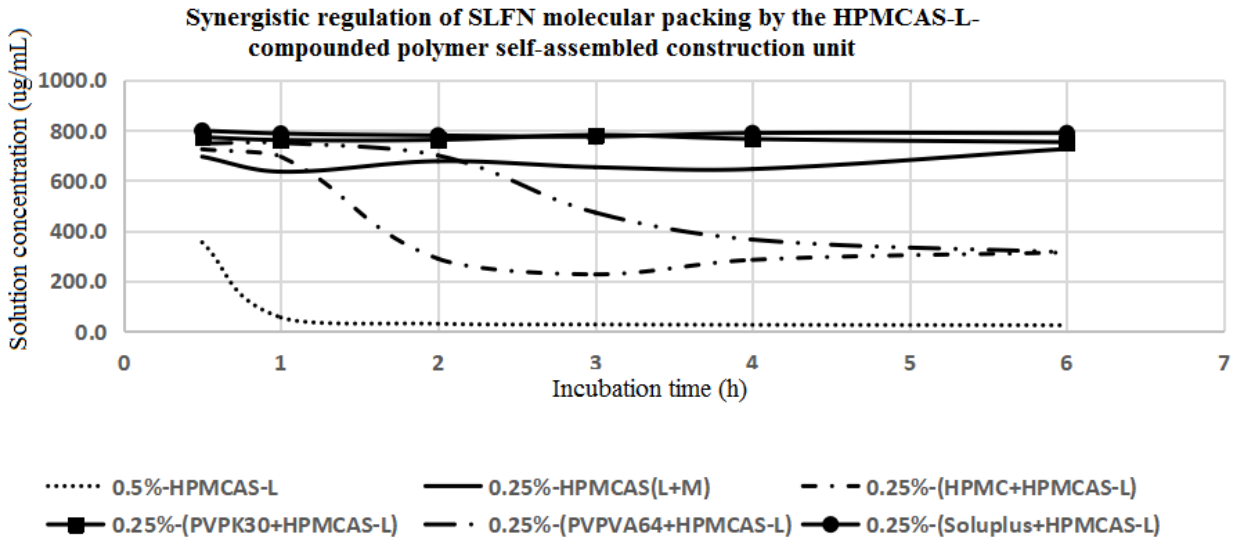

Synergistic regulation of SLFN molecular packing by the HPMCAS-L-compounded polymer self-assembled construction unit
Solution concentration (ug/mL)
1000.0
800.0
600.0
400.0
200.0
0.0
0
1
2
3
4
5
6
7
Incubation time (h)
0.5%-HPMCAS-L
0.25%-HPMCAS(L+M)
0.25%-(HPMC+HPMCAS-L)
0.25%-(PVPK30+HPMCAS-L)
0.25%-(PVPVA64+HPMCAS-L)
0.25%-(Soluplus+HPMCAS-L)

FIG. 10

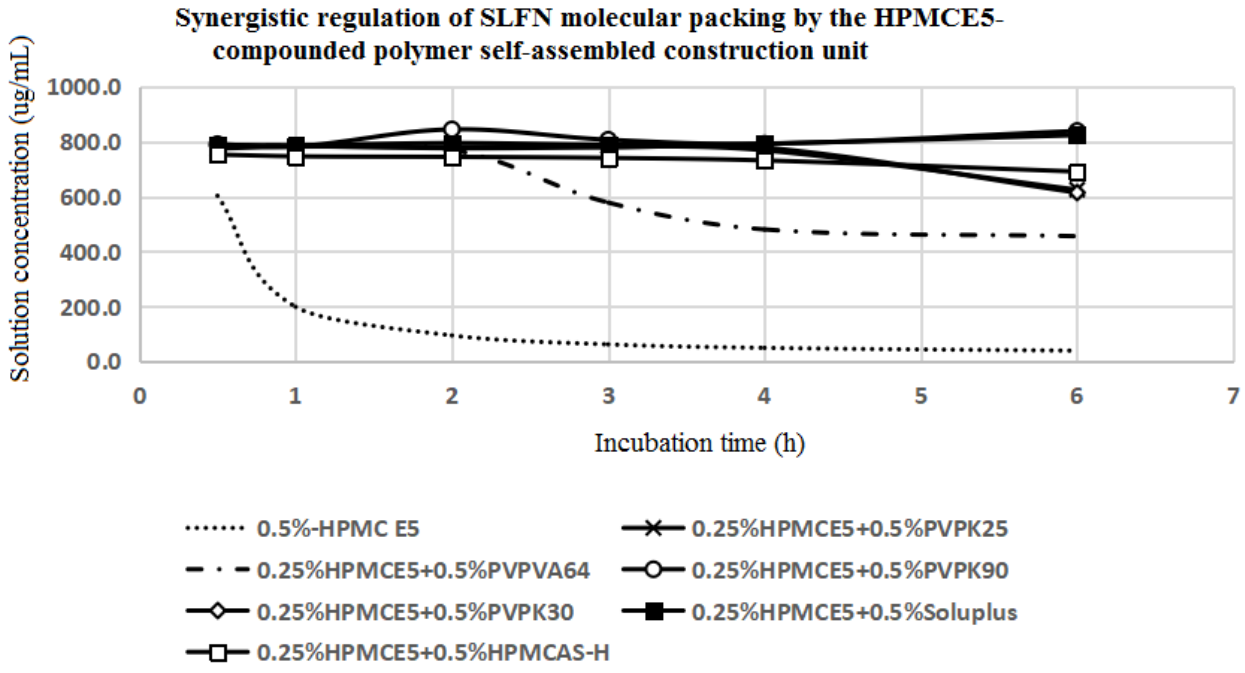

Synergistic regulation of SLFN molecular packing by the HPMCE5-compounded polymer self-assembled construction unit
Solution concentration (ug/mL)
1000.0
800.0
600.0
400.0
200.0
0.0
0
1
2
3
4
5
6
7
Incubation time (h)
0.5%-HPMC E5
0.25%HPMCE5+0.5%PVPK25
0.25%HPMCE5+0.5%PVPVA64
0.25%HPMCE5+0.5%PVPK90
0.25%HPMCE5+0.5%PVPK30
0.25%HPMCE5+0.5%Soluplus
0.25%HPMCE5+0.5%HPMCAS-H

FIG. 11

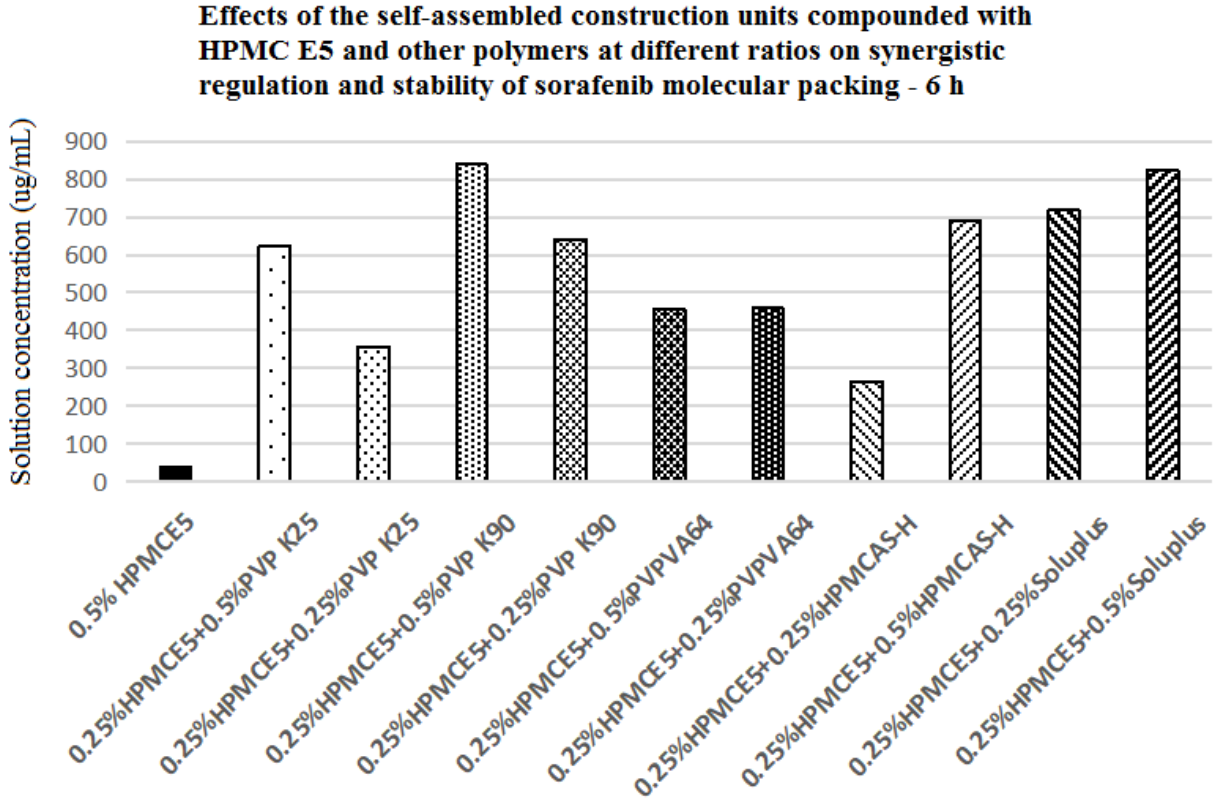

Effects of the self-assembled construction units compounded with HPMC E5 and other polymers at different ratios on synergistic regulation and stability of sorafenib molecular packing - 6 h
Solution concentration (ug/mL)
900
800
700
600
500
400
300
200
100
0
0.5% HPMCE5
0.25%HPMCE5+0.5%PVP K25
0.25%HPMCE5+0.25%PVP K25
0.25%HPMCE5+0.5%PVP K90
0.25%HPMCE5+0.25%PVP K90
0.25%HPMCE5+0.5%PVPVA64
0.25%HPMCE5+0.25%PVPVA64
0.25%HPMCE5+0.25%HPMCAS-H
0.25%HPMCE5+0.5%HPMCAS-H
0.25%HPMCE5+0.25%Soluplus
0.25%HPMCE5+0.5%Soluplus

FIG. 12

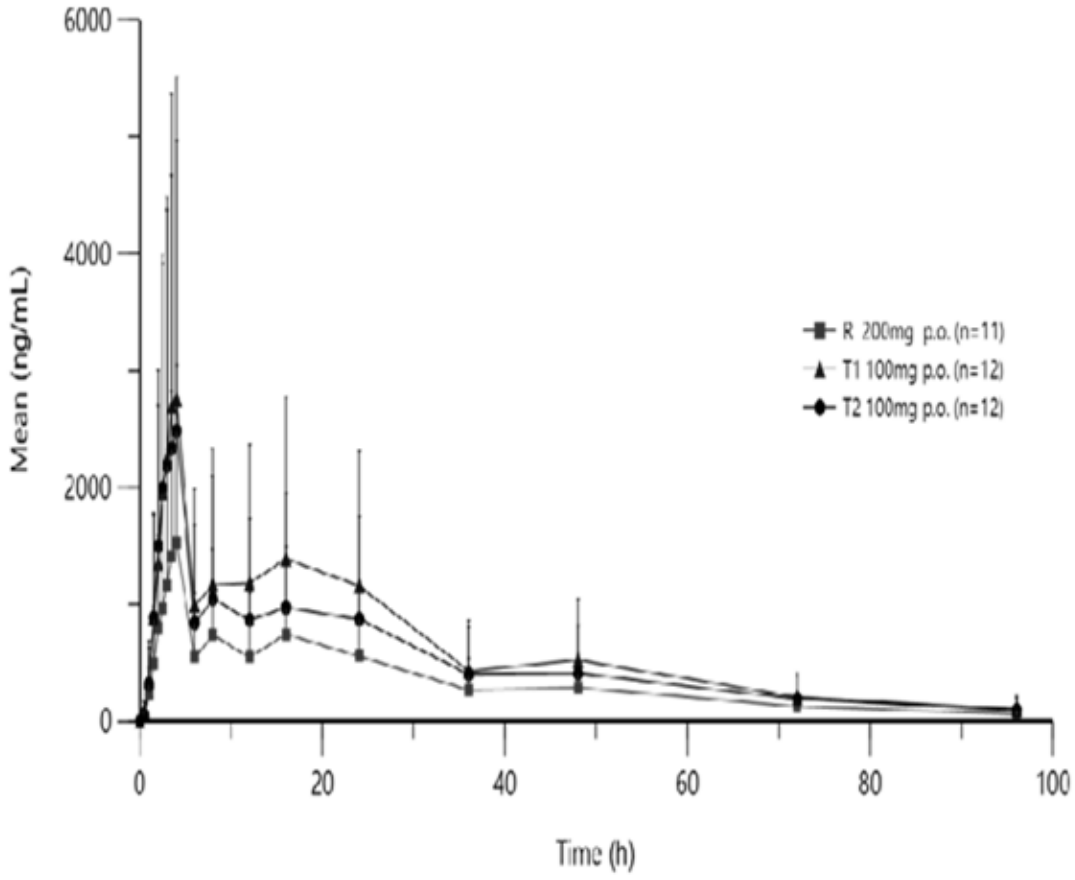

6000
4000
2000
0
Mean (ng/mL)
0
20
40
60
80
100
Time (h)
R 200mg p.o. (n=11)
T1 100mg p.o. (n=12)
T2 100mg p.o. (n=12)

FIG. 13

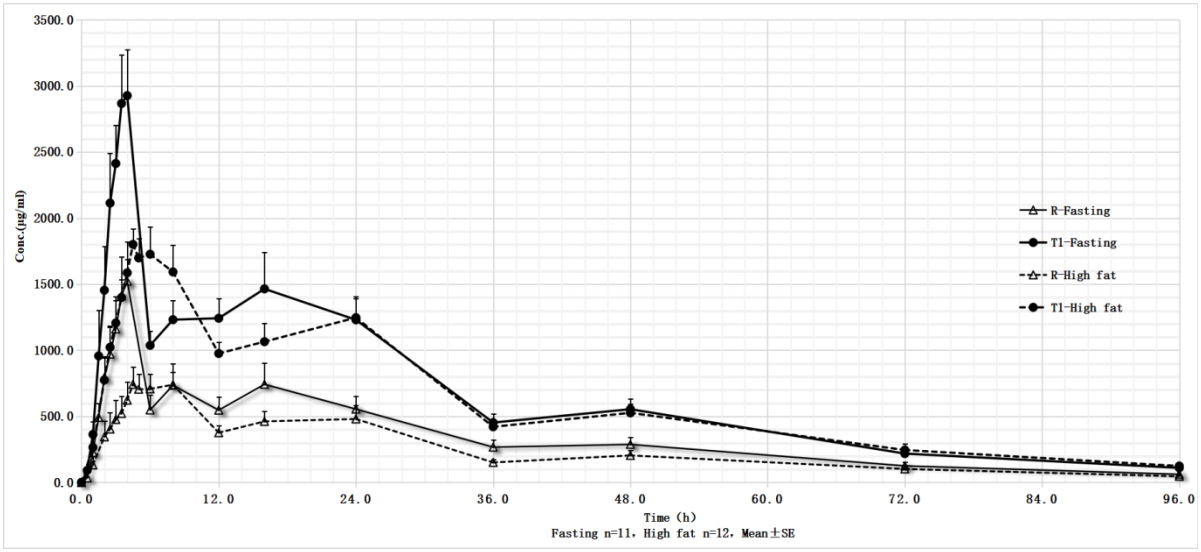

3500.0
3000.0
2500.0
2000.0
1500.0
1000.0
500.0
0.0
Conc.(μg/ml)
0.0
12.0
24.0
36.0
48.0
60.0
72.0
84.0
96.0
Time (h)
Fasting n=11, High fat n=12, Mean±SE
R-Fasting
T1-Fasting
R-High fat
T1-High fat

FIG. 14