

Supplemental material

Chrysin Directing an Enhanced Solubility through the Formation of a Supramolecular Cyclodextrin–Calixarene Drug Delivery System: A Potential Strategy in Antifibrotic Diabetes Therapeutics

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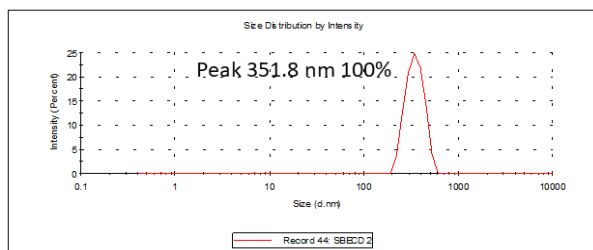
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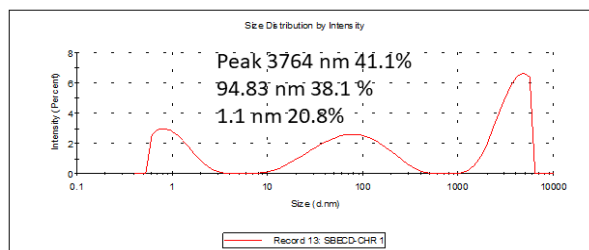
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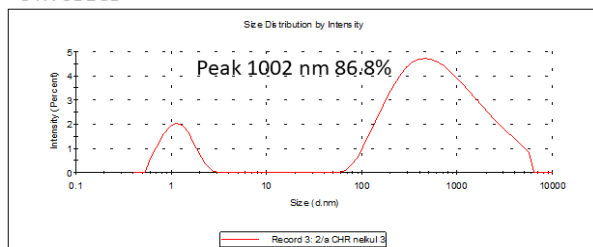
SBECD



CHR-SBECD



OTX-SBECD



CHR-OTX-SBECD

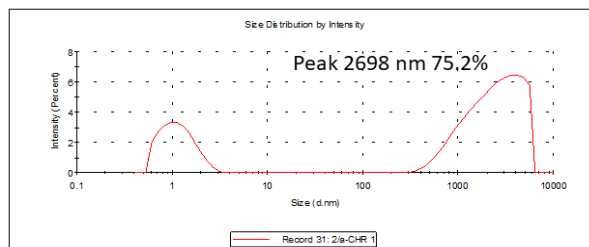


Figure S1. Size distribution of the molecular associates of SBECD, OTX008-SBECD and CHR-OTX008-SBECD in water. The associates were characterized by dynamic light scattering. X-axis: size (nm); Y-axis: intensity distribution (%).

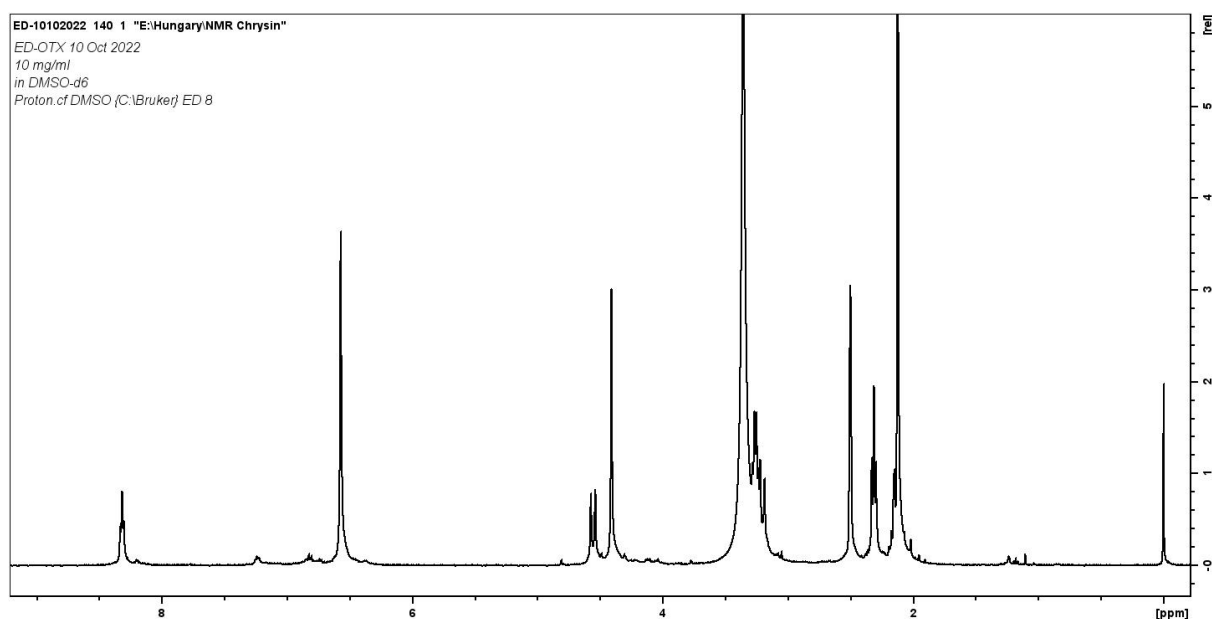


Figure S2. ^1H NMR spectrum of OTX008 in DMSO- d_6 .

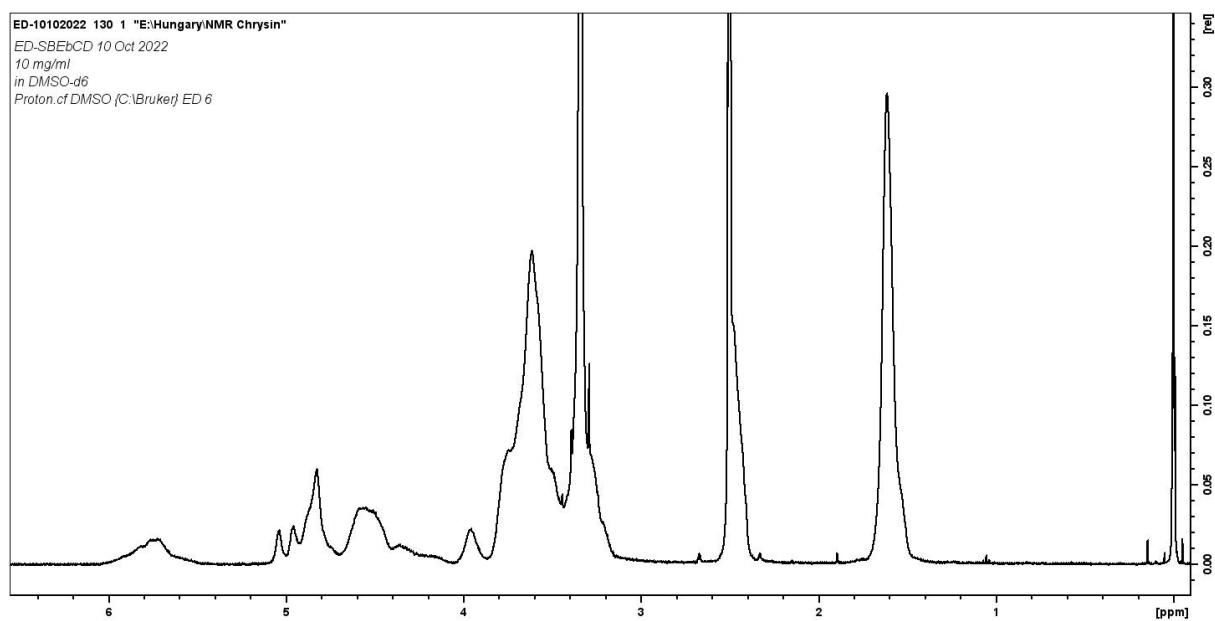


Figure S3. ^1H NMR spectrum of SBECD in DMSO-d_6 .

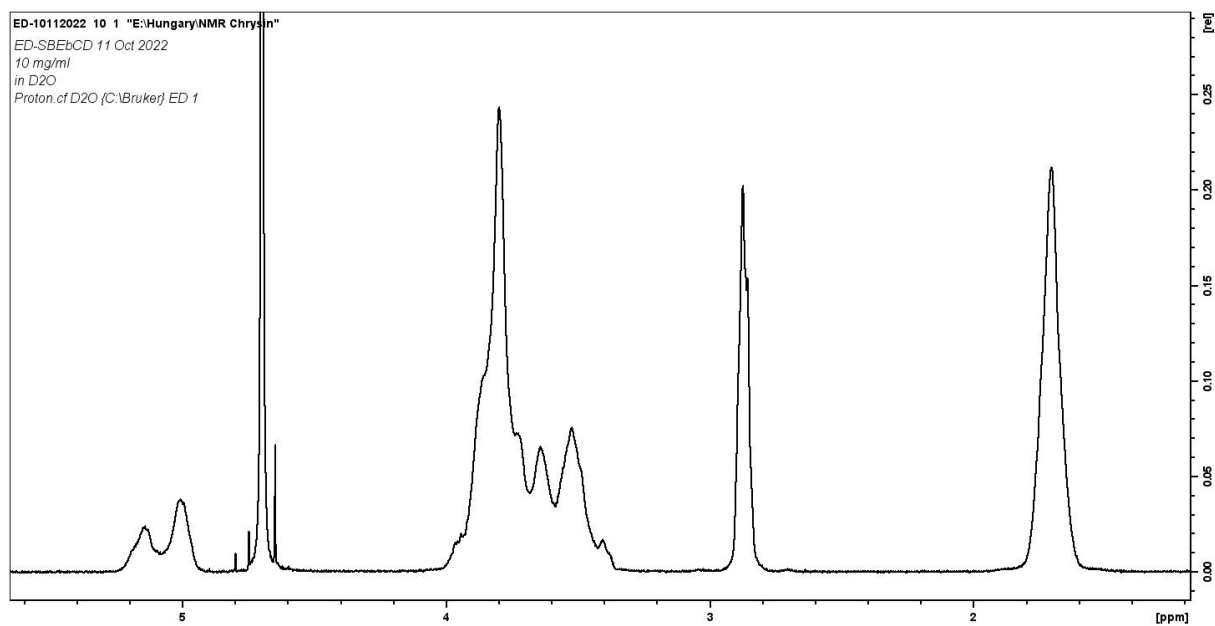


Figure S4. ^1H NMR spectrum of SBECD in D_2O .

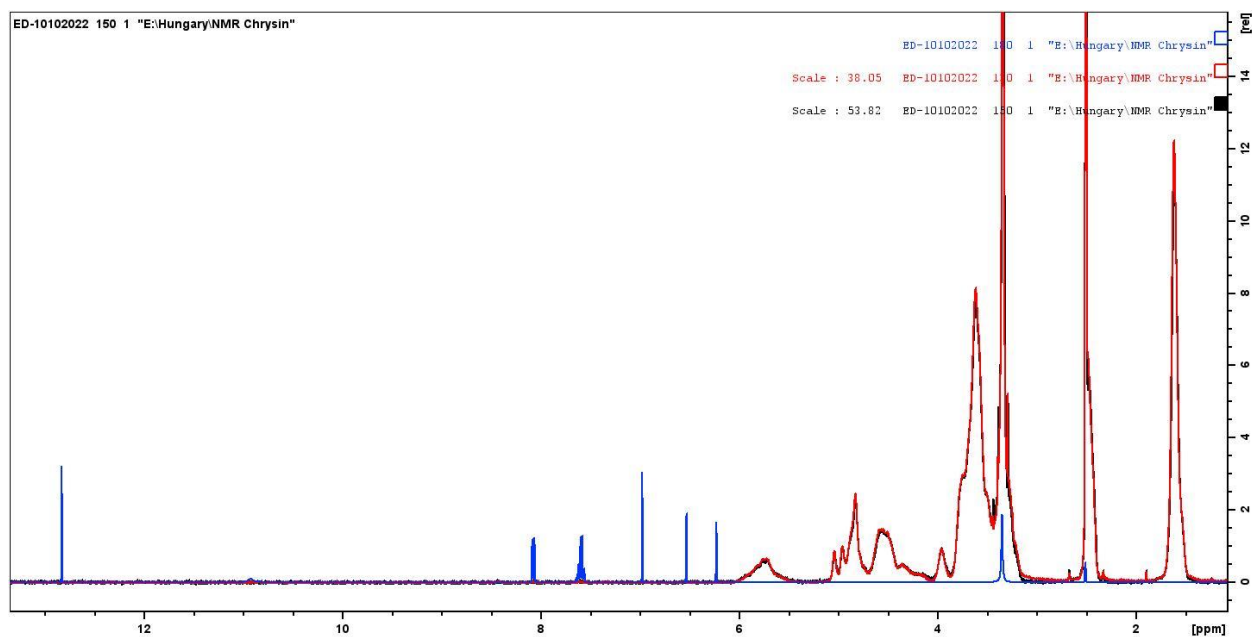


Figure S5. ^1H NMR spectra of CHR-SBECD mixture (black line), CHR (Blue line) and SBECD (Red line) in DMSO-d_6 .

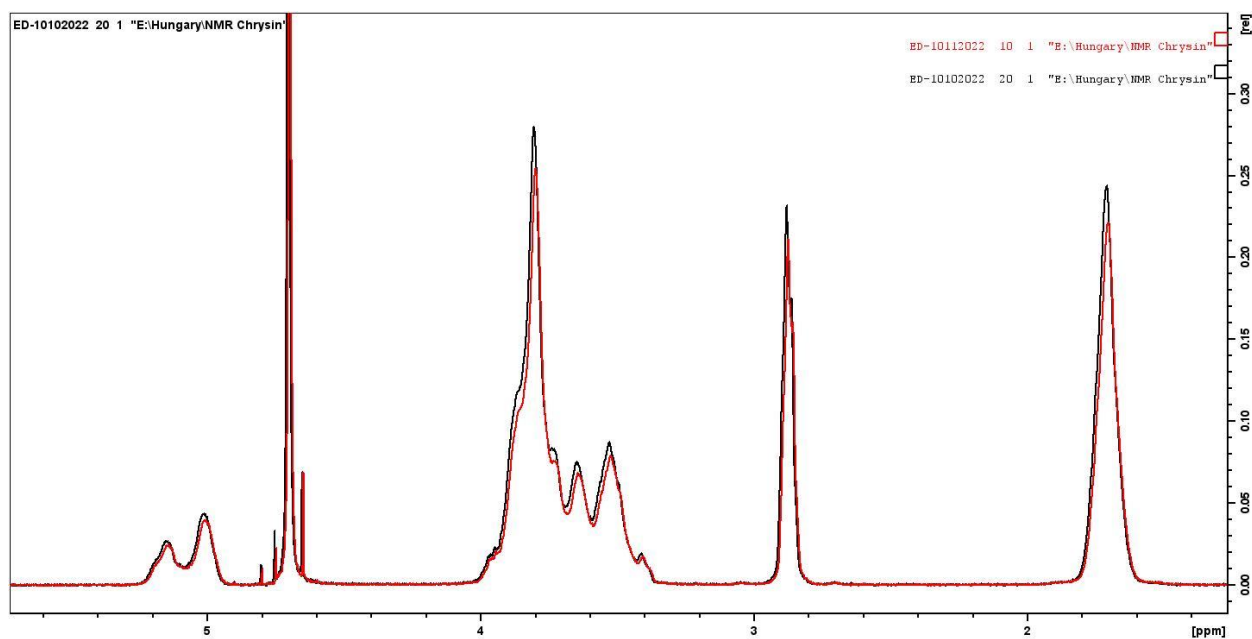


Figure S6. ^1H NMR spectra of CHR-SBECD mixture (black line) and SBECD (Red line) in D_2O .

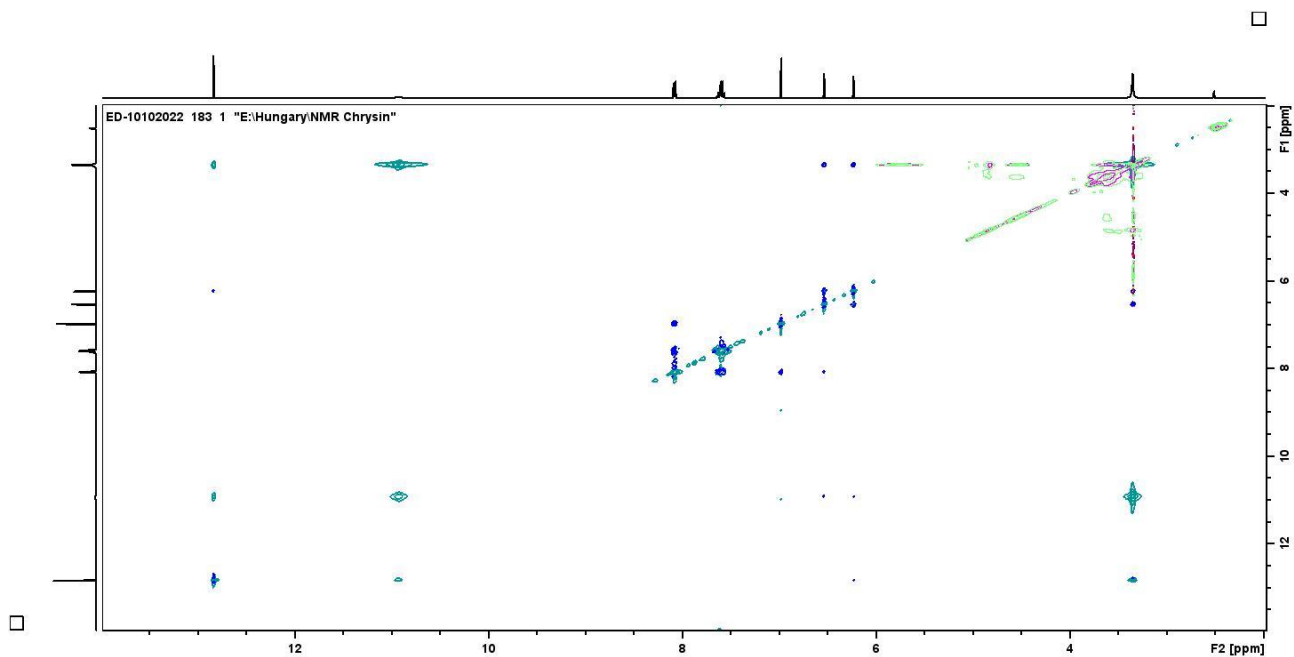


Figure S7. NOESY NMR spectra of CHR (Blue/Dark green line), CHR-SBECD mixture (Purple line) and SBECD (Light green line) in DMSO-d₆.

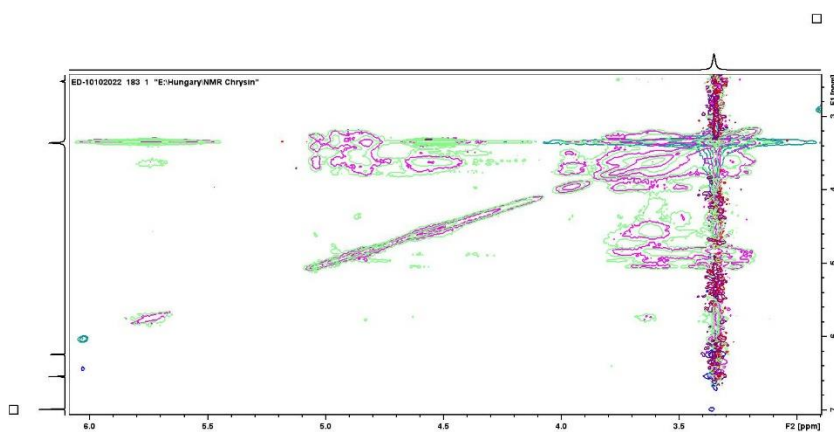


Figure S8. Expanded area of the NOESY spectra Figure S7.

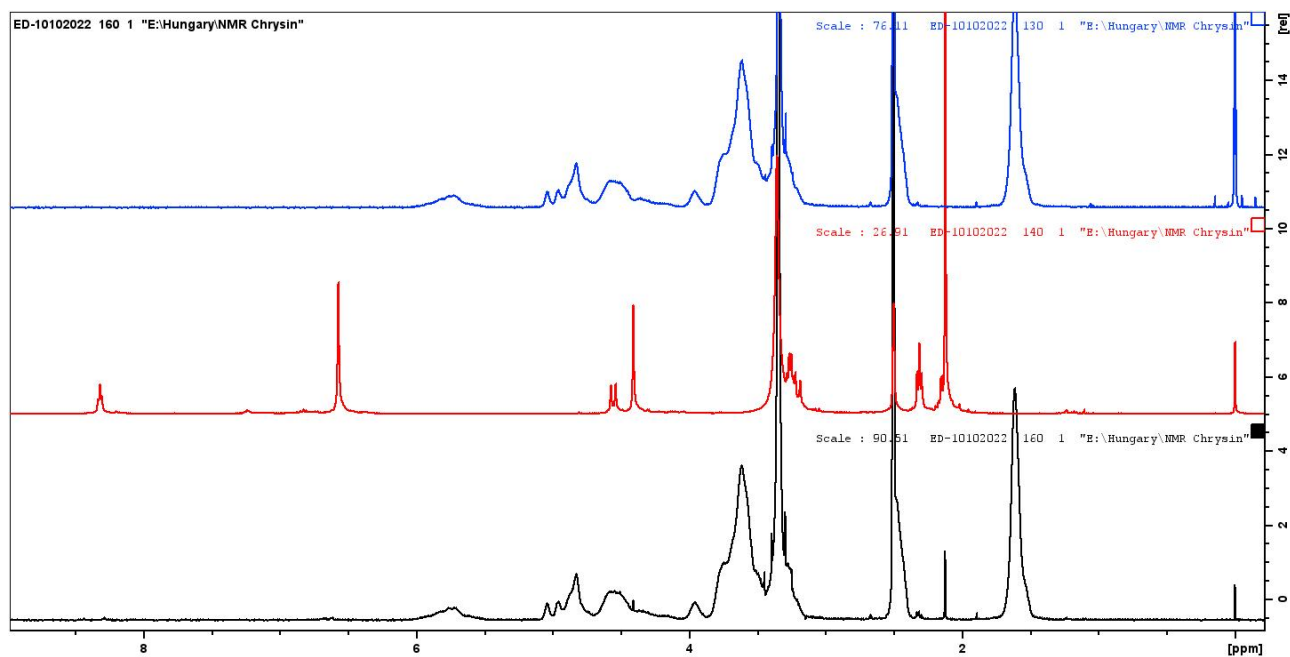


Figure S9. ^1H NMR spectra of OTX008-SBECD mixture (Black line), OTX008 (Red line) and SBECD (Blue line) in DMSO-d_6 .

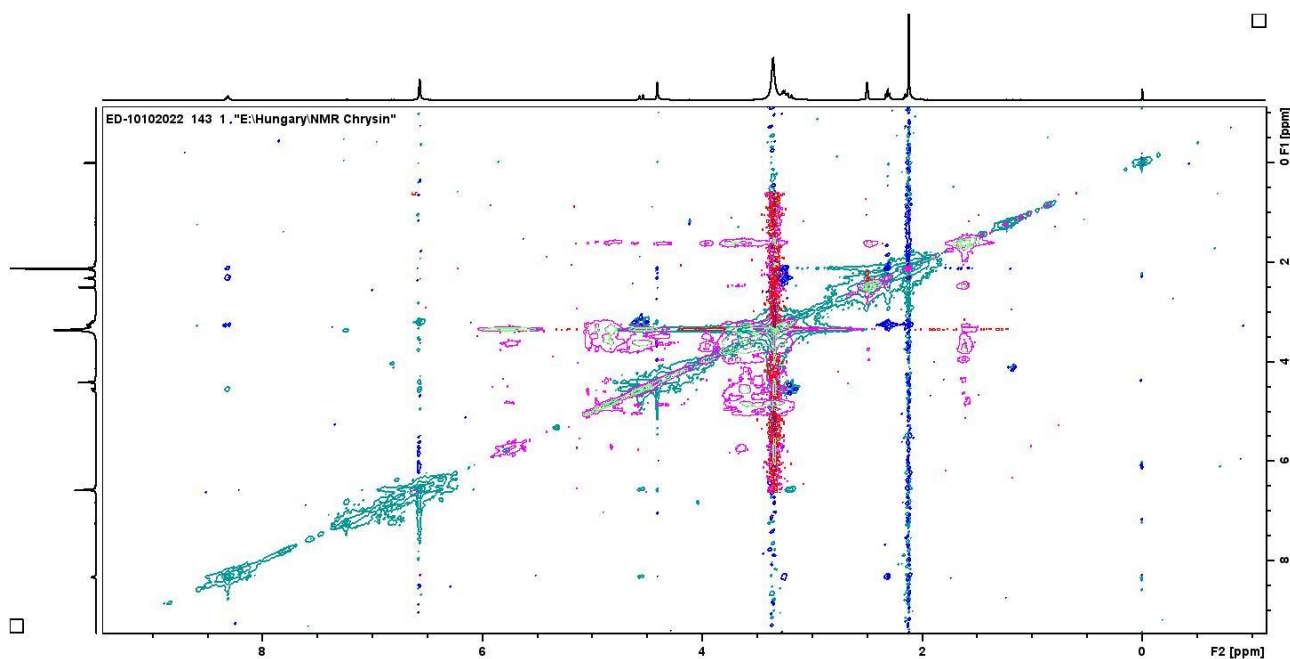


Figure S10. NOESY spectra of OTX008-SBECD mixture (Black line), OTX008 (Red line) and SBECD (Blue line) in DMSO-d_6 .

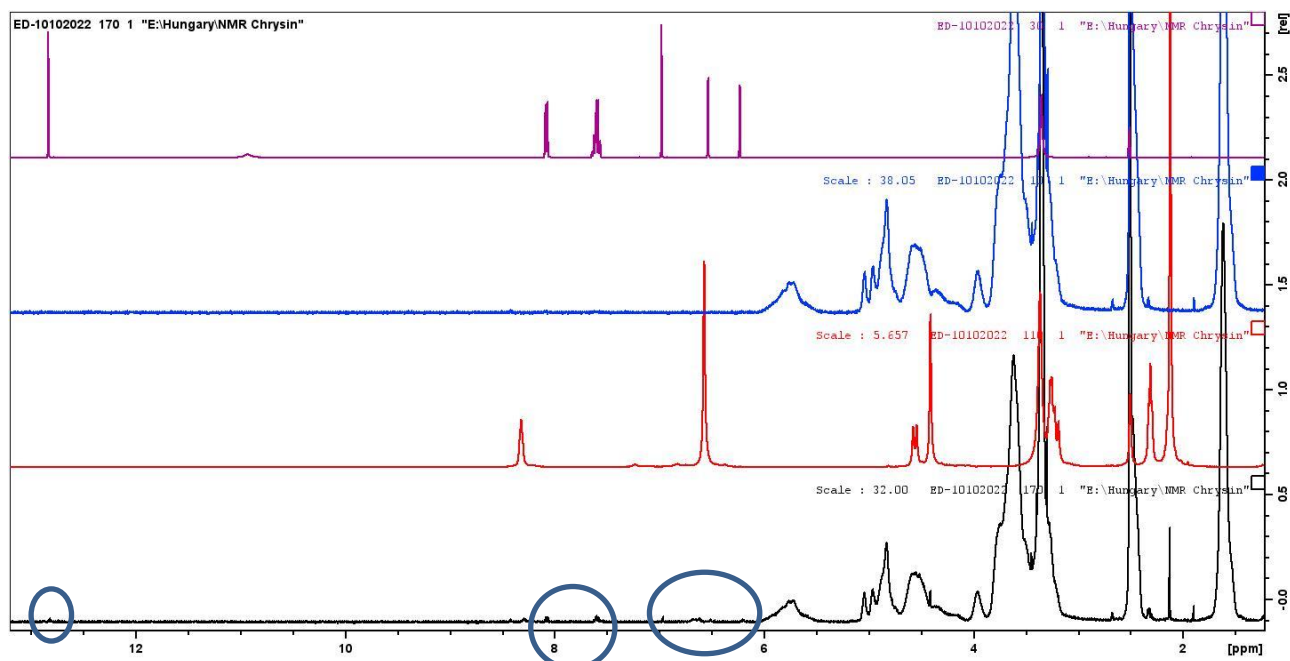


Figure S11. ^1H NMR spectra of CHR-OTX008-SBEDD mixture (Black line), OTX008 (Red line) SBEDD (B, Blue line) and CHR (Purple line) in DMSO-d_6 .

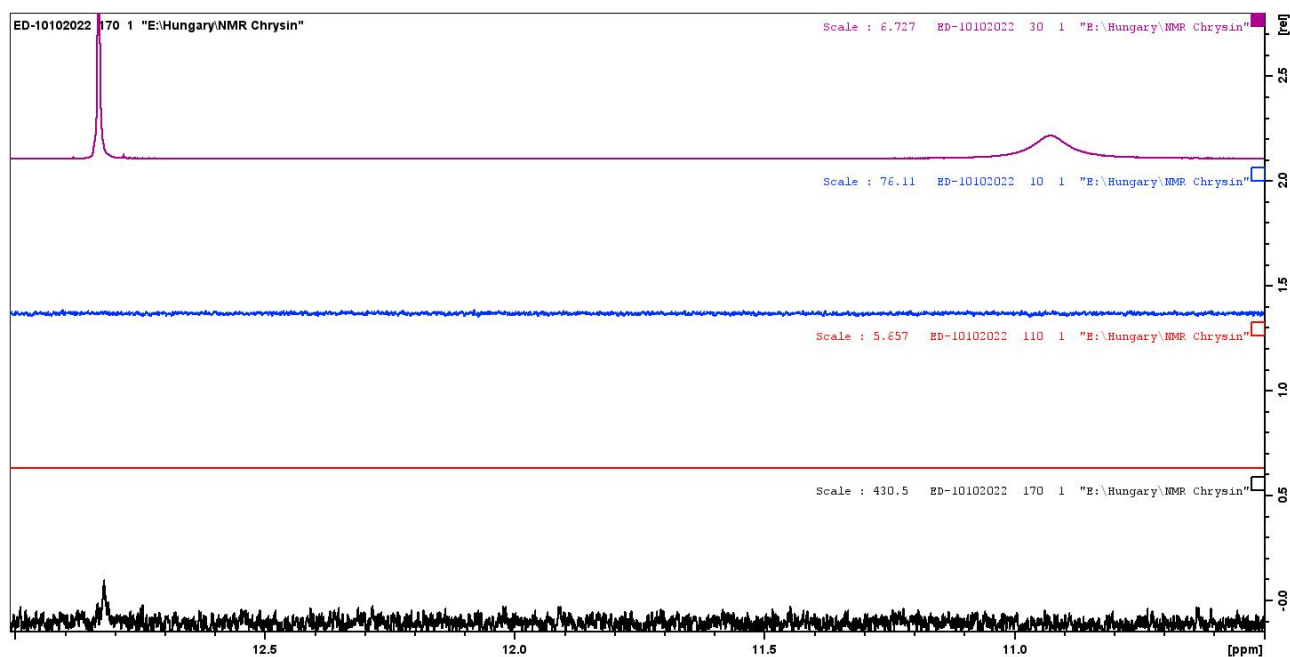


Figure S12. Expanded area of ^1H NMR spectra of CHR-OTX008-SBEDD mixture (Black line), OTX008 (Red line) SBEDD (B, Blue line) and CHR (Purple line) in DMSO-d_6 .

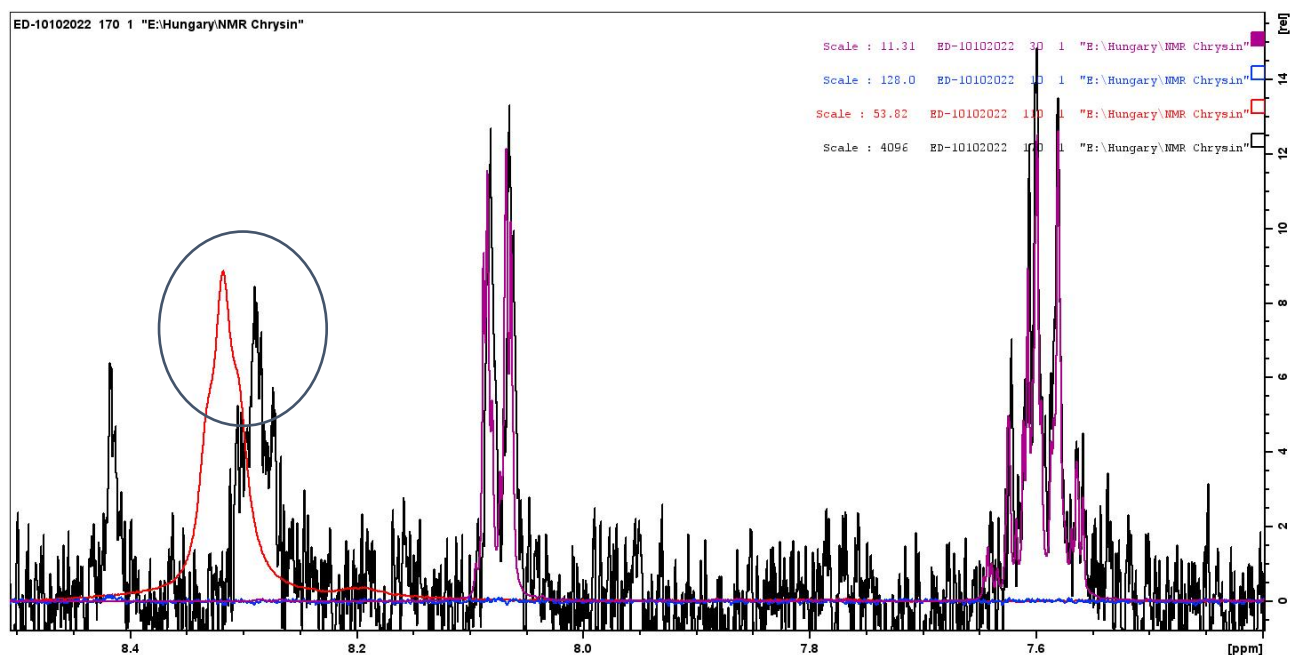


Figure S13. Expanded area of ^1H NMR spectra of CHR-OTX008-SBECD mixture (Black line), OTX008 (Red line) SBECD (B, Blue line) and CHR (Purple line) in DMSO-d_6 .

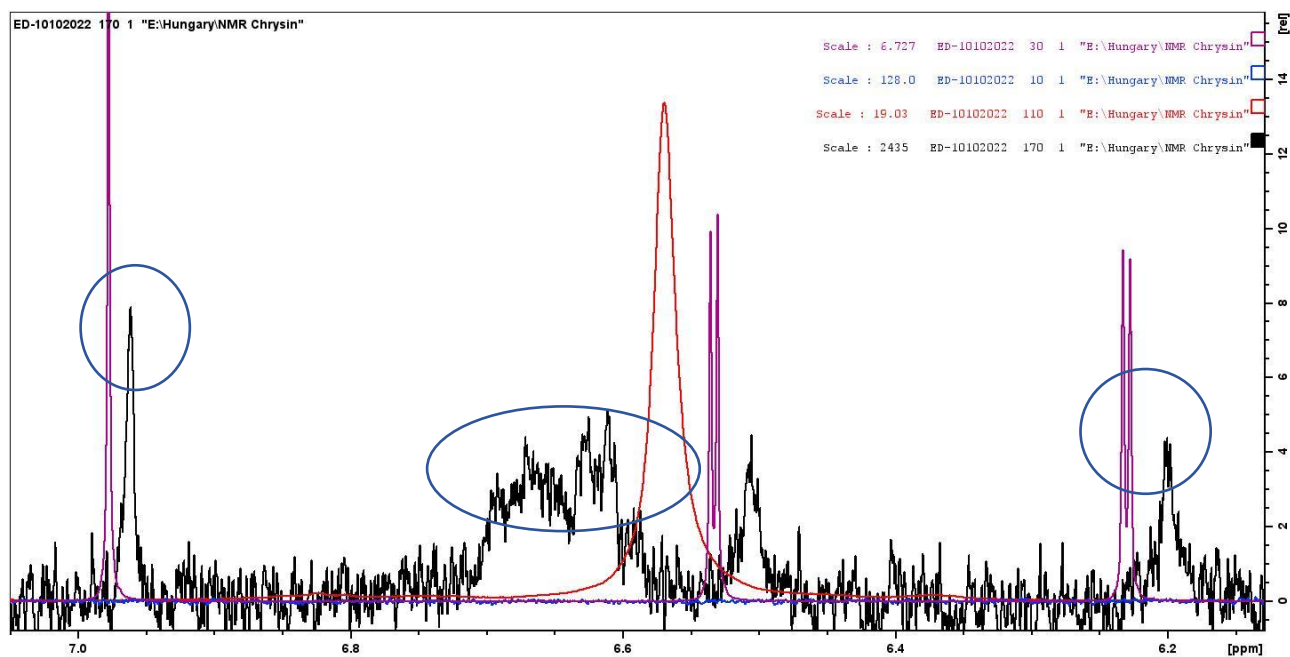


Figure S14. Expanded area of ^1H NMR spectra of CHR-OTX008-SBECD mixture (Black line), OTX008 (Red line) SBECD (B, Blue line) and CHR (Purple line) in DMSO-d_6 .

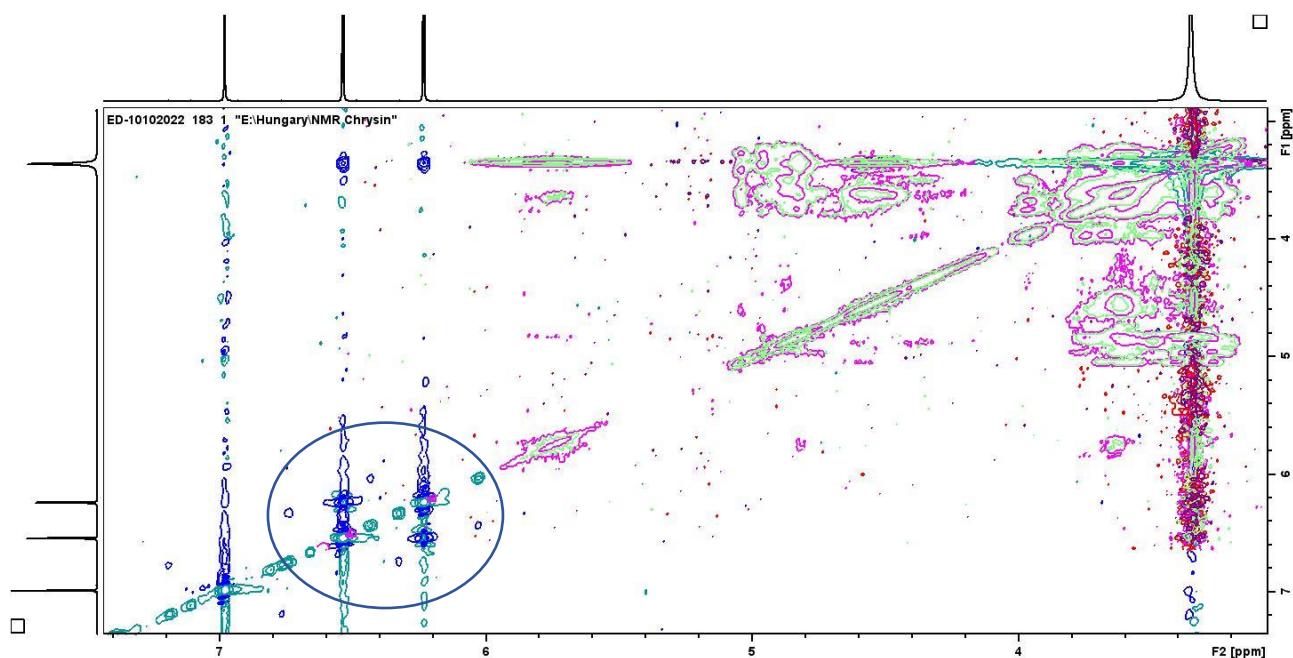


Figure S15. Comparison of NOESY spectra of CHR (Blue/Dark green line), CHR-OTX008-SBECD mixture (purple line) and binary CHR-SBECD mixture (Light green line) in DMSO- d_6 . The framed parts of the spectrum shown the presense of CHR molecules in a different situation when it is in ternary mixture.

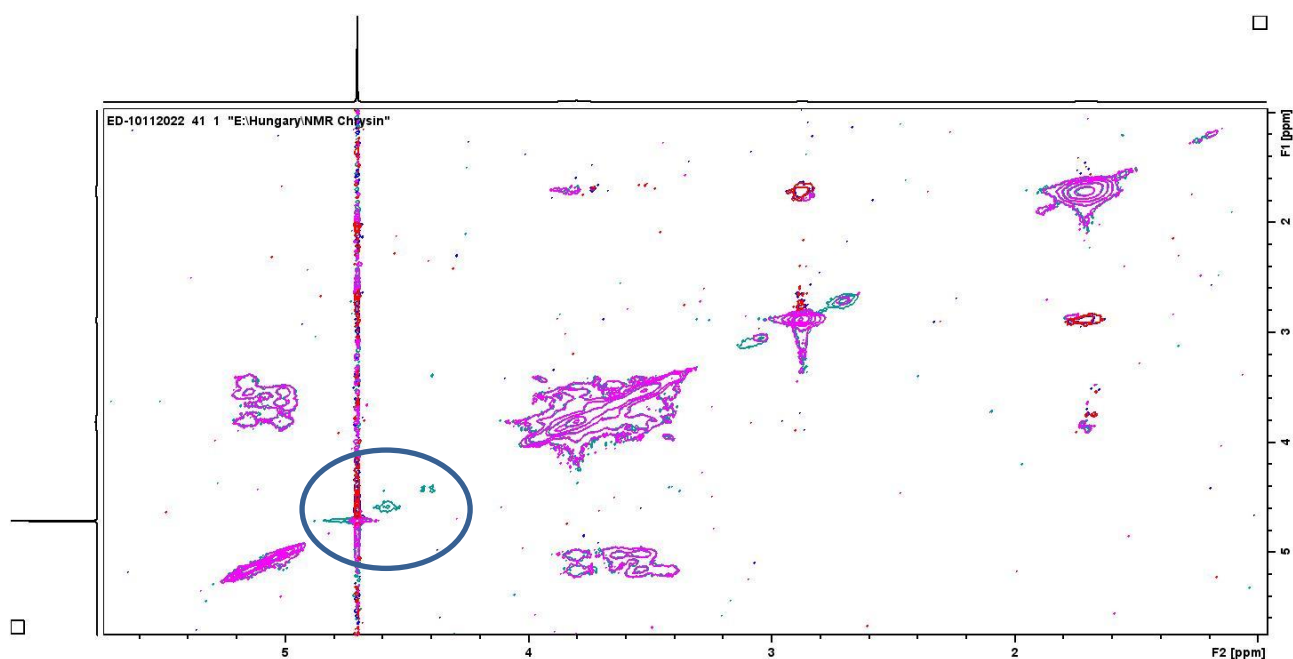


Figure S16. NOESY spectra CHR-OTX008-SBECD mixture (Black line) and SBECD (Red line) in D_2O showing the presense of CHR and OTX008 in the ternary structure.

Table S1. Results of thermal analysis.

Samples and mixtures	T _m	T _d
CHR	290	-
OTX1008	218	306
SBECD	272	281
Binary CHR- SBECD	272, 362	281
Binary OTX008- SBECD	290, 362	299
Ternary mixture CHR- OTX008- SBECD	293	300

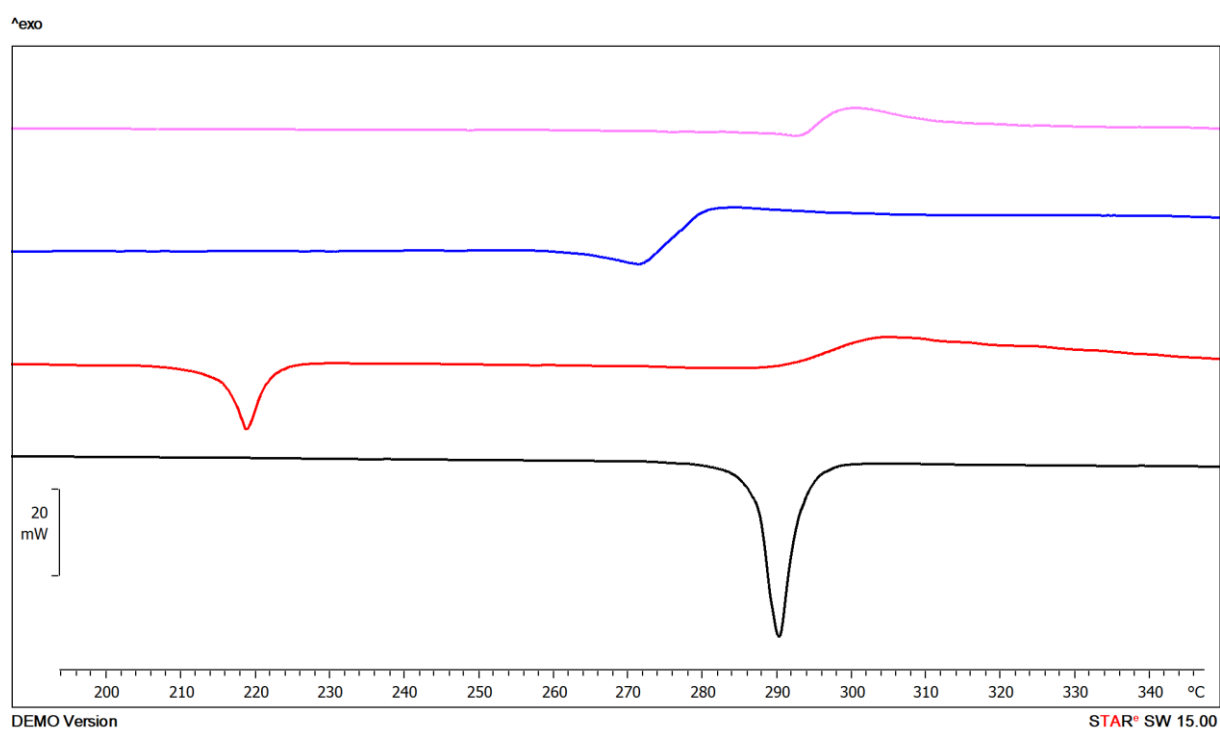


Figure S17. Zoomed view of DSC thermograms of CHR (Black line), OTX008 (Red line), SBECD (Blue line) CHR-OTX008-SBECD (Purple line), at 190-350 °C, 10 °C/min, inert N₂.

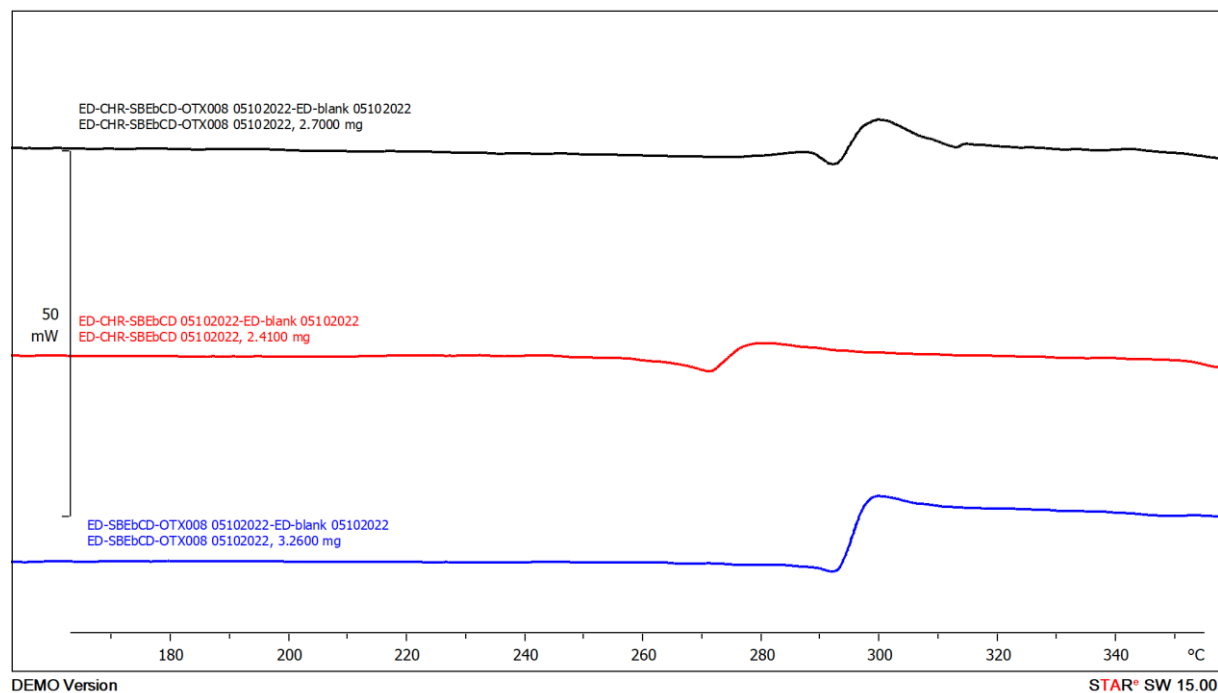


Figure S18. Comparison of zoomed areas of DSC thermograms of SBECD-OTX008 mixture (Blue line), SBECD-CHR mixture (Red line) and CHR-SBECD-OTX008 mixture (Black line), at 160-350 °C, 10 °C/min, inert N₂.

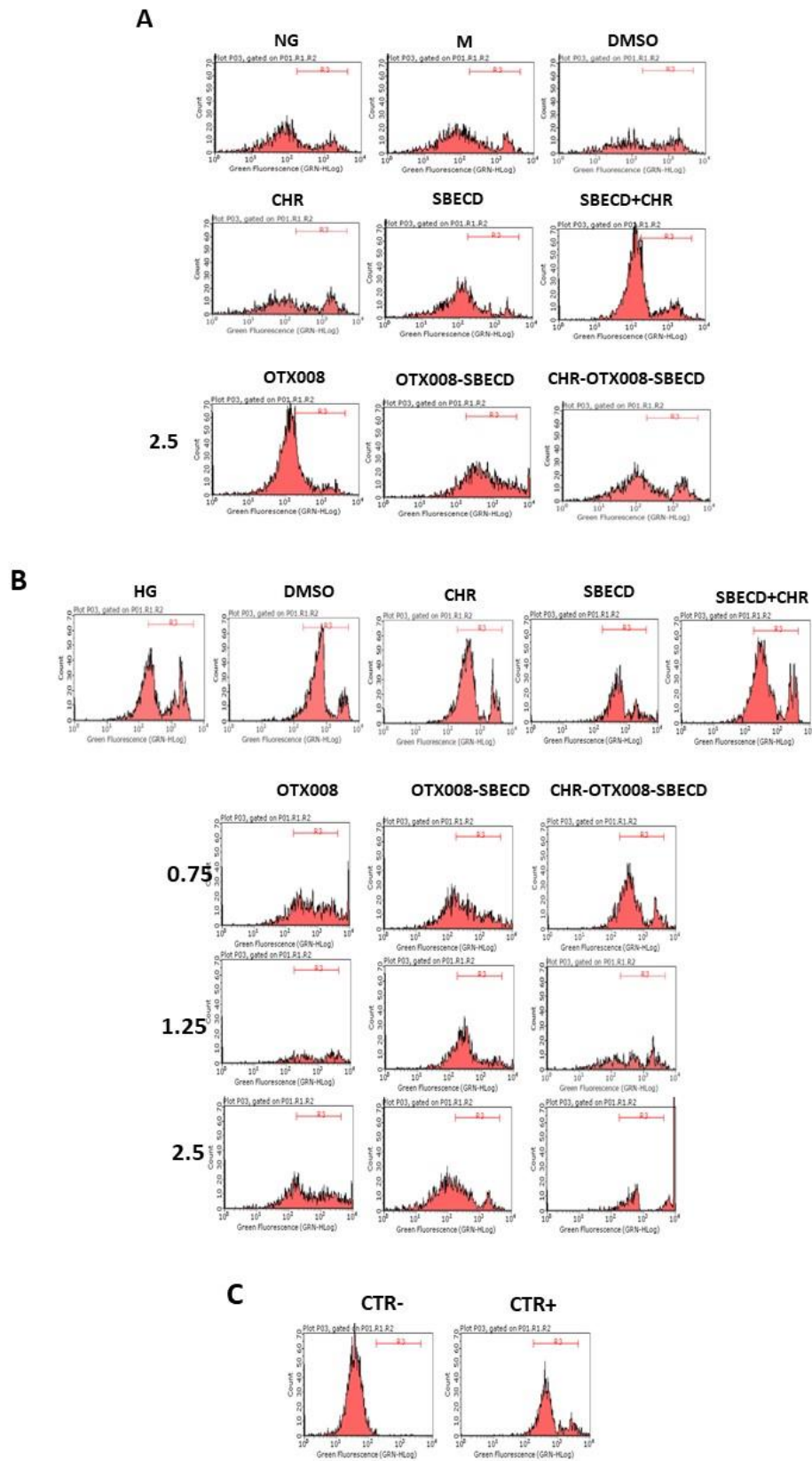


Figure S19. (A) Representative flow cytometer measures of total intracellular ROS levels assayed with DCFH-DA probe in NG or (B) HG medium. In NG cells, OTX008 was tested at

the maximum dose of 2.5 μM . In HG cells, OTX008 was tested at the doses of 2.5-1.25-0.75 μM ; (C) CTR $^-$ = negative control (5% FBS without DCFH-DA); CTR $^+$ = positive control (H₂O₂ 100 μM). R3 region = DCFH-DA-positive cells.

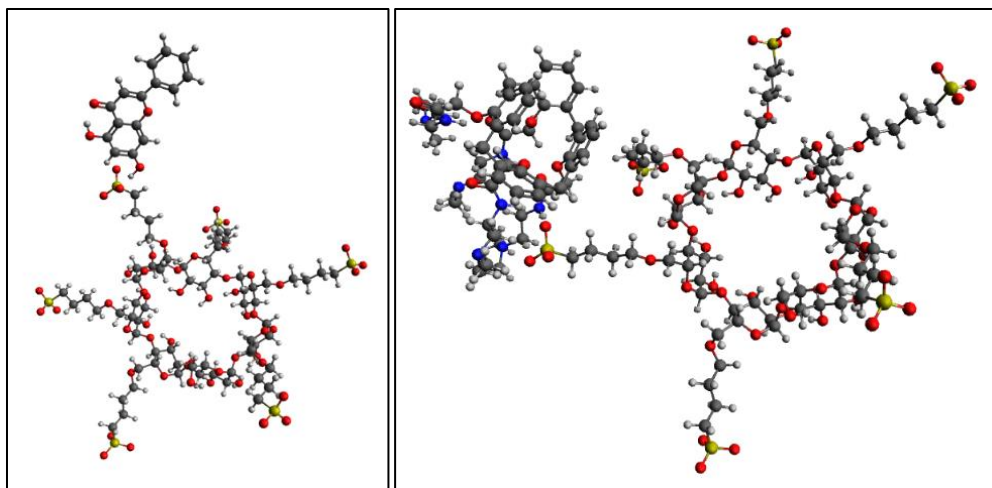


Figure S20. Interactions between SBECD and CHR (A). Interaction between OTX008 and SBECD (B).