SUPPORTING INFORMATION

Activated Microglia Targeting Dendrimer-minocycline Conjugate as Therapeutics for Neuroinflammation

Rishi Sharma[1], Soo-Young Kim[1], Anjali Sharma[1], Zhi Zhang[3], Siva Pramodh Kambhampati[1], Sujatha Kannan[1,3,4,5], Rangaramanujam M Kannan[1,2,4,5]

[1]*Center for Nanomedicine, Department of Ophthalmology, Wilmer Eye Institute Johns Hopkins University School of Medicine, Baltimore, MD 21231, USA;*

[2]*Department of Chemical and Biomolecular Engineering, Johns Hopkins University, Baltimore MD, 21218, USA;*

[3]*Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA;*

[4]*Hugo W. Moser Research Institute at Kennedy Krieger, Inc., Baltimore MD, 21205, USA;*

[5]*Kennedy Krieger Institute – Johns Hopkins University for Cerebral Palsy Research Excellence, Baltimore, MD 21218, USA;*

[*]Corresponding author:

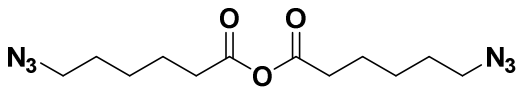
Rangaramanujam M. Kannan, Arnall Patz Distinguished Professor of Ophthalmology, Center for Nanomedicine at the Wilmer Eye Institute, 400 North Broadway, Baltimore, Maryland 21231, USA

Tel.: +1 443-287-8634; Fax: +1 443-287-8635; e-mail: krangar1@jhmi.edu

Contents

1. Characterization data of intermediates and dendrimer conjugates

Compound 3:



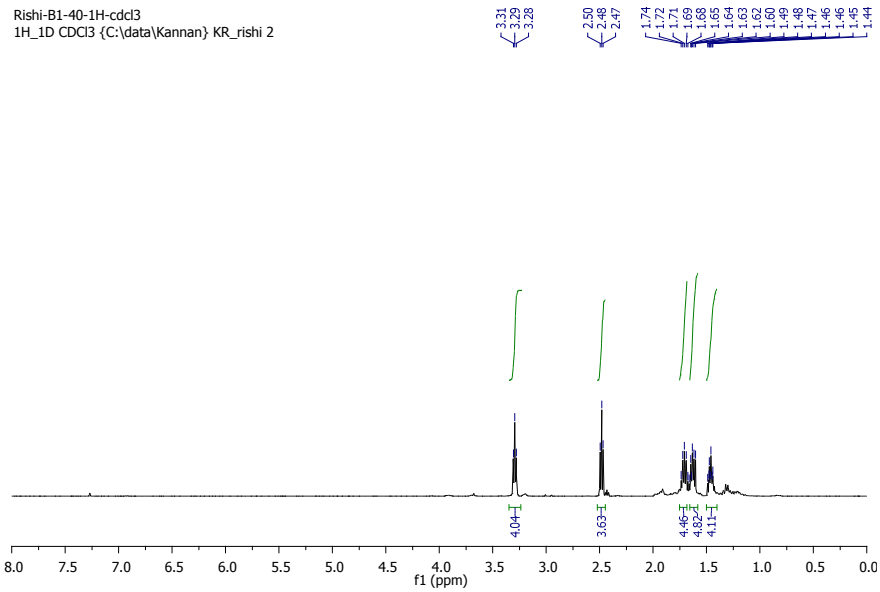


Figure S1. ^{1}H NMR spectrum of compound **3** ($CDCl_3$, 500 MHz).

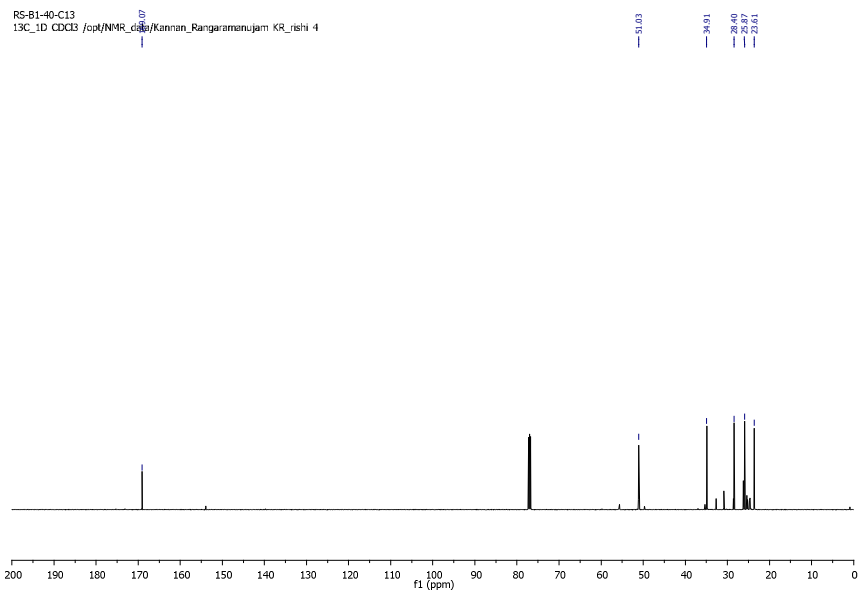
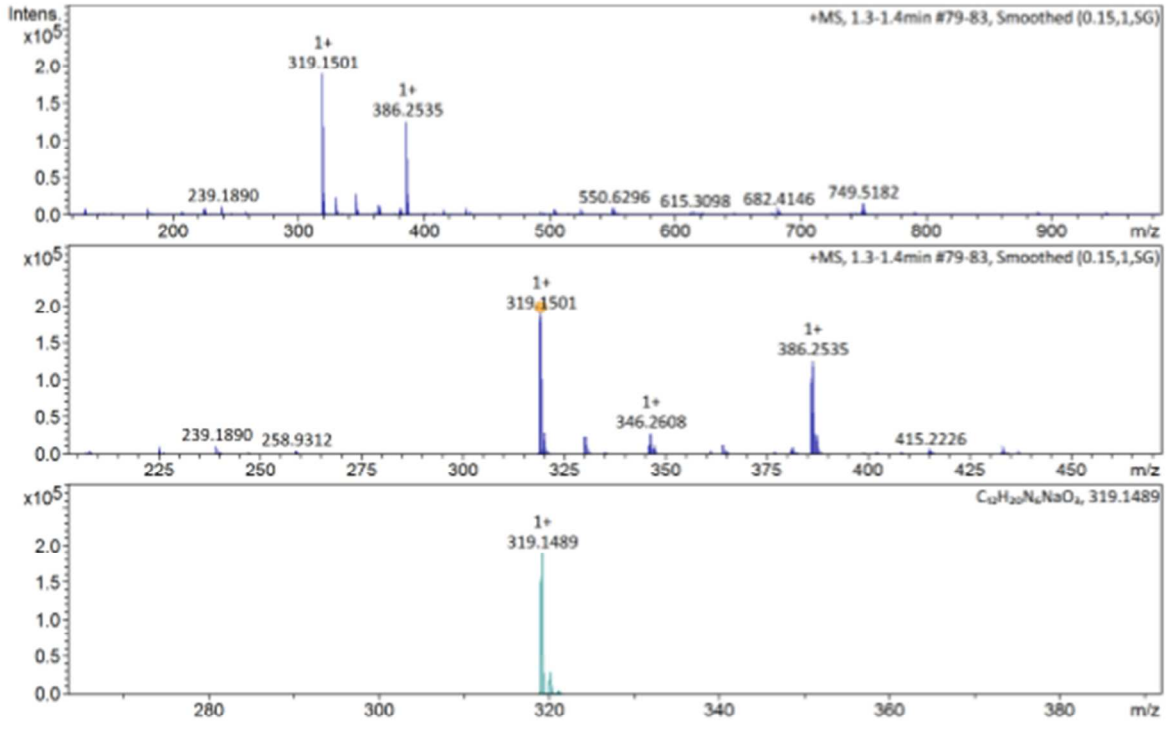


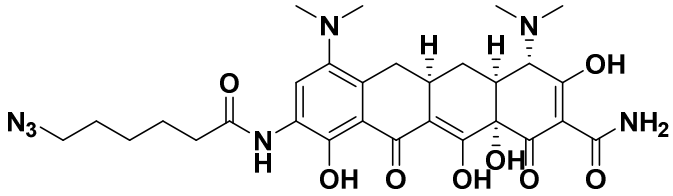
Figure S2. $^{13}C\{^{1}H\}$ NMR of compound **3** ($CDCl_3$, 75 MHz).



Meas. m/z	#	Ion Formula	m/z	err [ppm]	Mean err [ppm]	rdb	N-Rule	e⁻ Conf	mSigma	Std I	Std Mean m/z	Std I VarNorm	Std m/z Diff	Std Comb Dev
319.150116	1	C12H20N6NaO3	319.148909	-3.8	-5.4	5.5	ok	even	3.4	5.9	n.a.	n.a.	n.a.	n.a.

Figure S3. HRMS (ESI^+) spectrum of compound **3**.

Compound 5:



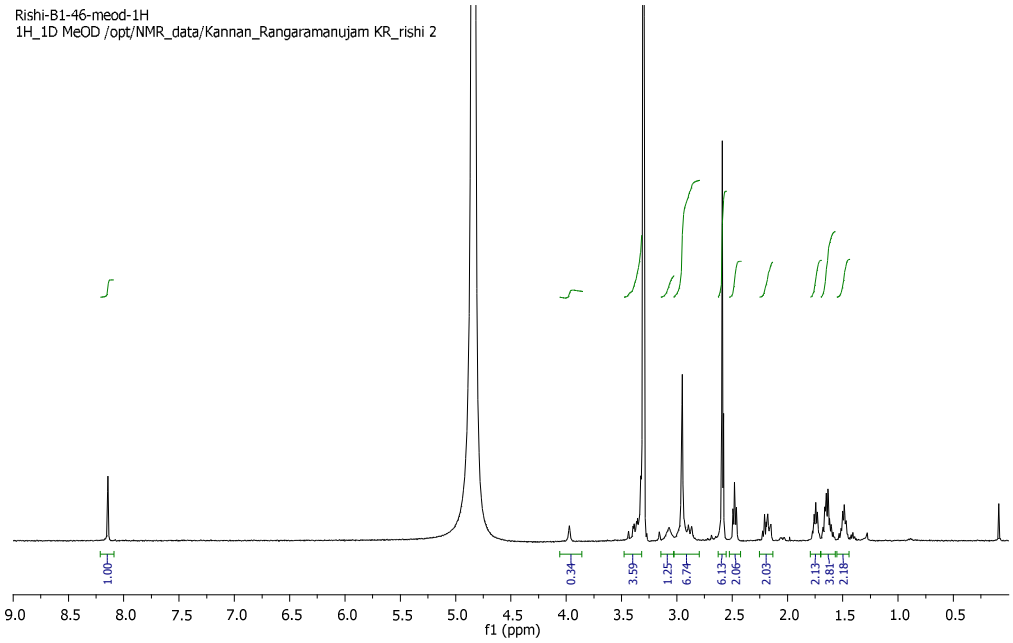


Figure S4. ^{1}H NMR spectrum of compound **5** (CD_3OD, 500 MHz).

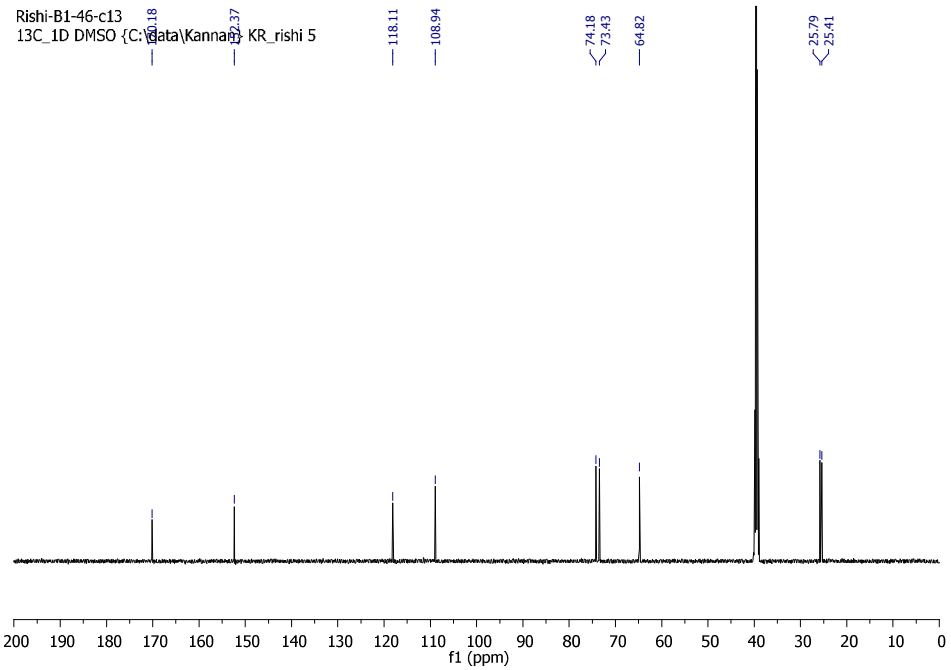
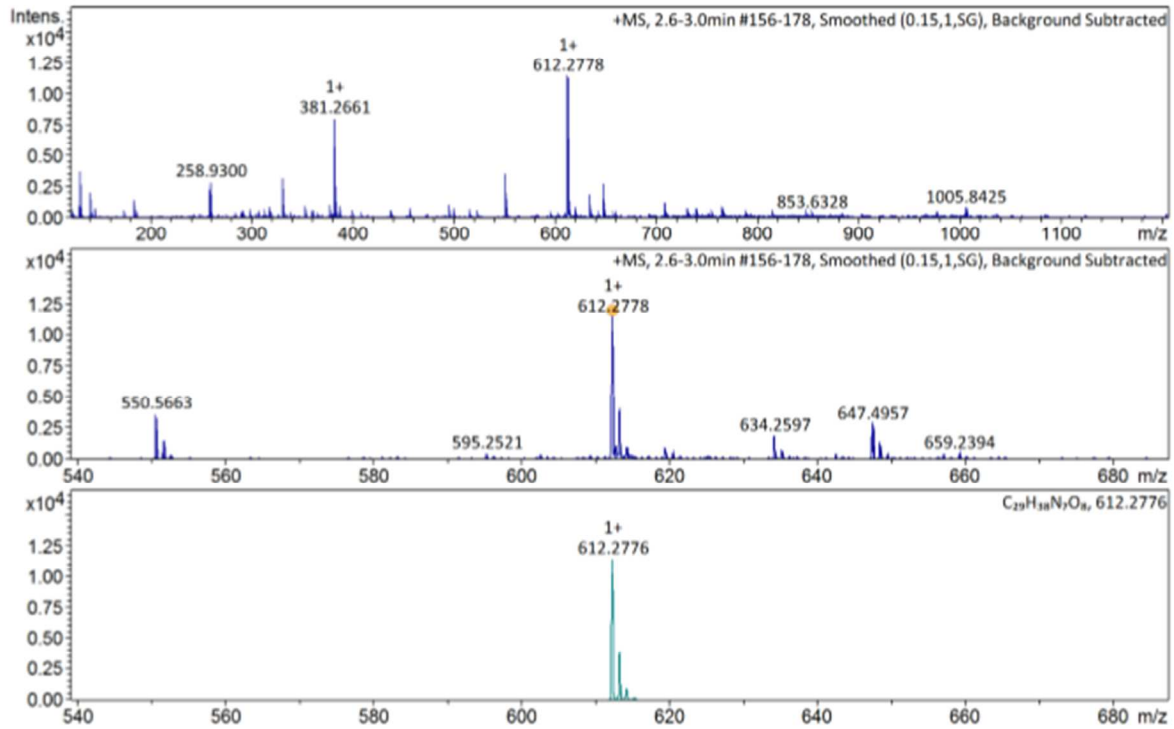
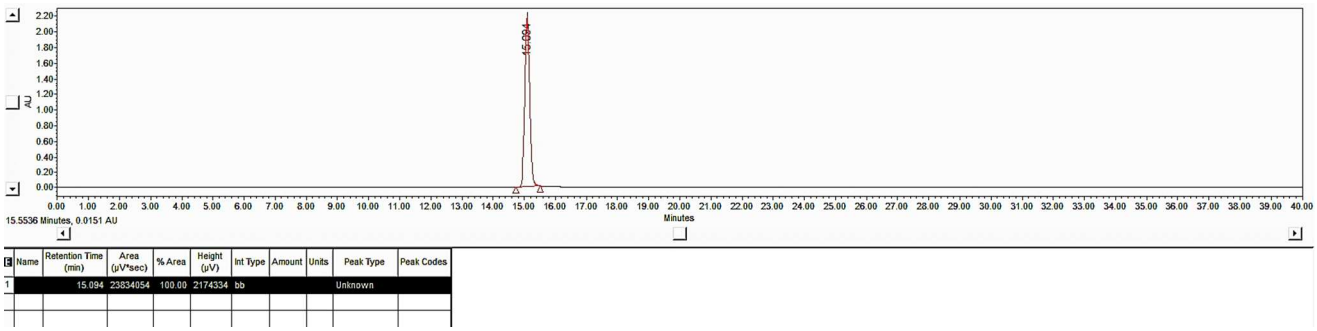


Figure S5. ^{13}C {^{1}H} NMR of compound **5** (DMSO, 75 MHz)



Meas. m/z	#	Ion Formula	m/z	err [ppm]	Mean err [ppm]	rdb	N-Rule	e⁻ Conf	mSigma	Std I a	Std Mean m/z	Std I VarNorm	Std m/z Diff	Std Comb Dev
612.277819	1	C29H38N7O8	612.277638	-0.3	796.2	14.5	ok	even	9.5	13.0	n.a.	n.a.	n.a.	n.a.

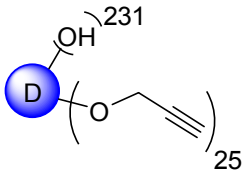
Figure S6.HRMS (ESI+) spectrum of compound **5**



	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		15.094	23834054	100.00	2174334	bb			Unknown	

Figure S7. HPLC trace of compound **5**

Compound 7:



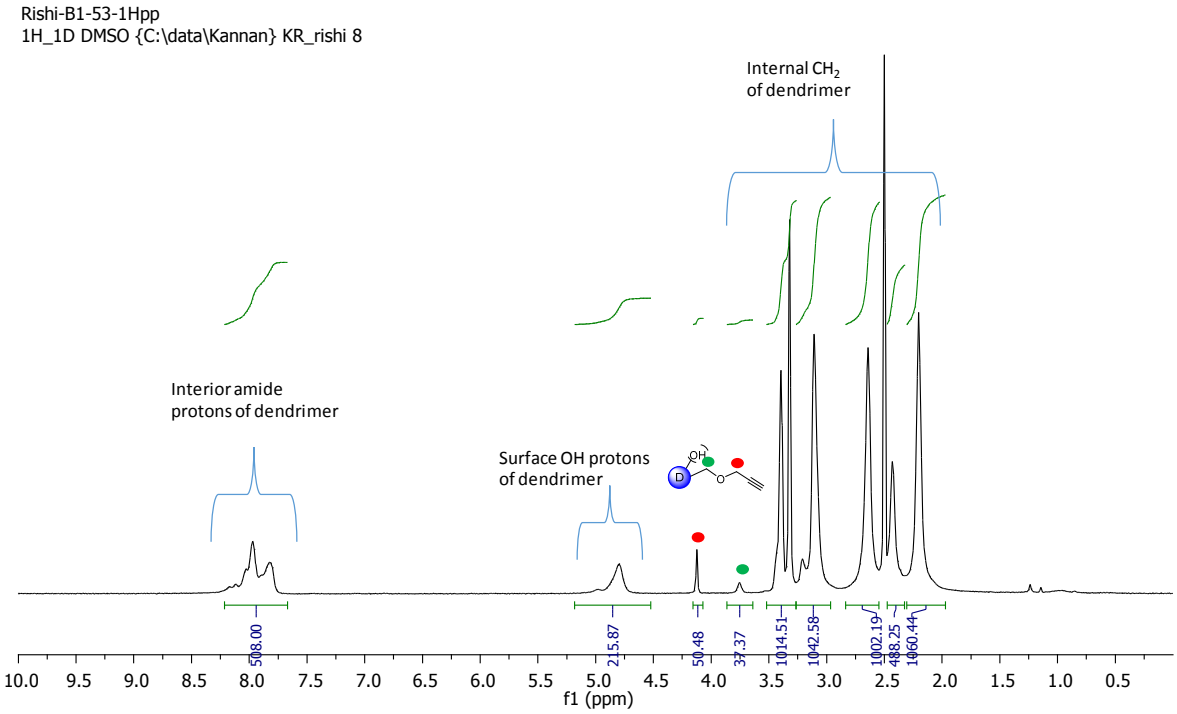
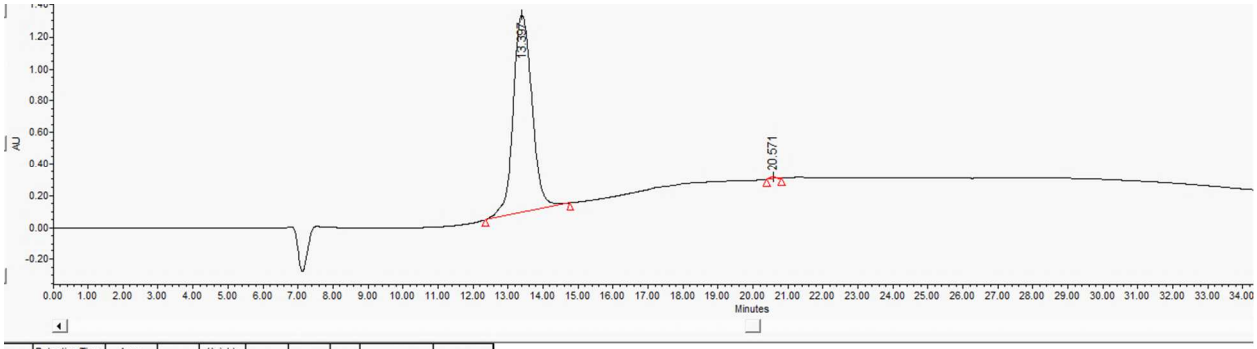


Figure S8. ^{1}H NMR spectrum of compound **7** (DMSO, 500 MHz).



Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
	13.397	46324193	99.70	1238265	bb			Unknown	
	20.571	137515	0.30	12626	bb			Unknown	

Figure S9. HPLC trace of compound **7**.

Compound 8:

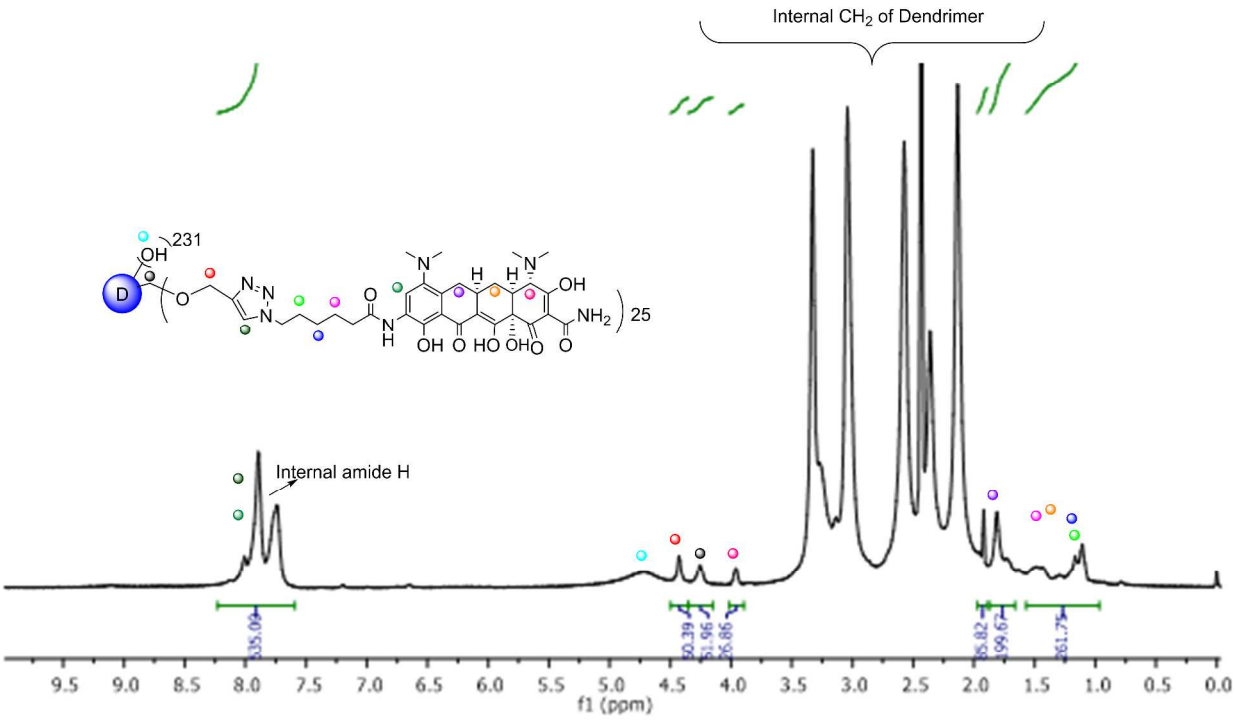


Figure S10. ^{1}H NMR spectrum of compound **8** (DMSO, 500 MHz).

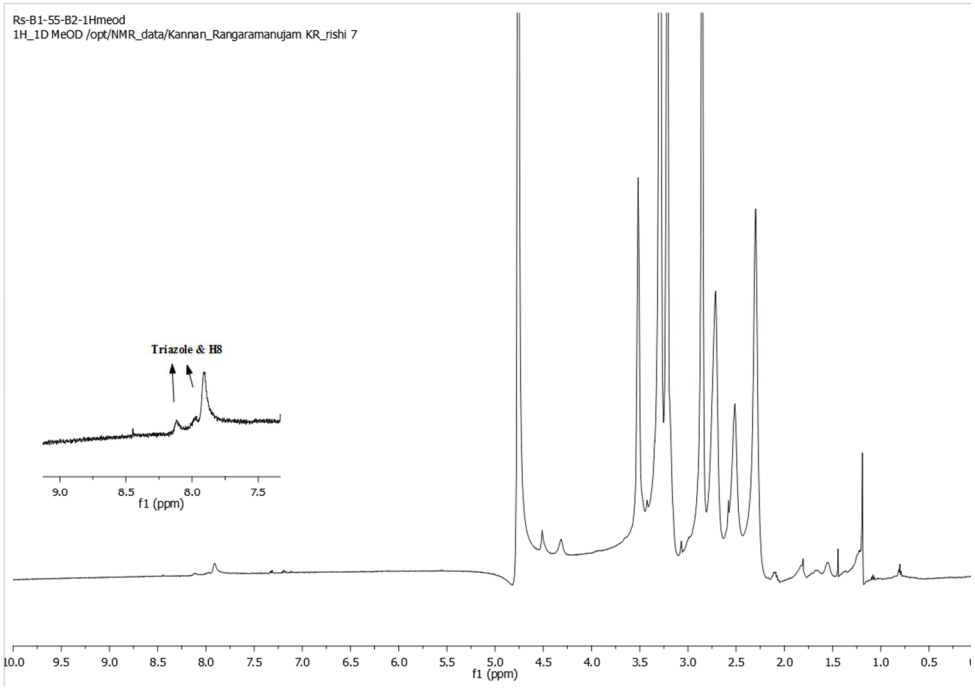


Figure S11. ^{1}H NMR spectrum of compound **8** (CD_3OD, 500 MHz).

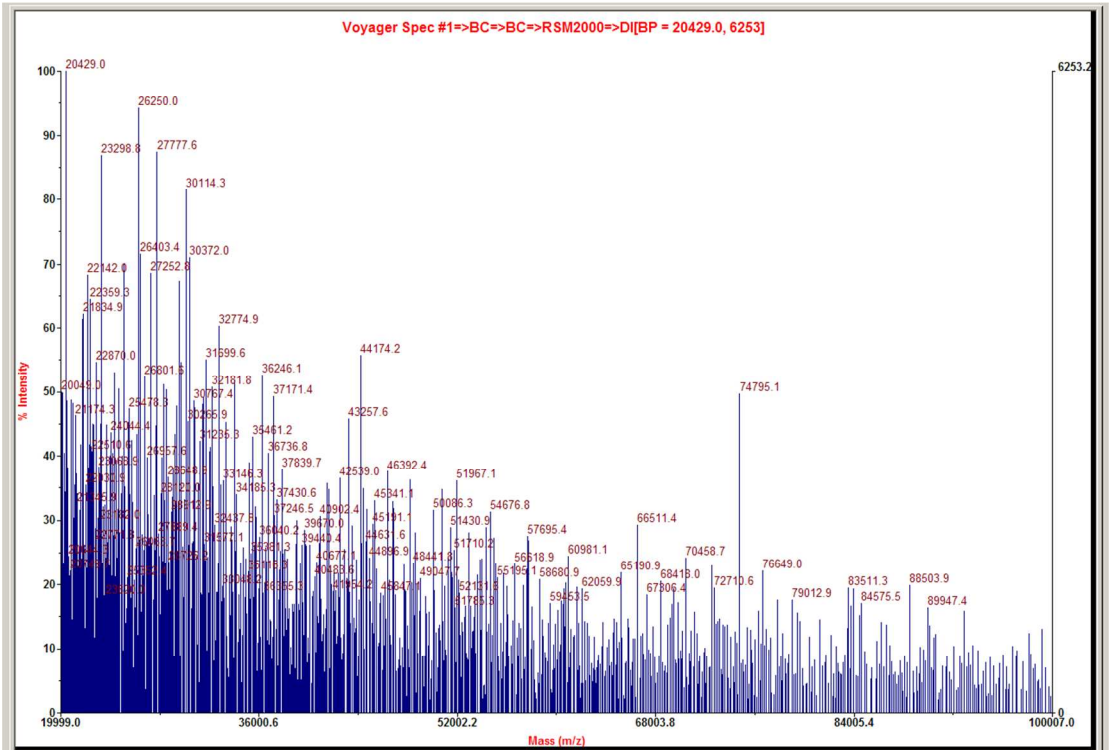
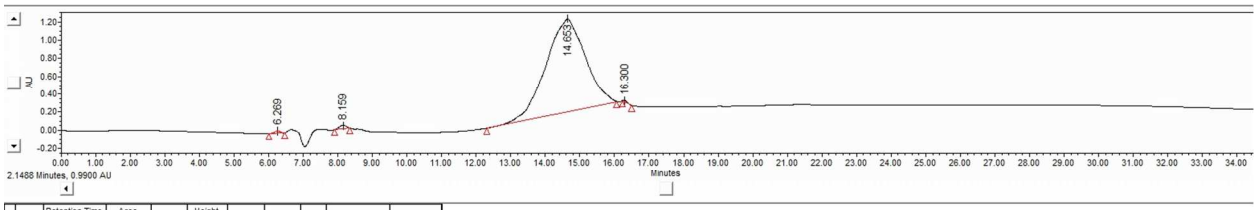
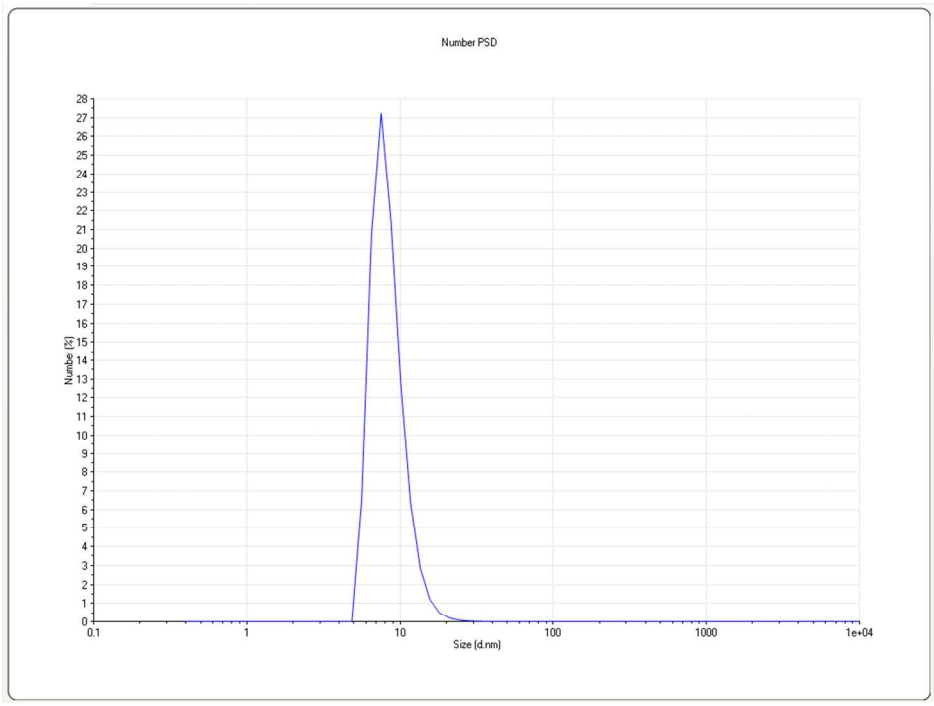


Figure S12. MALDI-TOF trace for compound **8** (DHB matrix).



	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		6.269	293988	0.36	27489	bb			Unknown	
2		8.159	552829	0.67	37262	bb			Unknown	
3		14.653	81805372	98.82	1027995	bb			Unknown	
4		16.300	129372	0.16	17794	bb			Unknown	I08

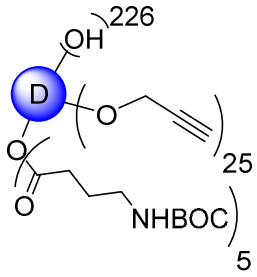
Figure S13. HPLC trace of compound **8**.



Mean 2,4,5				25.0	49.41	8.279	115.8	12.93	0.536	182.3
Std Dev				0.0	4.170	0.6453	16.16	1.294	0.006	4.6

Figure S14. DLS size distribution of dendrimer **8** in water at 25°C.

Compound 9:



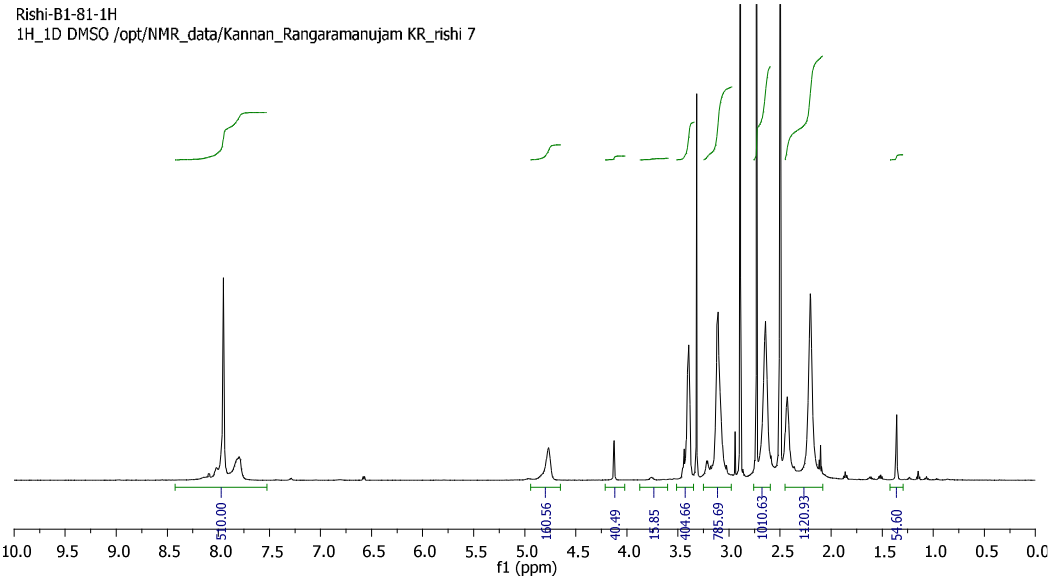


Figure S15. ^{1}H NMR spectrum of compound **9** (DMSO, 500 MHz).

Compound 11:

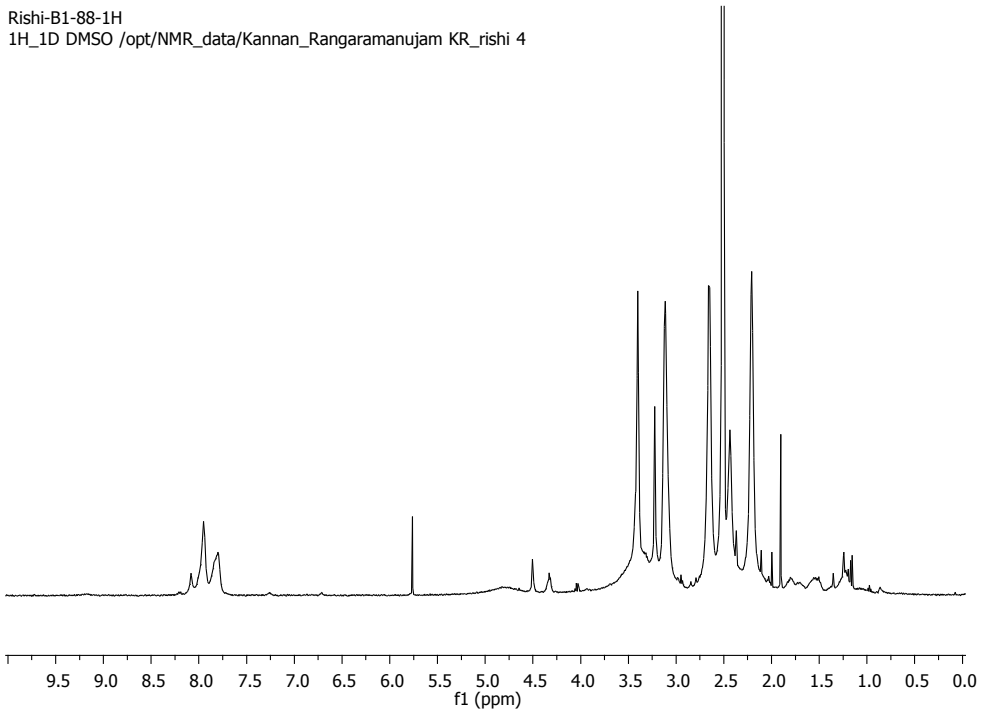
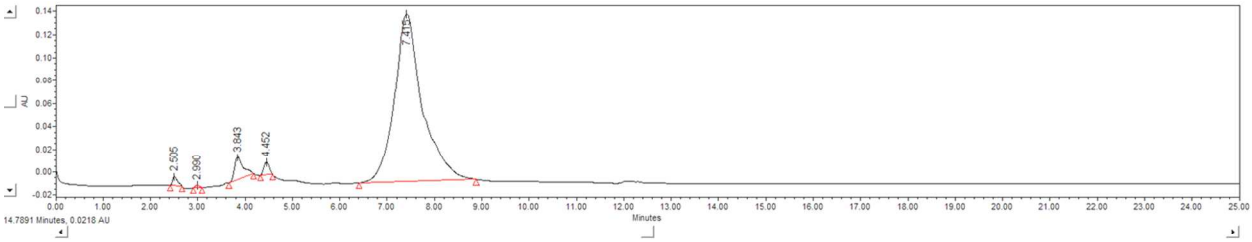


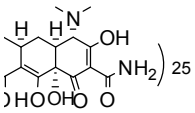
Figure S16. ^{1}H NMR spectrum of compound **11** (DMSO, 500 MHz).



Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
	2.505	56147	0.88	7752	bb			Unknown	
	2.990	11721	0.18	2111	bb			Unknown	
	3.843	242914	3.82	19372	bb			Unknown	
	4.452	86845	1.37	10970	bb			Unknown	
	7.415	5954854	93.74	145424	bb			Unknown	

Figure S17. HPLC trace of compound **11**.

Compound 12:



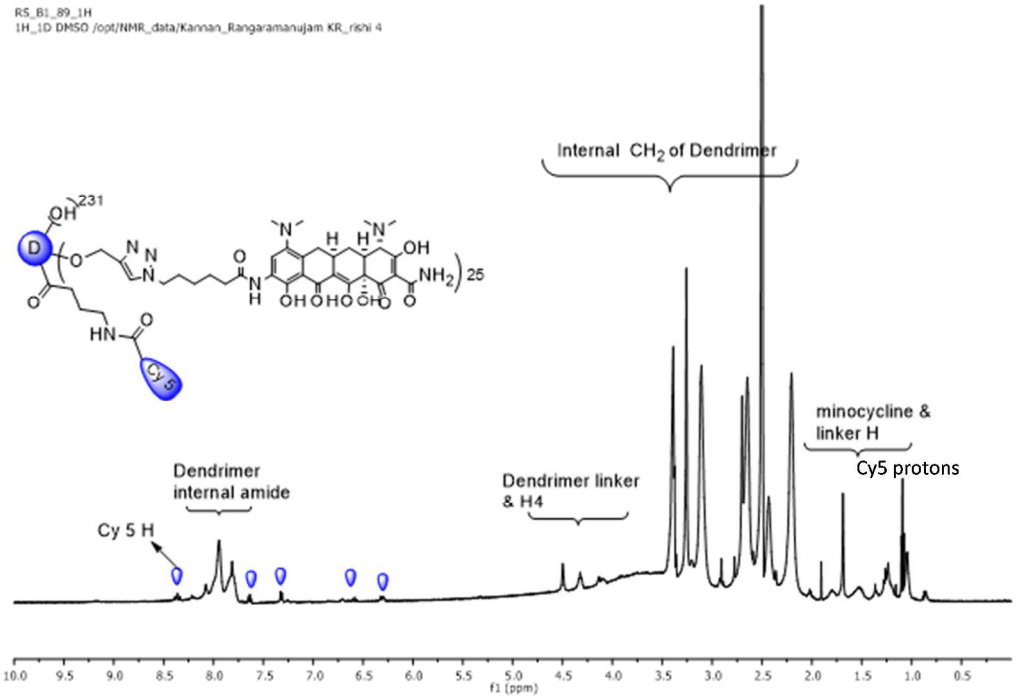
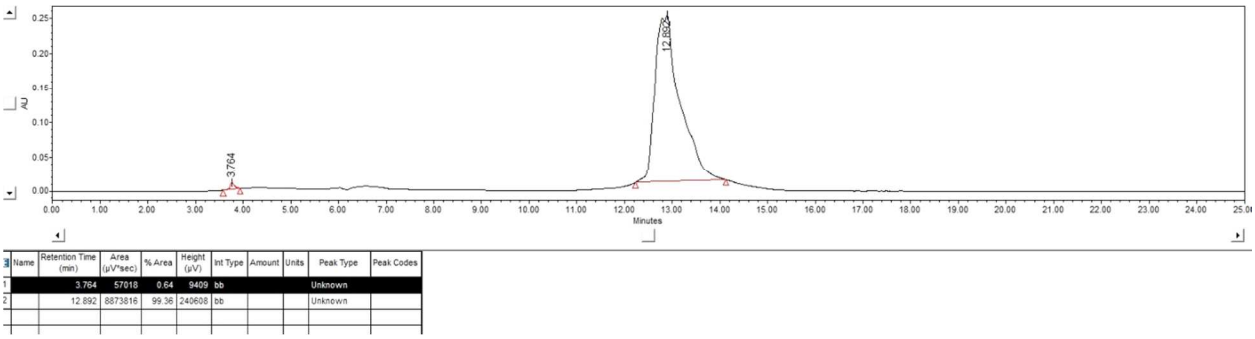


Figure S18. ^{1}H NMR spectrum of compound **12** (DMSO, 500 MHz).



Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
	3.764	57018	0.64	9409	bb			Unknown	
	12.892	8873816	99.36	240608	bb			Unknown	

Figure S19. HPLC trace of compound **12** at 650 nm.