

Supporting Information

Design, Synthesis and Evaluation of Novel Ferulic Acid Derivatives as Multi Target Directed Ligands for the Treatment of Alzheimer's Disease

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Representative ^1H , ^{13}C NMR, and HR-ESI-MS spectra for the synthesized compounds

Table S1. MNLC of TM-10 determination (N=30)

Group	Concentration ($\mu\text{g/mL}$)	Death number	Mortality (%)
Untreated	-	0	0
Vehicle	-	0	0
	3.125	0	0
	6.25	30	100
TM-10	12.5	30	100
	25	30	100
	50	30	100
	100	30	100

Table S2. Incidences (%) of acute toxicity manifestations in zebrafish larvae (N = 30)

Common Defects	Untreated	Vehicle	μg/mL			
			0.35	1.04	3.125	4
Heart	Pericardial edema	-	-	-	10	30
	Bradycardia	-	-	-	-	-
Circulation	Absent blood flow	-	-	-	-	33.3
	Slow blood flow	-	-	-	-	-
Brain	□Hemorrhage/ thrombosis	-	-	-	-	-
	Small or misshapen	-	-	-	-	-
Jaw	Short or misshapen jaw	-	-	-	-	-
Eye	Small or misshapen eye(s)	-	-	-	-	-
	Absent	-	-	-	-	-
	Abnormal size	-	-	-	-	-
Liver	Presence of dark brown,	-	-	-	-	-
	Yolk sac absorption delay	-	-	-	30	80
Kidney	Edema	-	-	-	-	13.3
Intestine	Abnormal	-	-	-	-	-
Trunk /tail/notochord	Abnormal	-	-	-	-	-
Trunk muscle/ somite	Degenerating muscle within the somites	-	-	-	-	-
	Pigmentation, Abnormal	-	-	-	-	-
Pigmentation, Body shape	Body shape	-	-	-	-	-
	Death	-	-	-	-	-

Table S3. MTC of TM-10 determination (n=30)

Group	Toxicity	Death number	Mortality (%)
Untreated	-	0	0
Model	-	0	0
1 µg/mL	-	0	0
2.5 µg/mL	3 roll over, 1 renal edema and pericardium edema	0	0
5 µg/mL	8roll over, 1 renal edema and pericardium edema	0	0
10 µg/mL	14roll over, 3 renal edema and pericardium edema	0	0
25 µg/mL	-	30	100
50 µg/mL	-	30	100
100 µg/mL	-	30	100
200 µg/mL	-	30	100

Table S4. Efficacy of TM-10 on vascular injury in zebrafish (n=15)

Group	Concentration (μ g/mL)	Vascular injury number	Vascular integrity number	Vascular injury rate	
				(%)	Efficecy (%)
Untreated	-	0	15	0	-
Model	-	11	4	73	-
	0.11	12	3	80	-9
TM-10	0.33	10	5	67	9
	1	10	5	67	9

Representative ^1H , ^{13}C NMR, HR-ESI-MS and HPLC spectra for the synthesized compounds













