

	Observed Efficacy (µg/ml)
Age-Impaired Rats	1.9 – 3.9
aMCI	2.9 – 4.4

	No Efficacy (µg/mL)
Age-Impaired Rats	7.9
aMCI	8.0

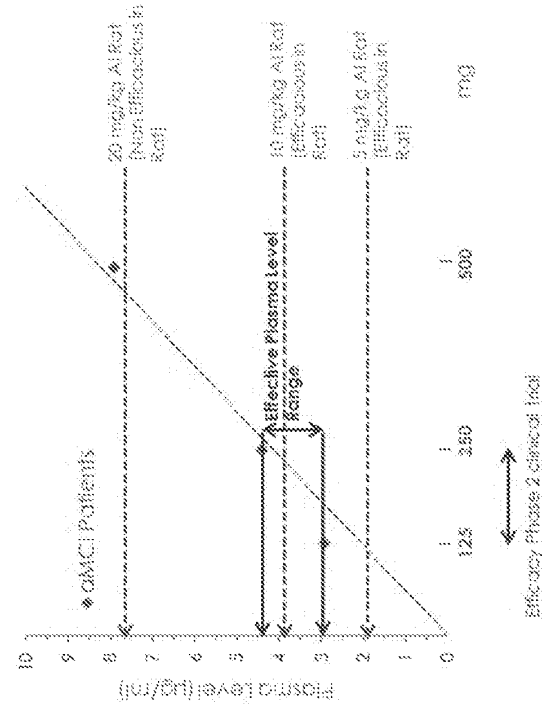


FIG. 1

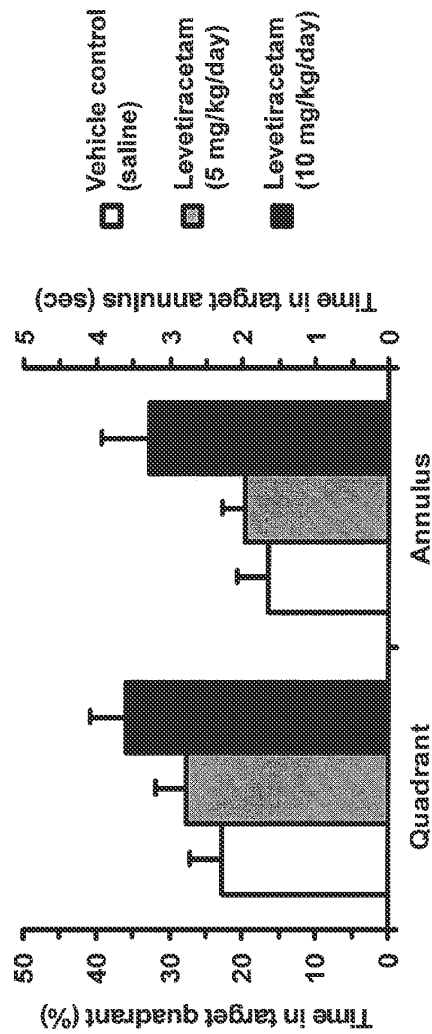
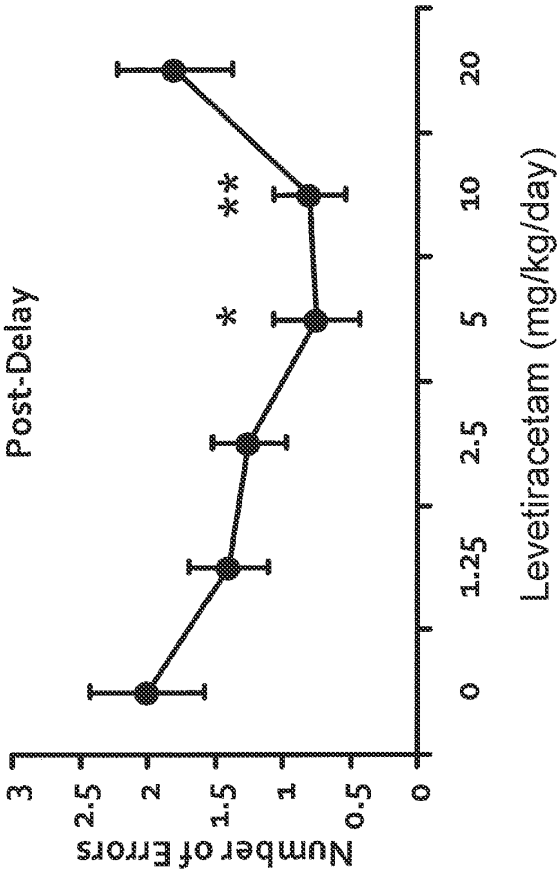


FIG. 2



* $t(9) = 2.18, p = 0.057$

** $t(9) = 2.37, p = 0.042$

FIG. 3

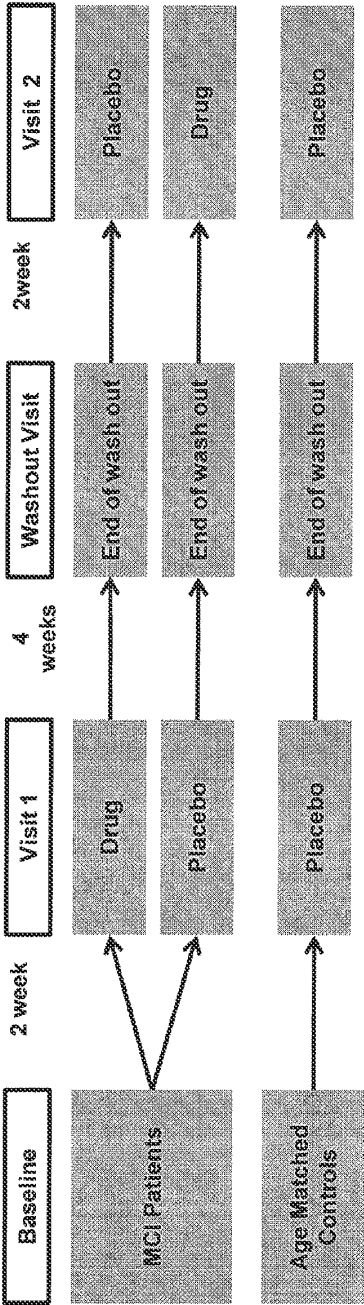


FIG. 4

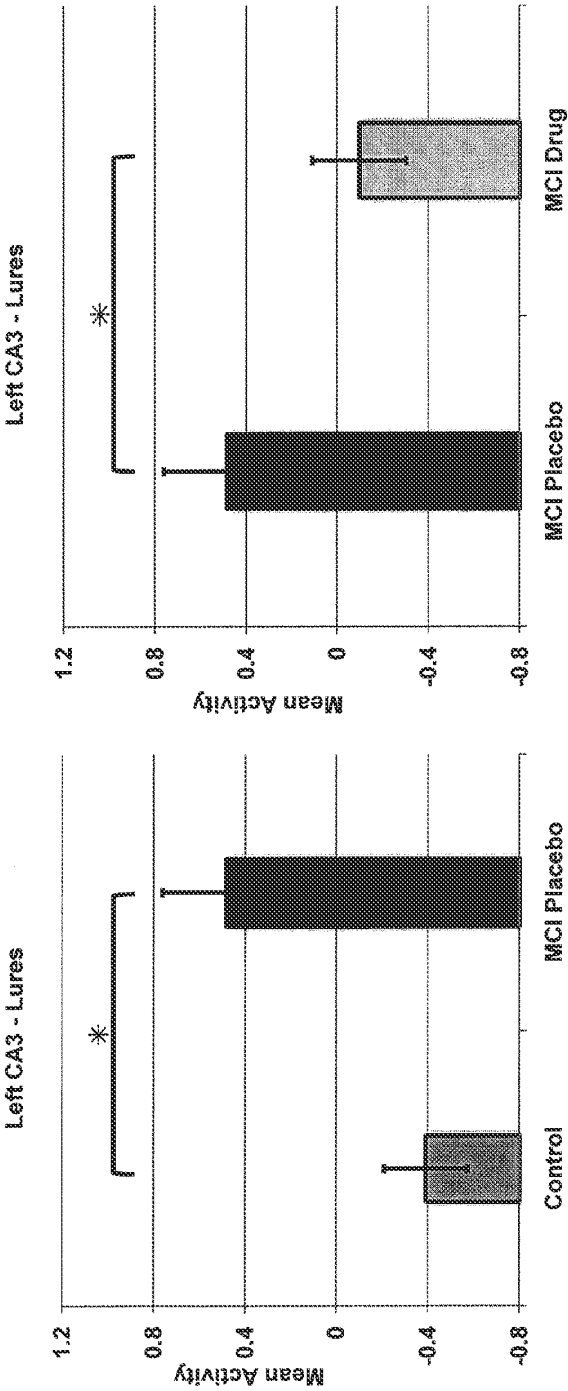


FIG. 5A

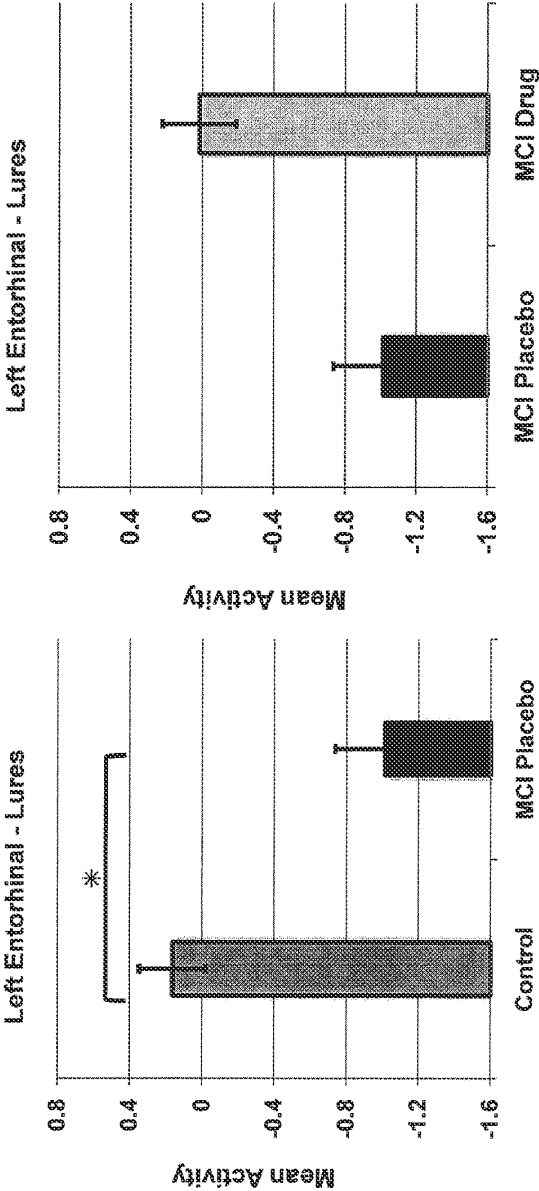
FIG. 5B

Left CA3 Lures

Group	Mean Activity	Standard Error
Control	-0.39129	0.182628
MCI Placebo	0.48440	0.277487
MCI Drug	-0.09653	0.205892

FIG. 5C

fMRI entorhinal activation in amnesic MCI is normalized by drug treatment



*Independent samples t-test: $t = 3.278$, $p = 0.003$

Paired samples t-test: $t = -1.600$, $p = 0.129$

FIG. 6A

FIG. 6B

Left Entorhinal Lures

Group	Mean Activity	Standard Error
Control	0.16444	0.143864
MCI Placebo	-1.01273	0.329062
MCI Drug	0.016291	0.411762

FIG. 6C

Reduced memory in task that taxes pattern separation

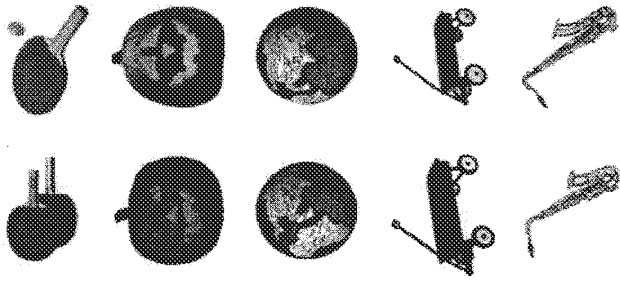


FIG. 7B

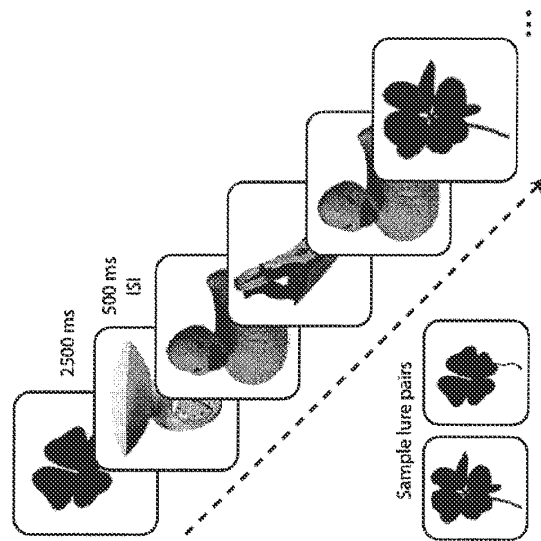
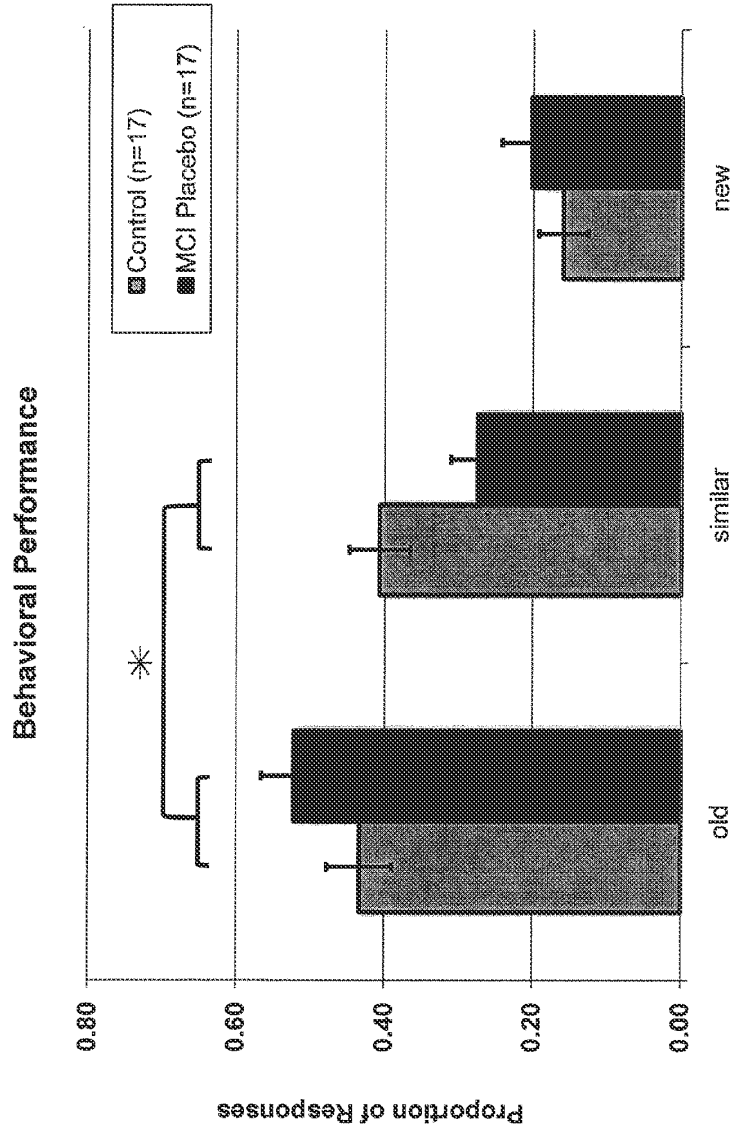


FIG. 7A



Control vs. MCI Placebo by Old vs. Similar: $F = 7.687, p = 0.009$

FIG. 8

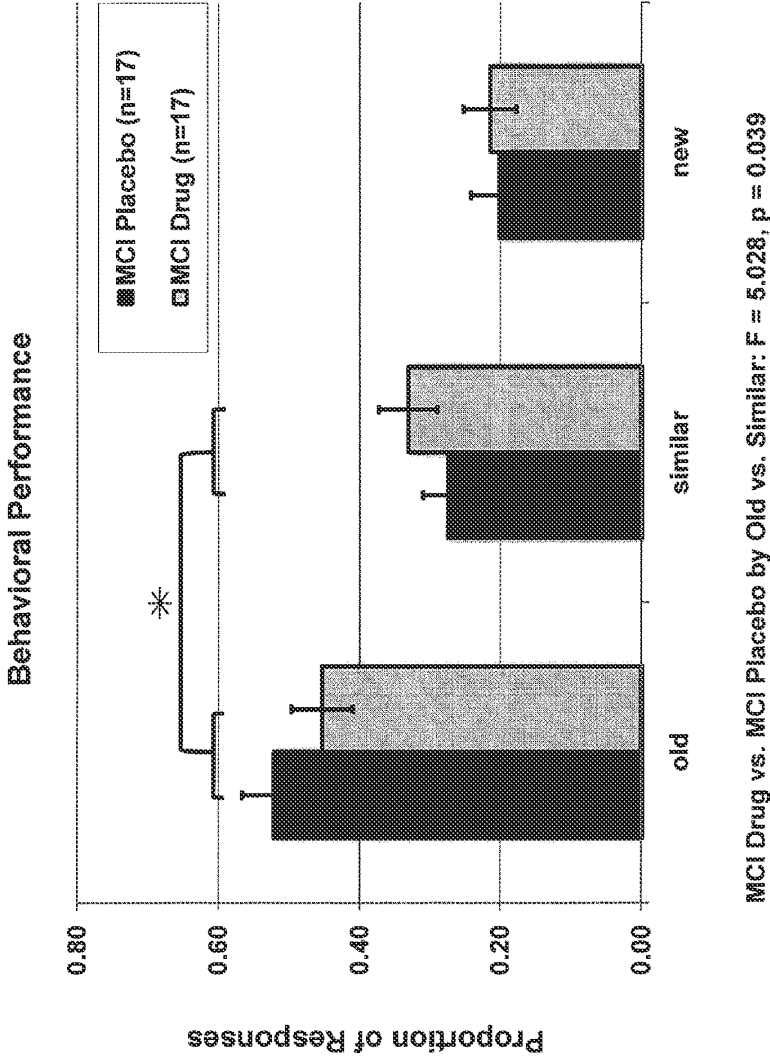
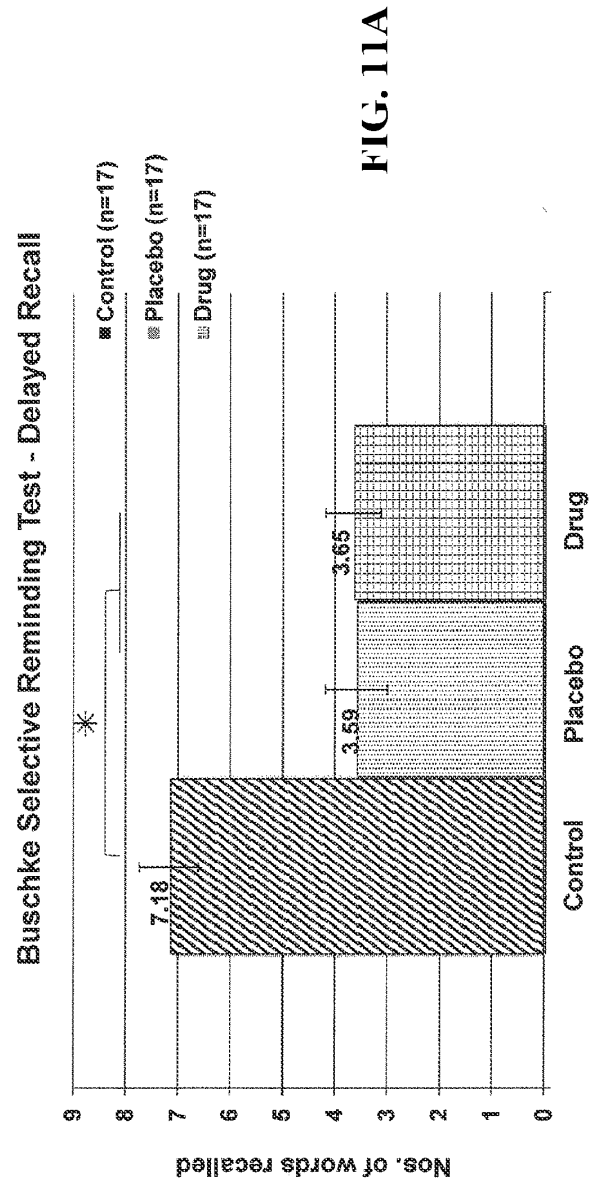


FIG. 9

Behavioral Performance

Control Subjects	Proportion of Responses	Standard Error
Old	0.433676	0.04426
Similar	0.406771	0.04135
New	0.159553	0.03312
MCI Placebo Subjects	Proportion of Responses	Standard Error
Old	0.52262	0.04871
Similar	0.27549	0.03956
New	0.20188	0.04528
MCI Drug Subjects	Proportion of Responses	Standard Error
Old	0.45361	0.04825
Similar	0.33144	0.04592
New	0.21494	0.04202

FIG. 10



Group	Mean	Standard Error	Delayed (p-value)
Control	7.18	0.56	Control vs. Placebo: <0.001
MCI Placebo	3.59	0.59	
MCI Drug	3.65	0.53	Placebo vs. Drug: 0.887

FIG. 11B

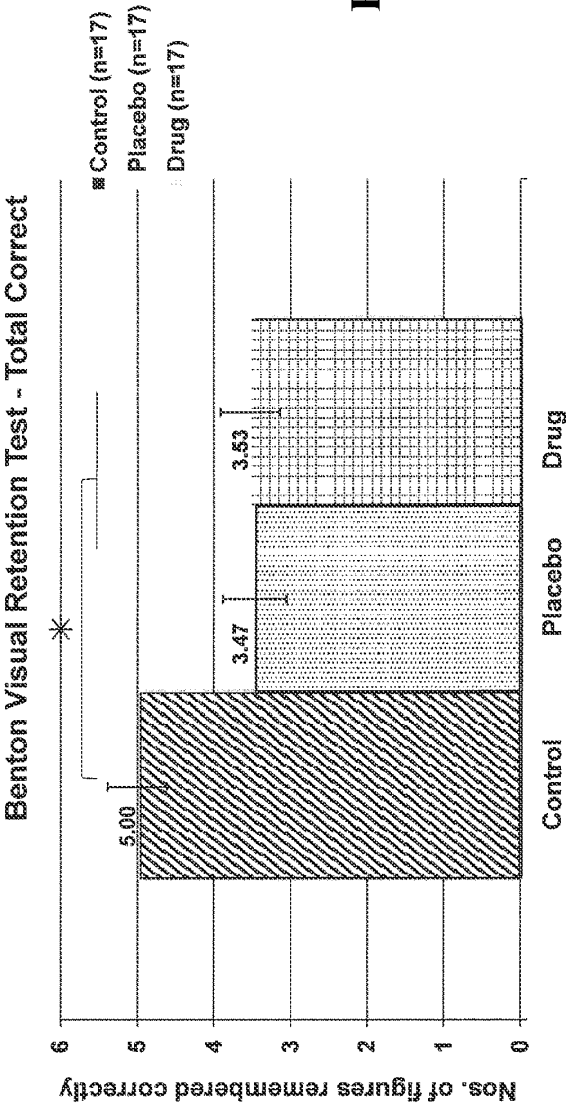


FIG. 12A

Group	Mean	Standard Error	Total Correct (p-value)
Control	5.00	0.38	Control vs. Placebo: 0.011
MCI Placebo	3.47	0.41	Control vs. Drug: 0.011
MCI Drug	3.53	0.38	Placebo vs. Drug: 0.805

FIG. 12B

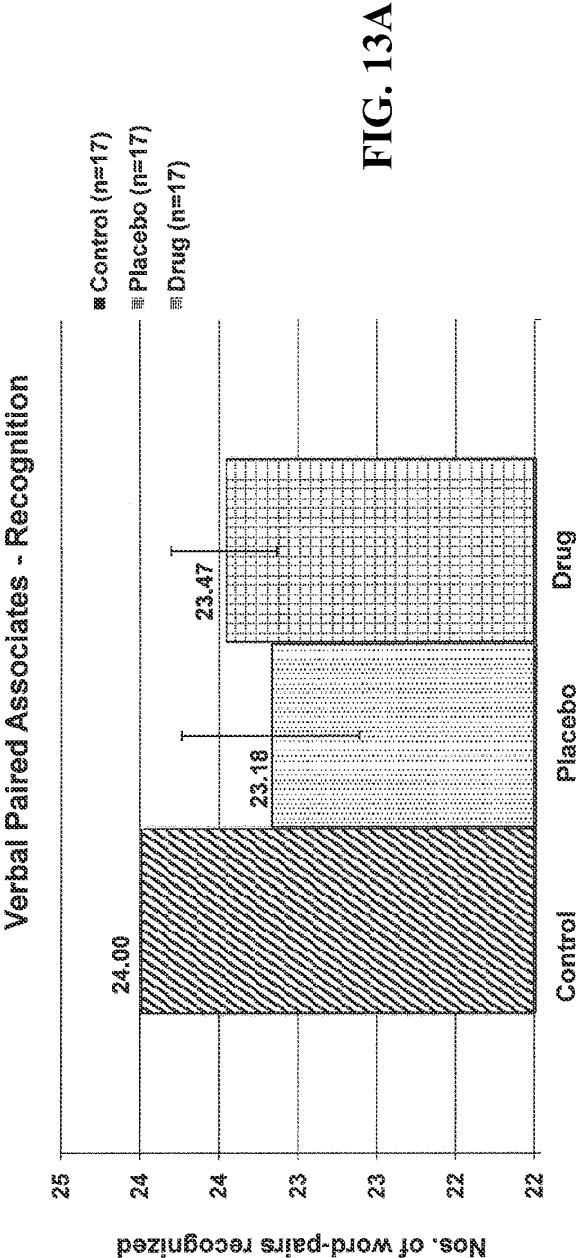


FIG. 13A

Group	Mean	Standard Error	Recognition (p-value)
Control	24.00	0.00	Control vs. Placebo: 0.154
MCI Placebo	23.18	0.56	Control vs. Drug: 0.122
MCI Drug	23.47	0.33	Placebo vs. Drug: 0.428

FIG. 13B

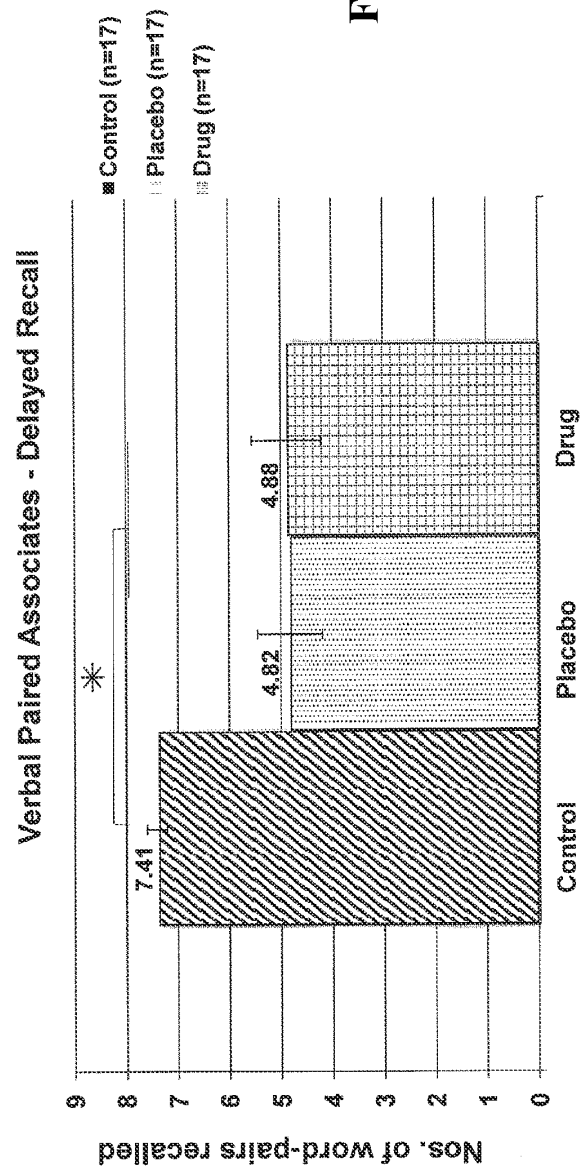


FIG. 14A

FIG. 14B

Study Status

	Control subjects	MCI subjects	Total subjects
Participated in screening	26	32	58
Screening failures	4	9	13
Enrolled	22	23	45
Removed or withdrew from study	5	5	11
Total subjects used in analysis	17	17	34

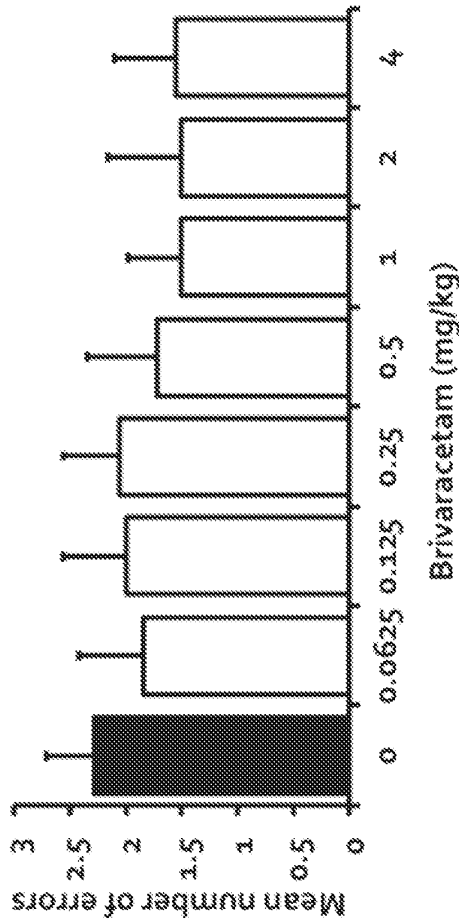
FIG. 15A

Characteristics of Study Samples

	Control Subjects	MCI Subjects	p
N	17	17	
Sex (M/F)	9/8	6/11	0.307
Age (yrs)	69.3 (7.0)	72.9 (8.9)	0.201
Education (yrs)	15.9 (2.6)	15.8 (2.9)	0.951
Race (Caucasian/African American)	17/0	14/3	0.074
Hispanic or Latino (y/n)	0/17	1/16	0.317

FIG. 15B

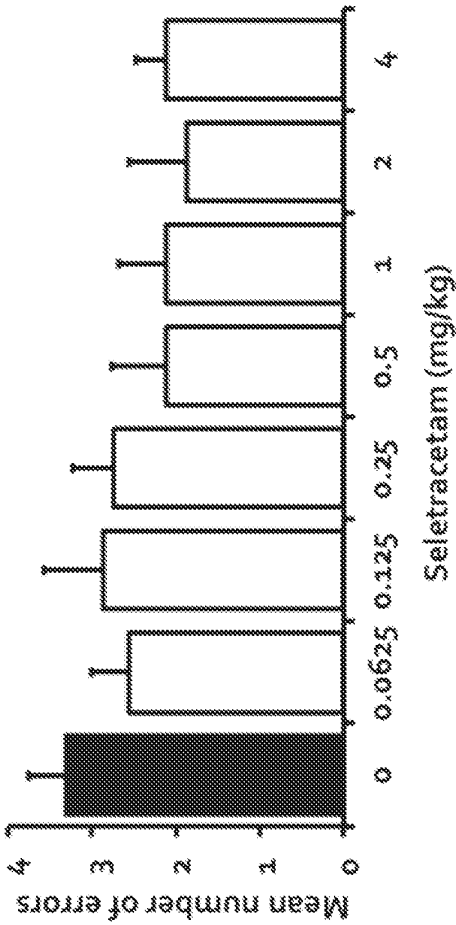
Brivaracetam Treatment: Radial Arm Maze Task



Repeated measures ANOVA for within-subject contrasts, $F(1, 8) = 6.046$, $p = 0.039$
Means and SEMs are shown

FIG. 16

Seletracetam Treatment: Radial Arm Maze Task



Repeated measures ANOVA for within-subject contrasts, $F(1, 7) = 12.577$, $p = 0.009$
Means and SEMs are shown

FIG. 17

Performance of cognitively-impaired aged rats (n = 3/group)
treated with brivaracetam (2 mg/kg/day after 14 days) in the water maze task

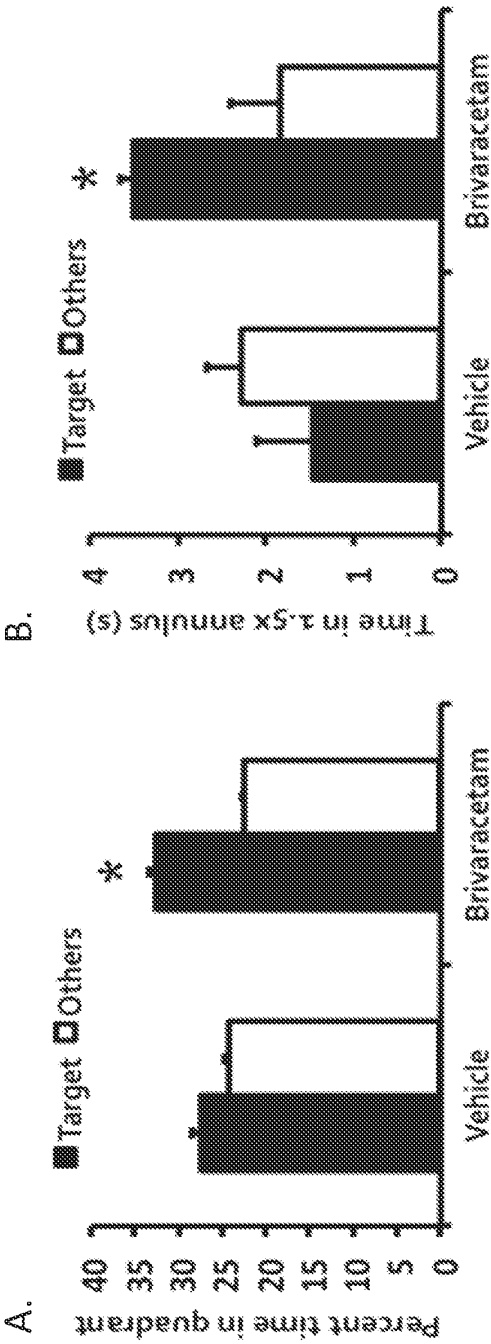


FIG. 18A

FIG. 18B

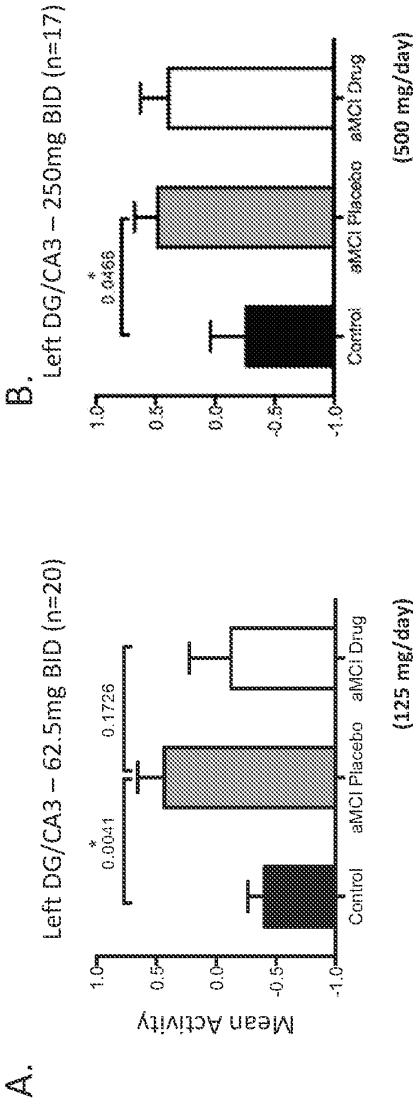


FIG. 19A

FIG. 19B

A. Behavior Performance – Lures (62.5 mg BID) B. Behavior Performance – Lures (250 mg BID)

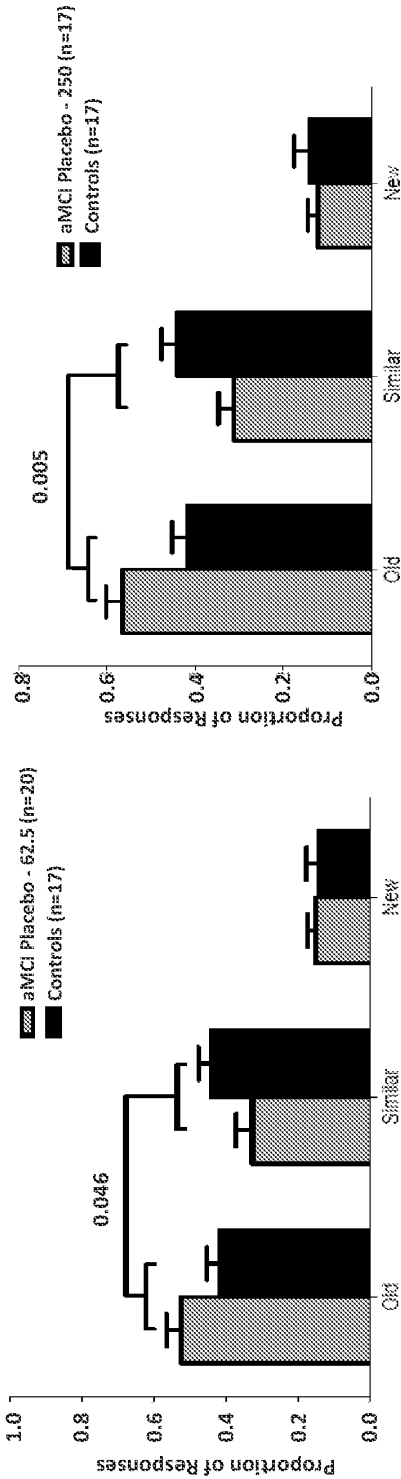


FIG. 20A

FIG. 20B

FIG. 21A

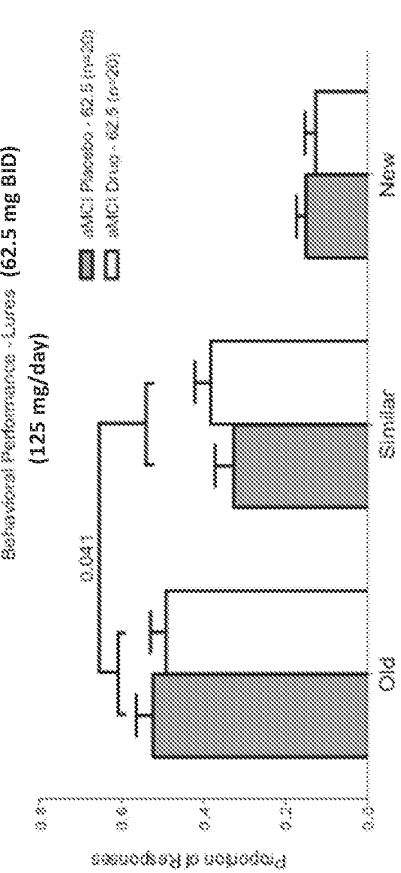
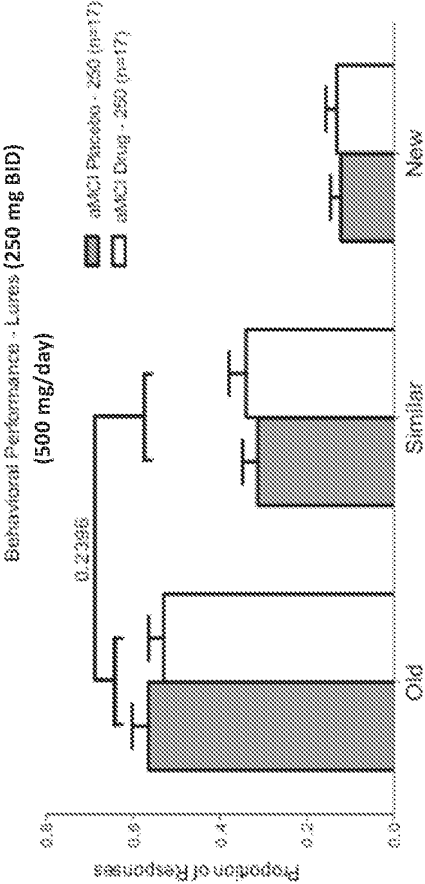


FIG. 21B



Chronic Treatment with Levetiracetam (10 mg/kg/day) in
AI Rats Restores Somatostatin in DG Hilus

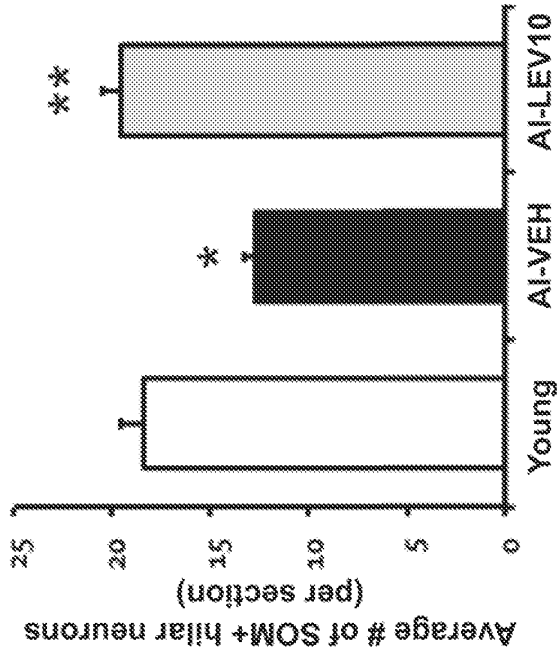


FIG. 22

Chronic Treatment with Levetiracetam (10 mg/kg/day) in
AI Rats Restores Reelin in Entorhinal Cortex (EC2)

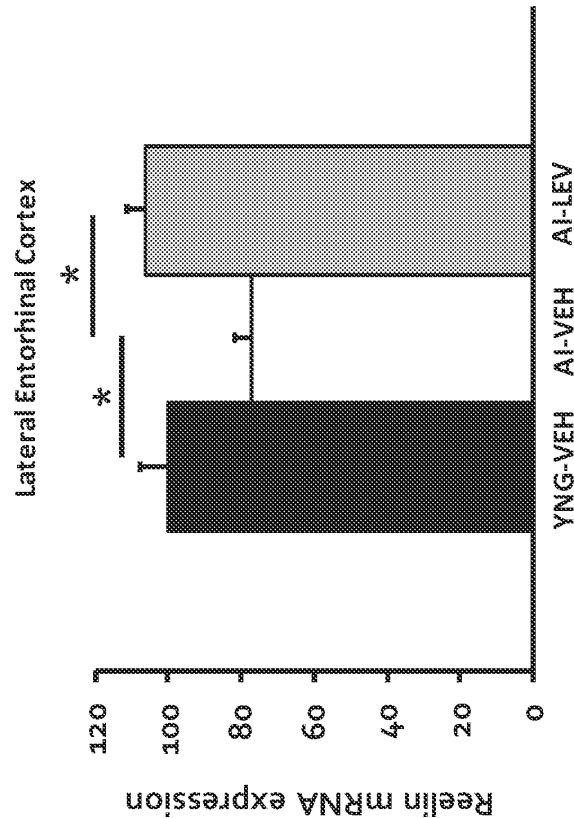
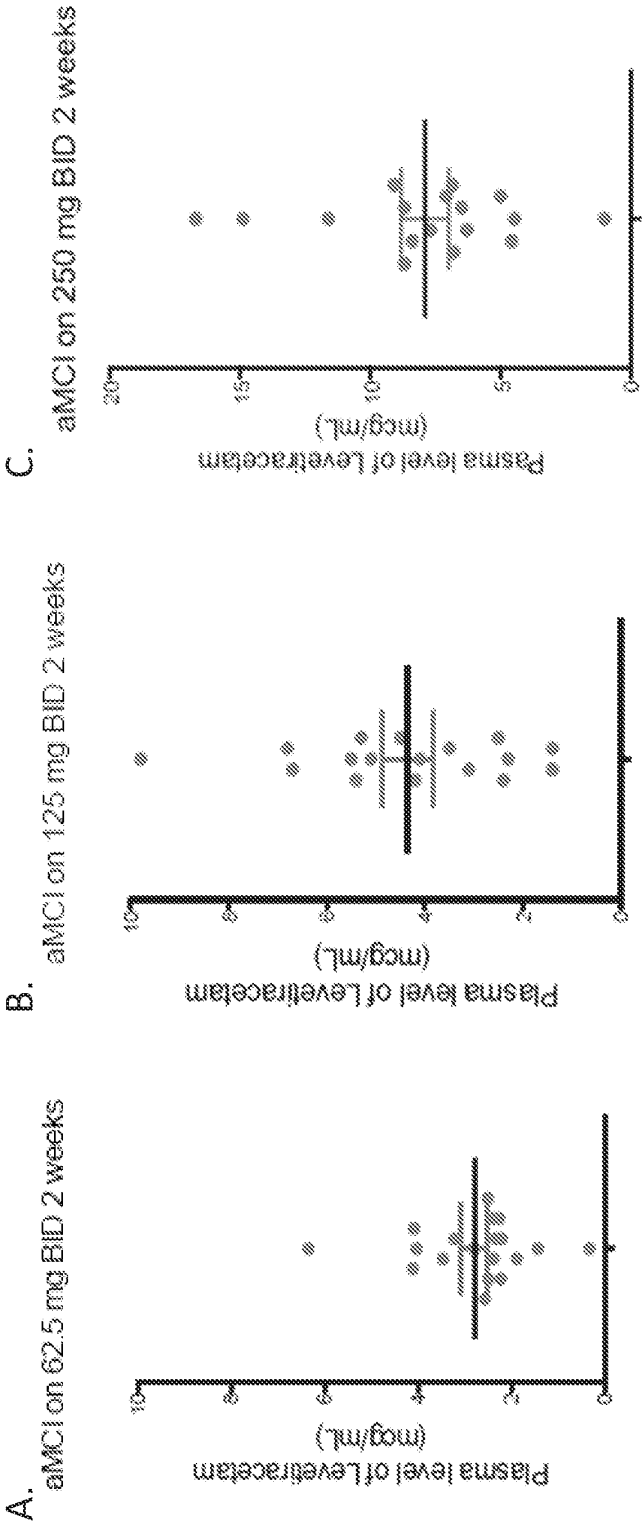


FIG. 23



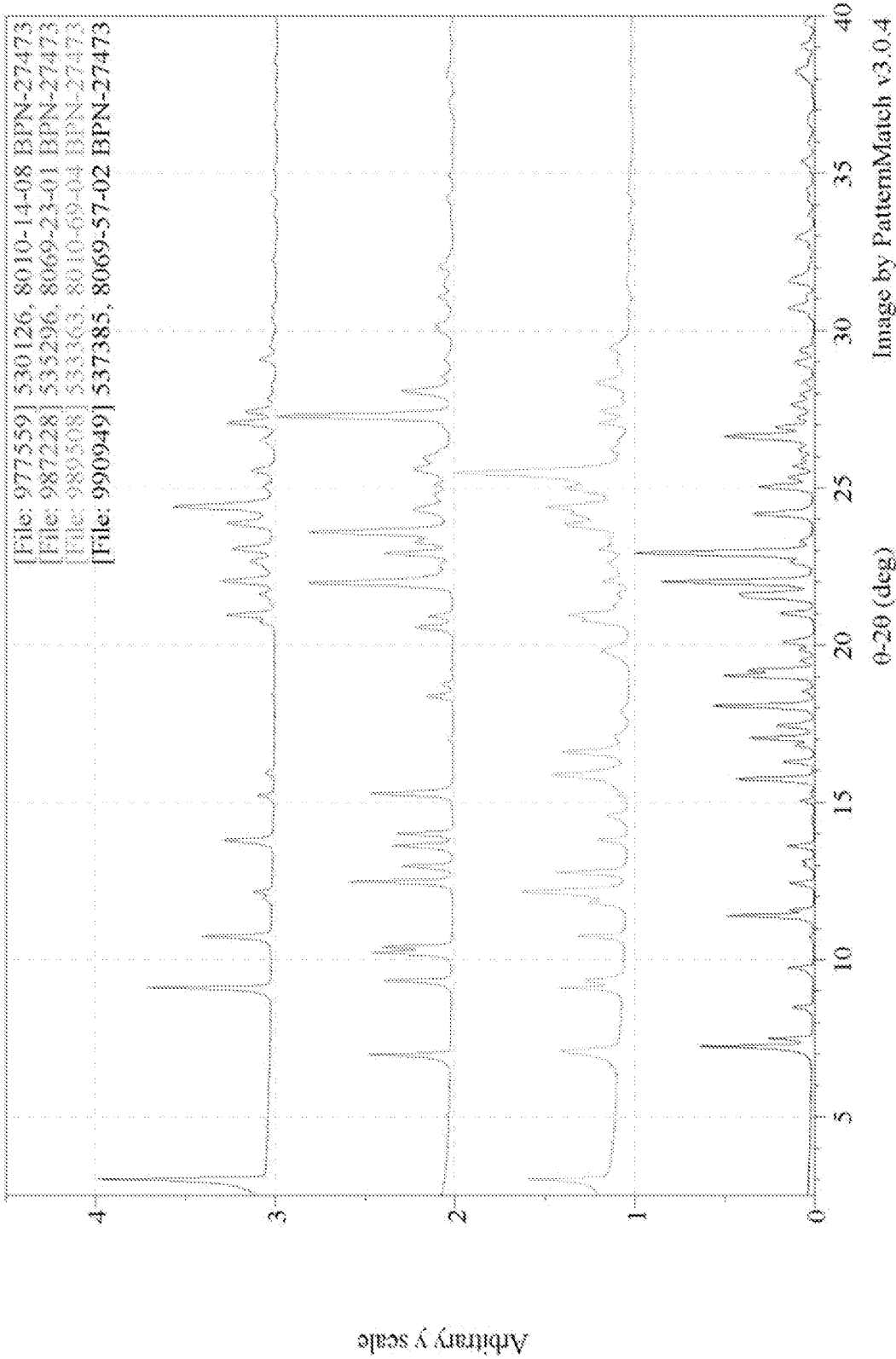


FIG. 25

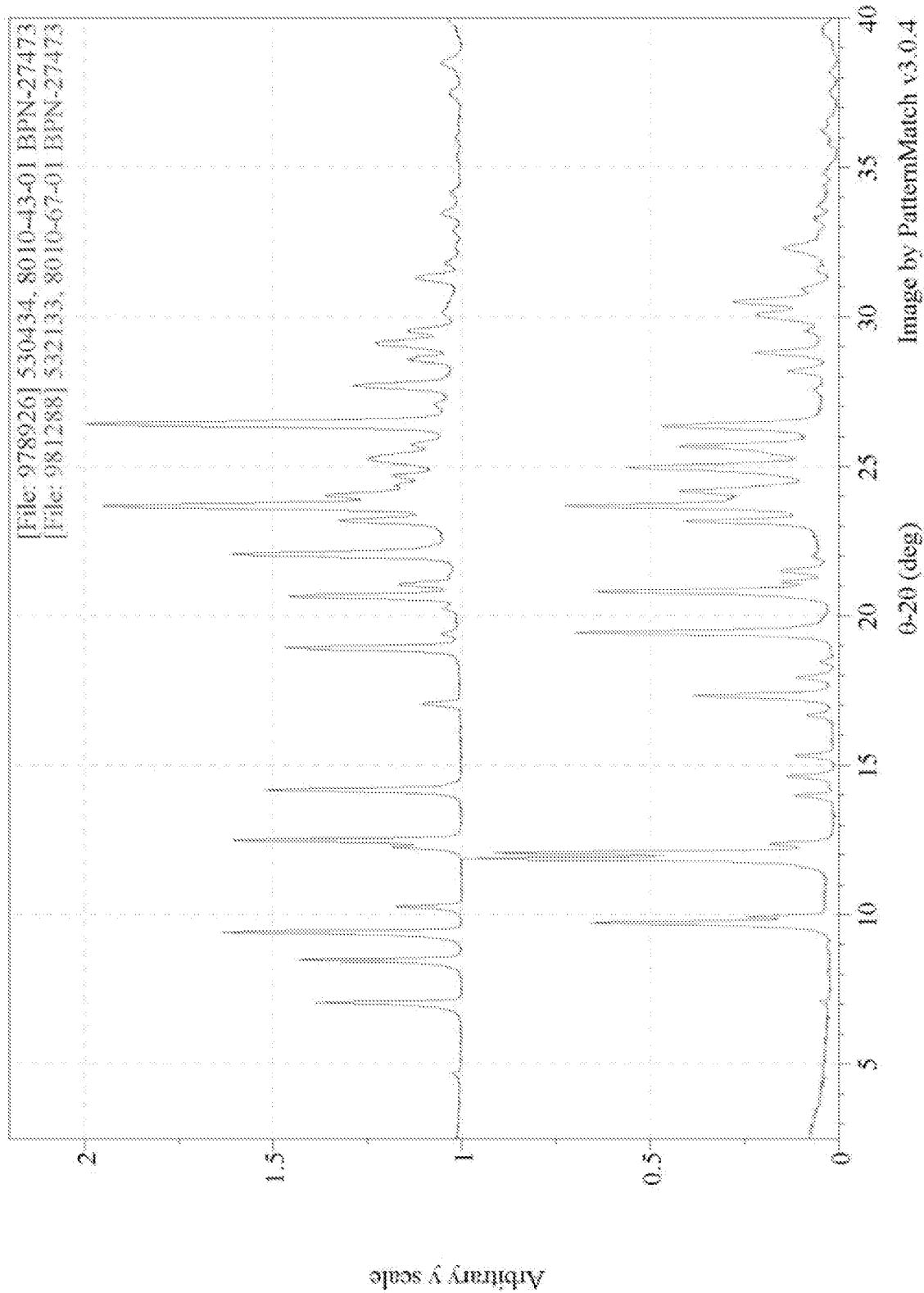


FIG. 26

FIG. 27A

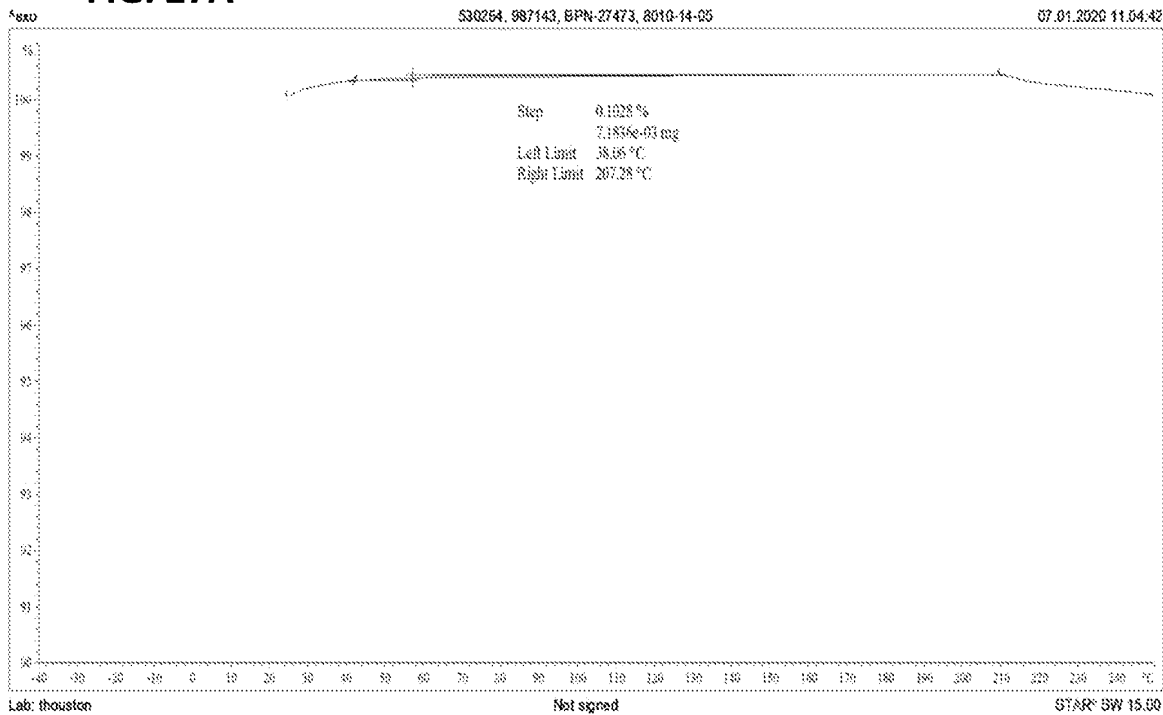
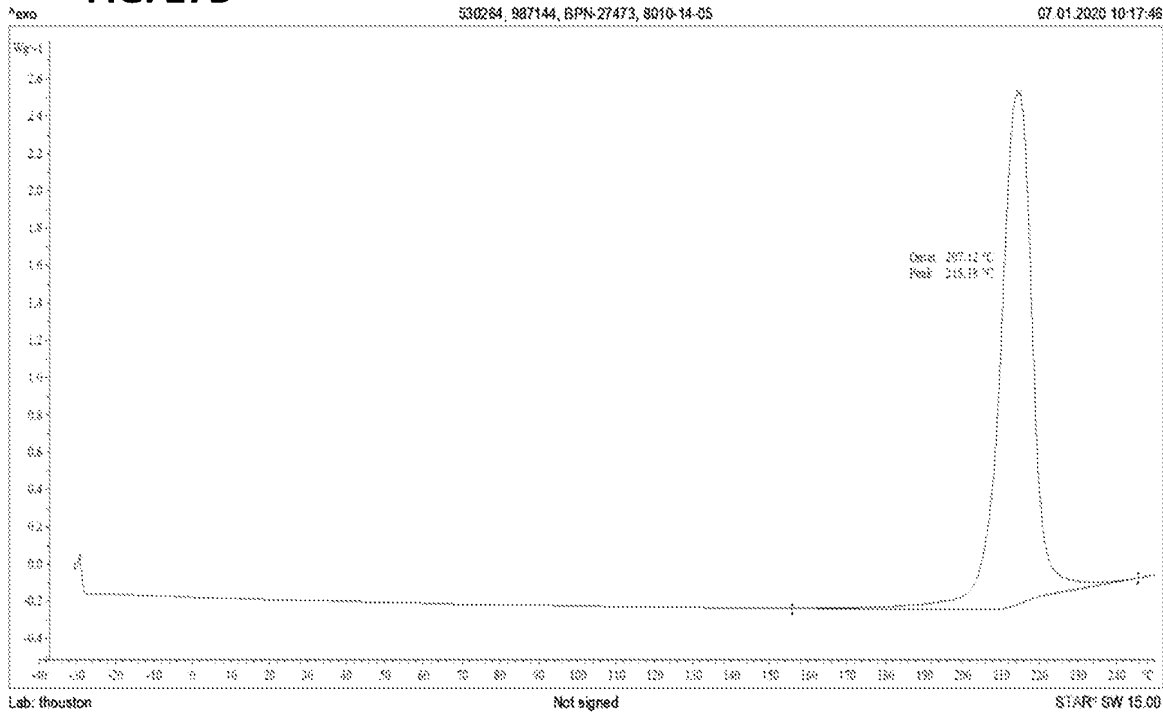


FIG. 27B



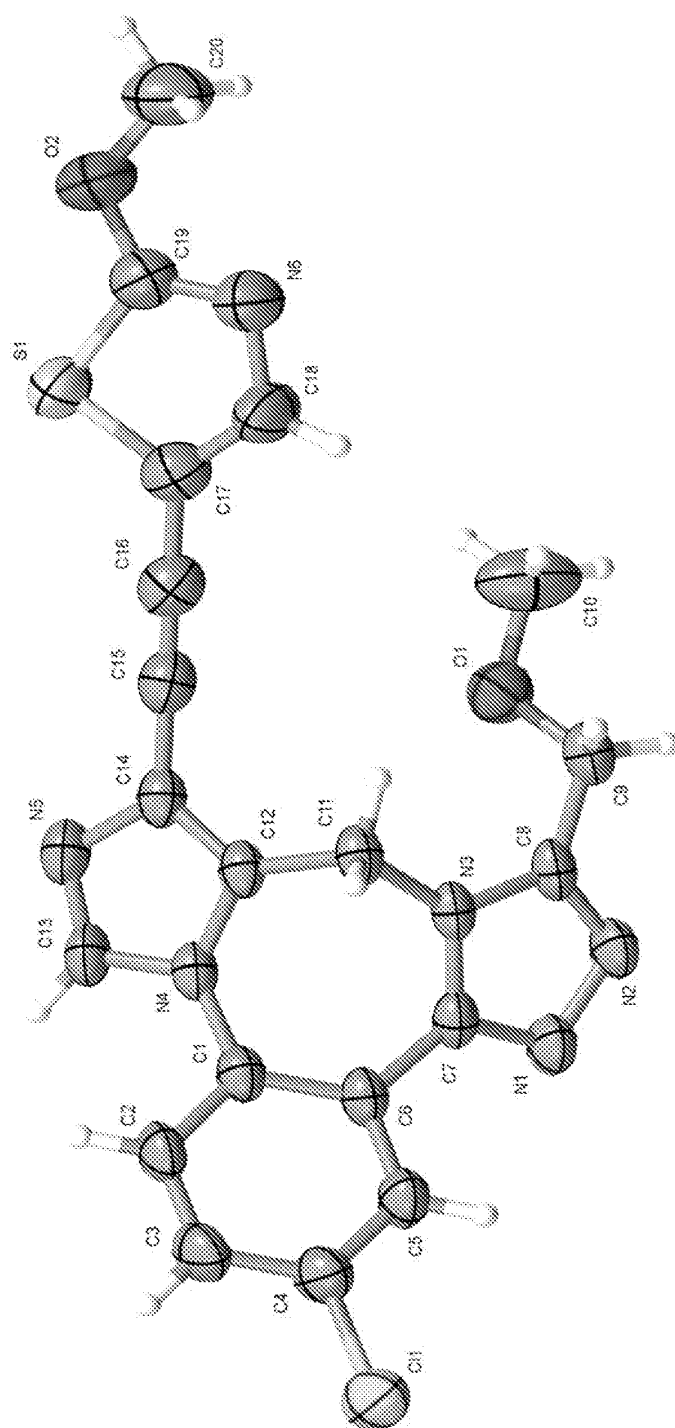


FIG. 28

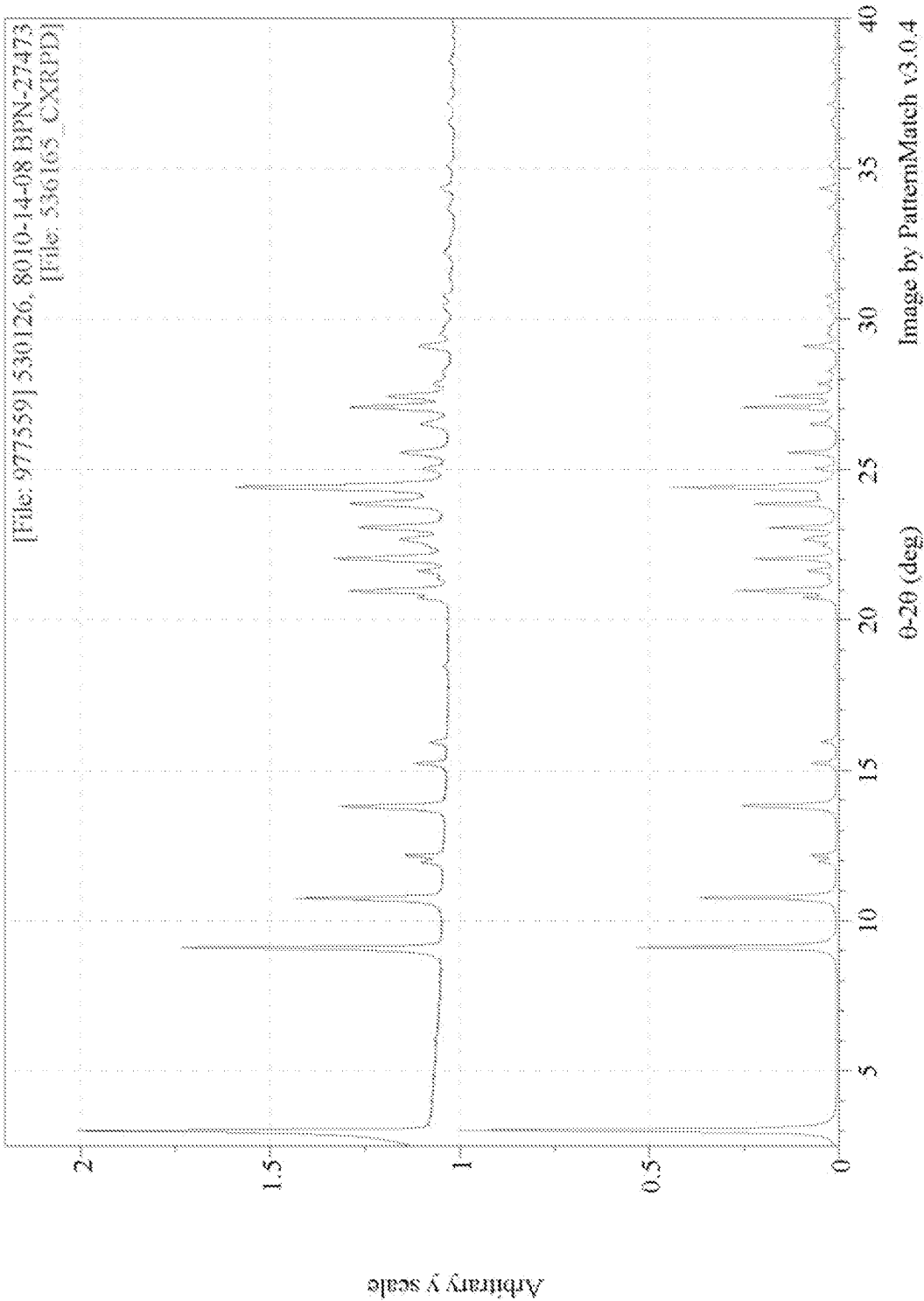


FIG. 29

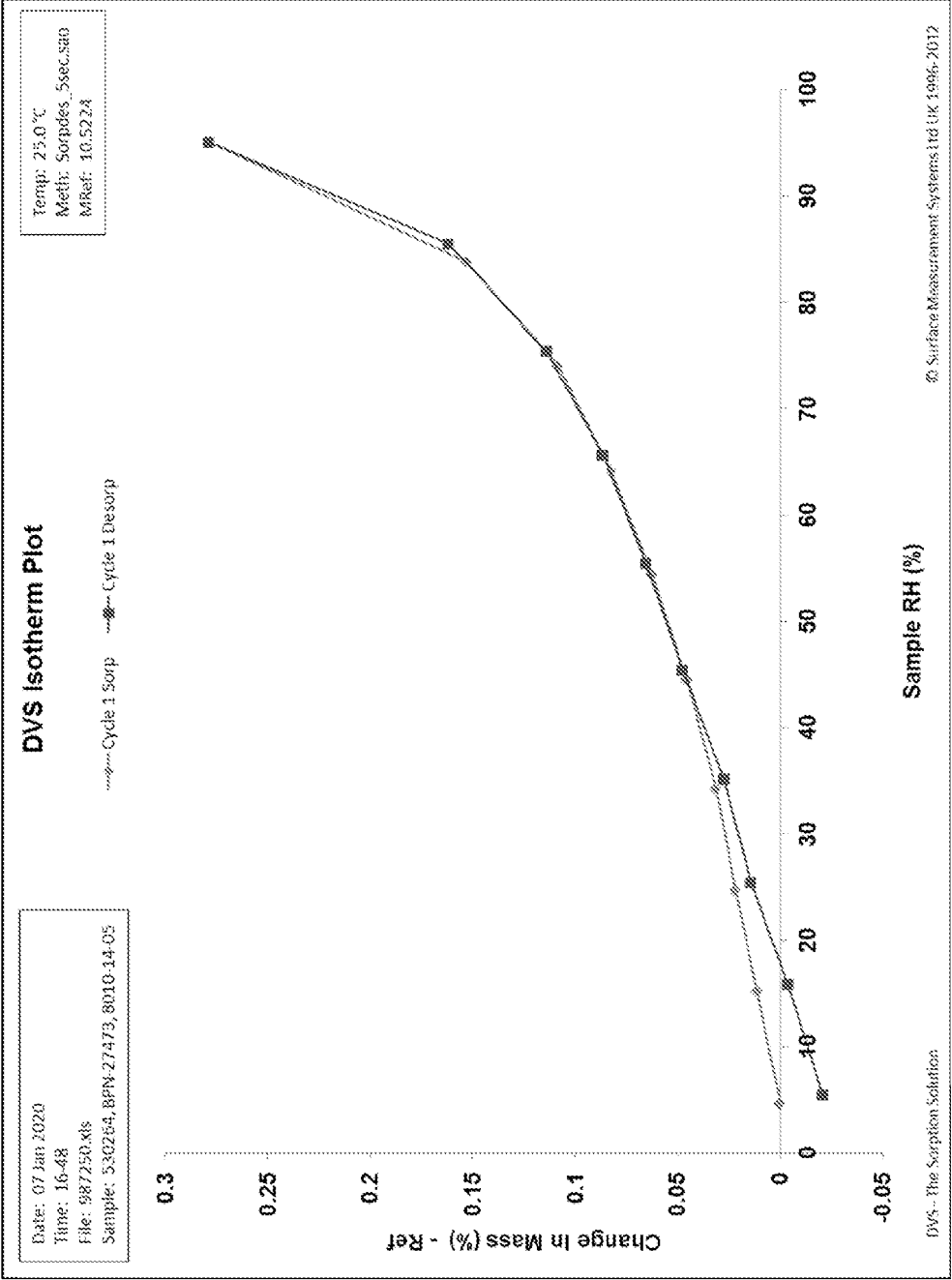
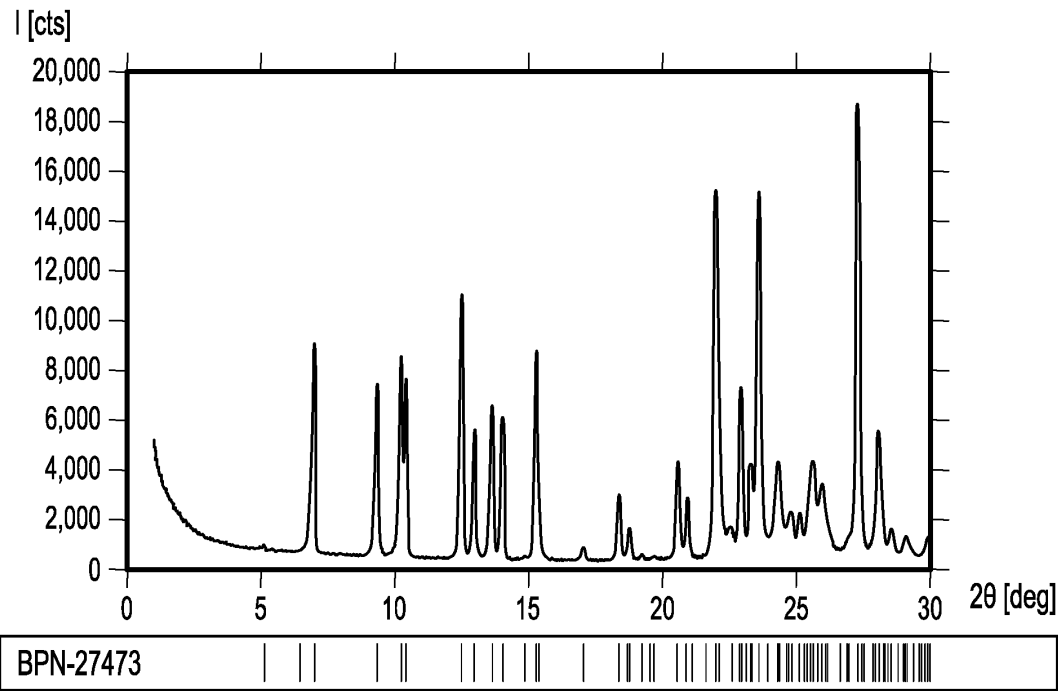


FIG. 30

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Indexing results for XRPD file 987228 collected with Cu-K α radiation



	BPN-27473
Bravais Type	Primitive Monoclinic
a [Å]	14.254
b [Å]	4.041
c [Å]	36.069
α [deg]	90
β [deg]	106.84
γ [deg]	90
Volume [Å ³ /cell]	1,988.5
Chiral Contents?	Not Specified
Extinction Symbol	P 1 c 1
Space Group(s)	Pc (7), P2/c (13)
Source	Manual Input

Indexing is a non-cGMP activity

FIG. 31

Output Rendered using Triads v2.1.1

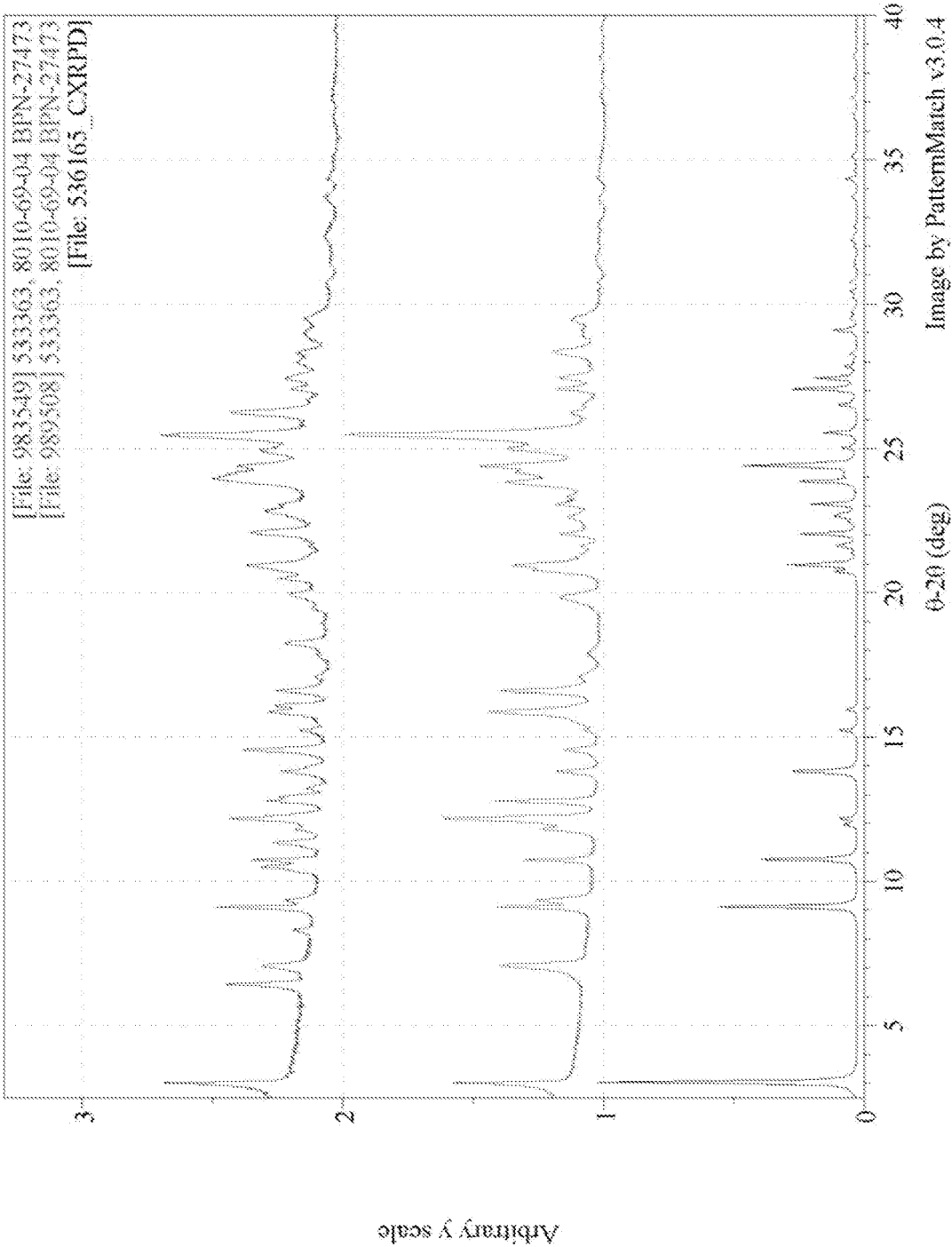


FIG. 32

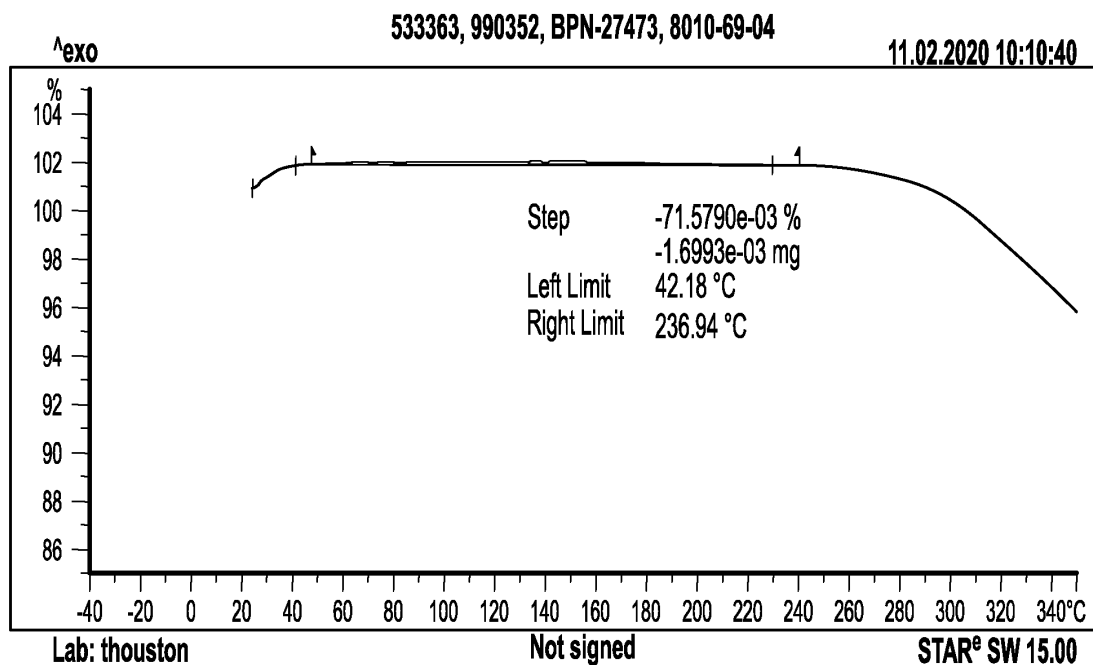


FIG. 33A

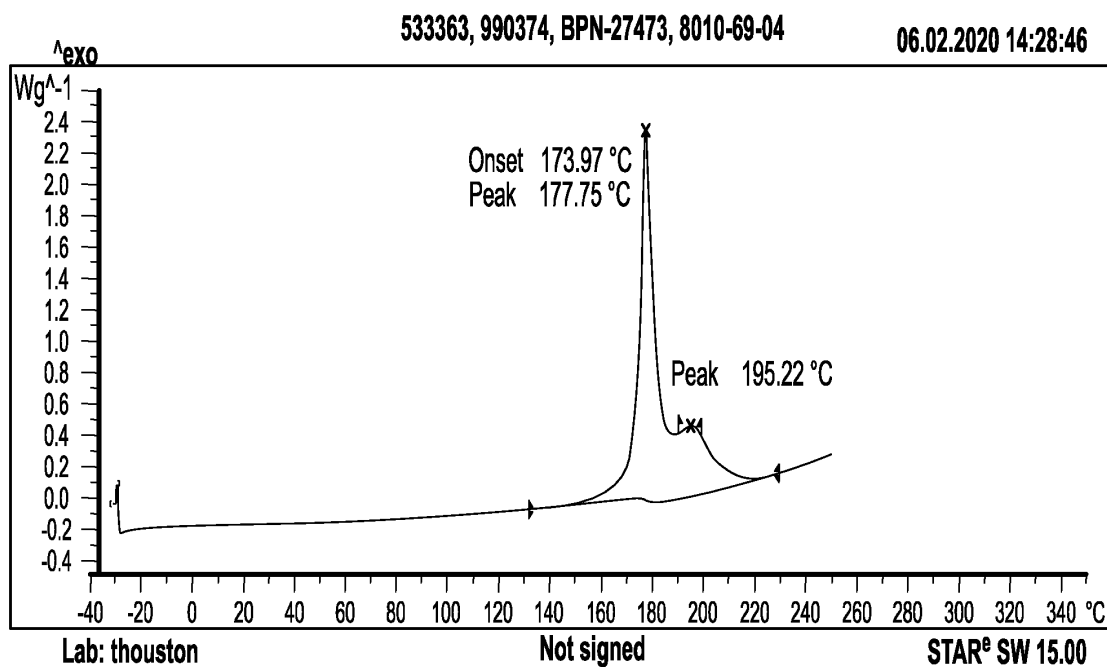


FIG. 33B

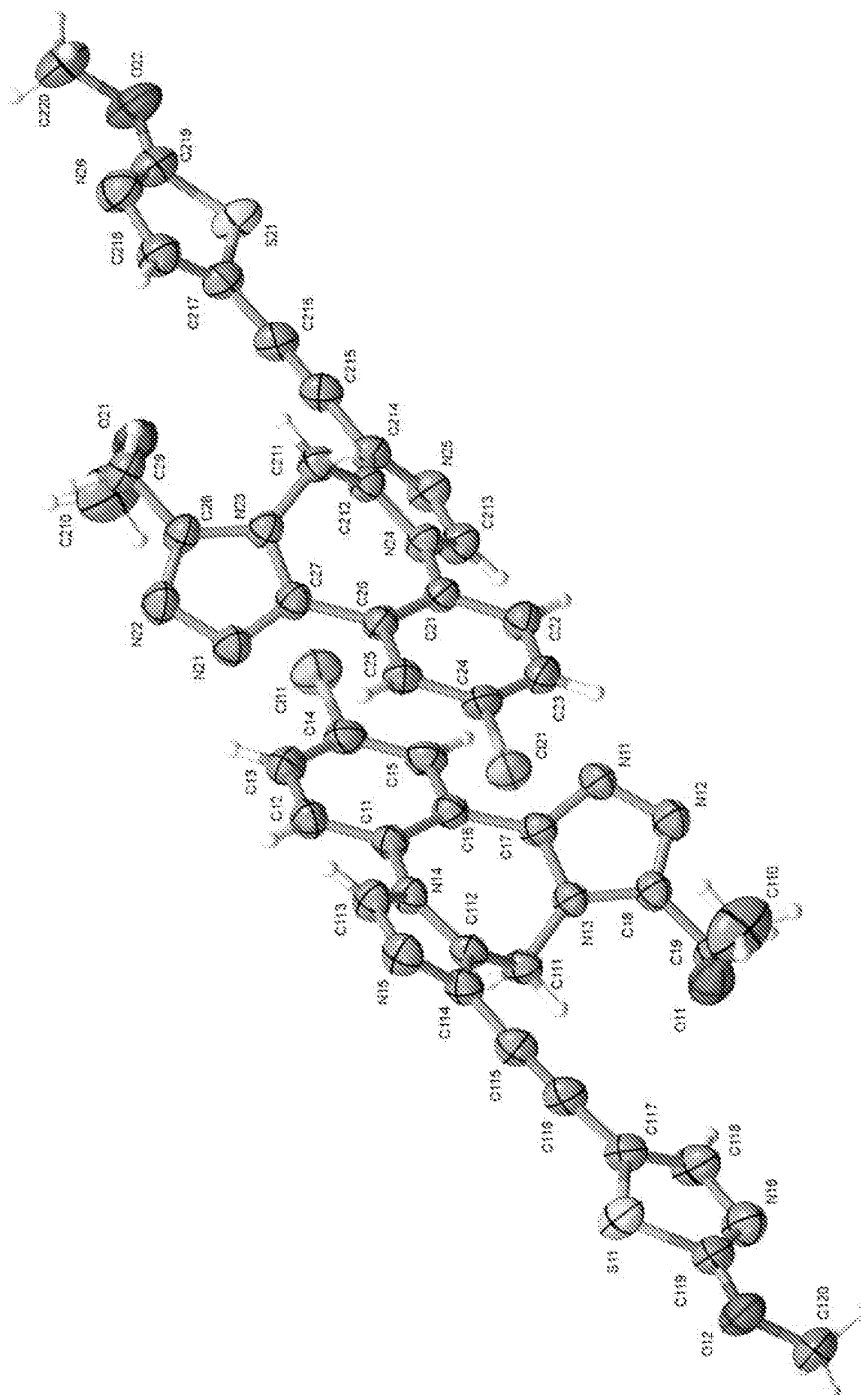


FIG. 34

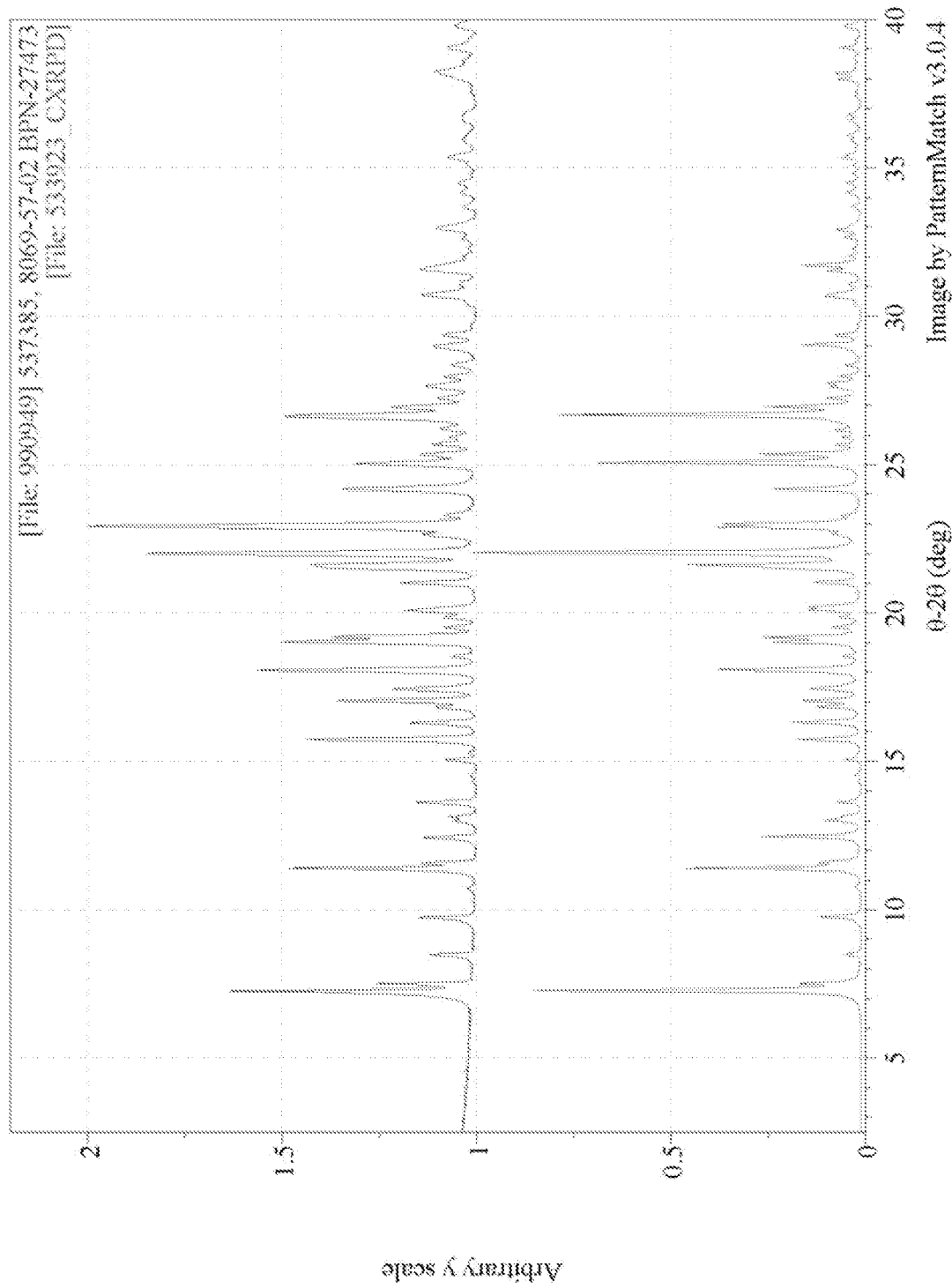


FIG. 35

FIG. 36A

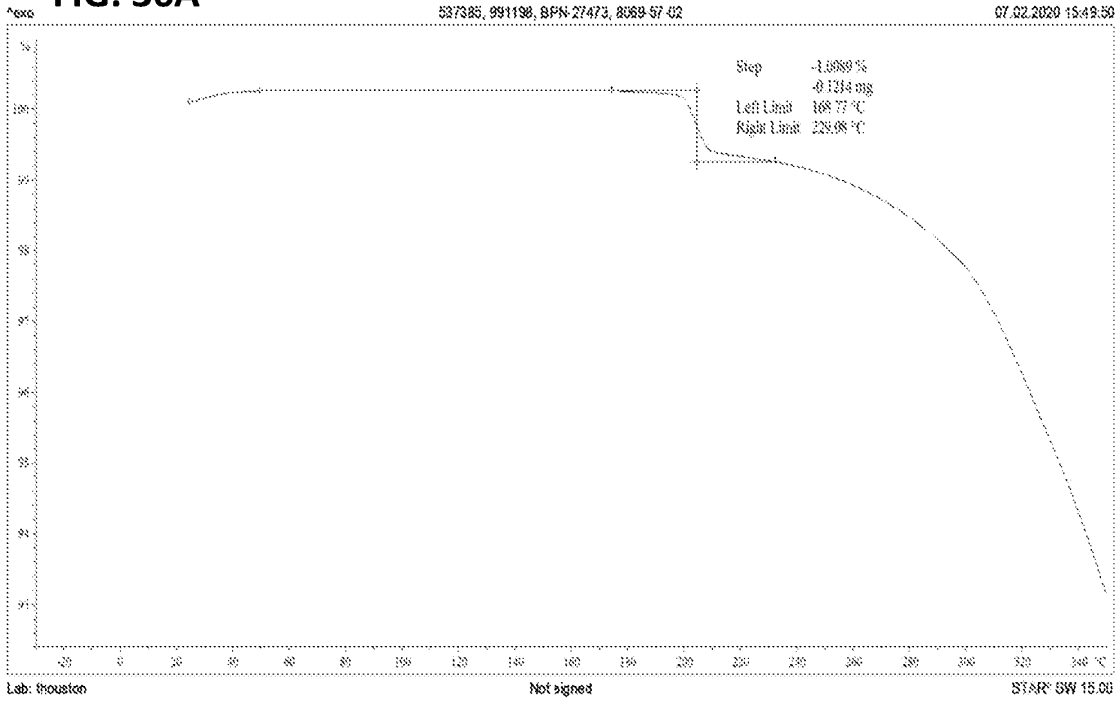
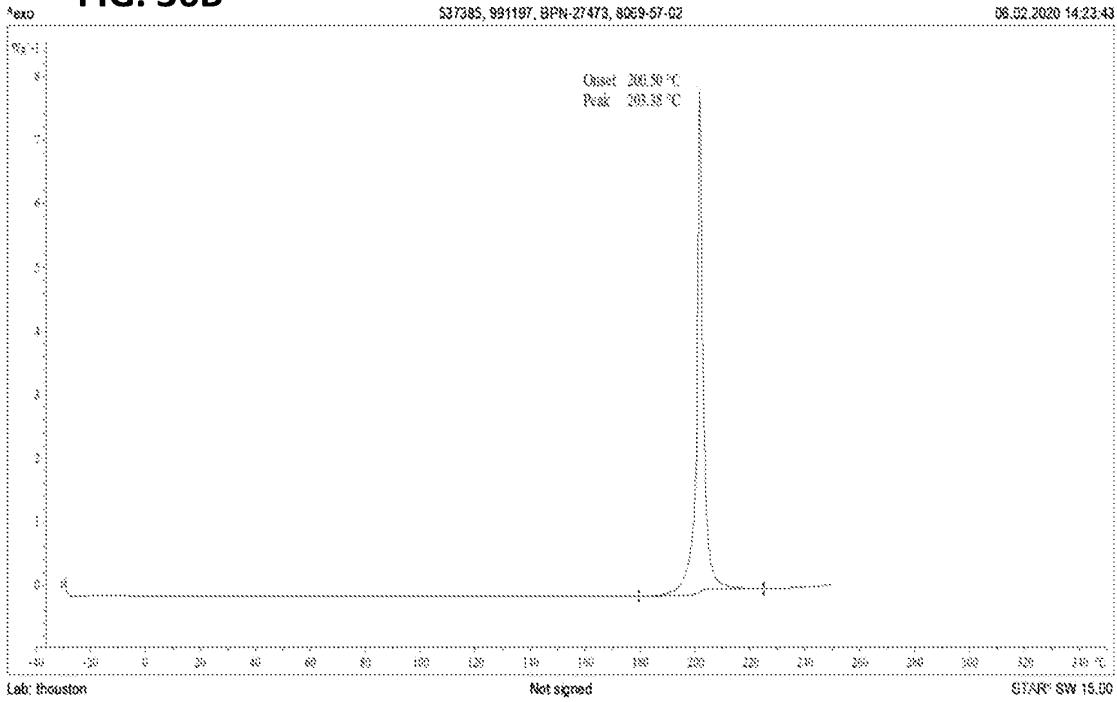


FIG. 36B



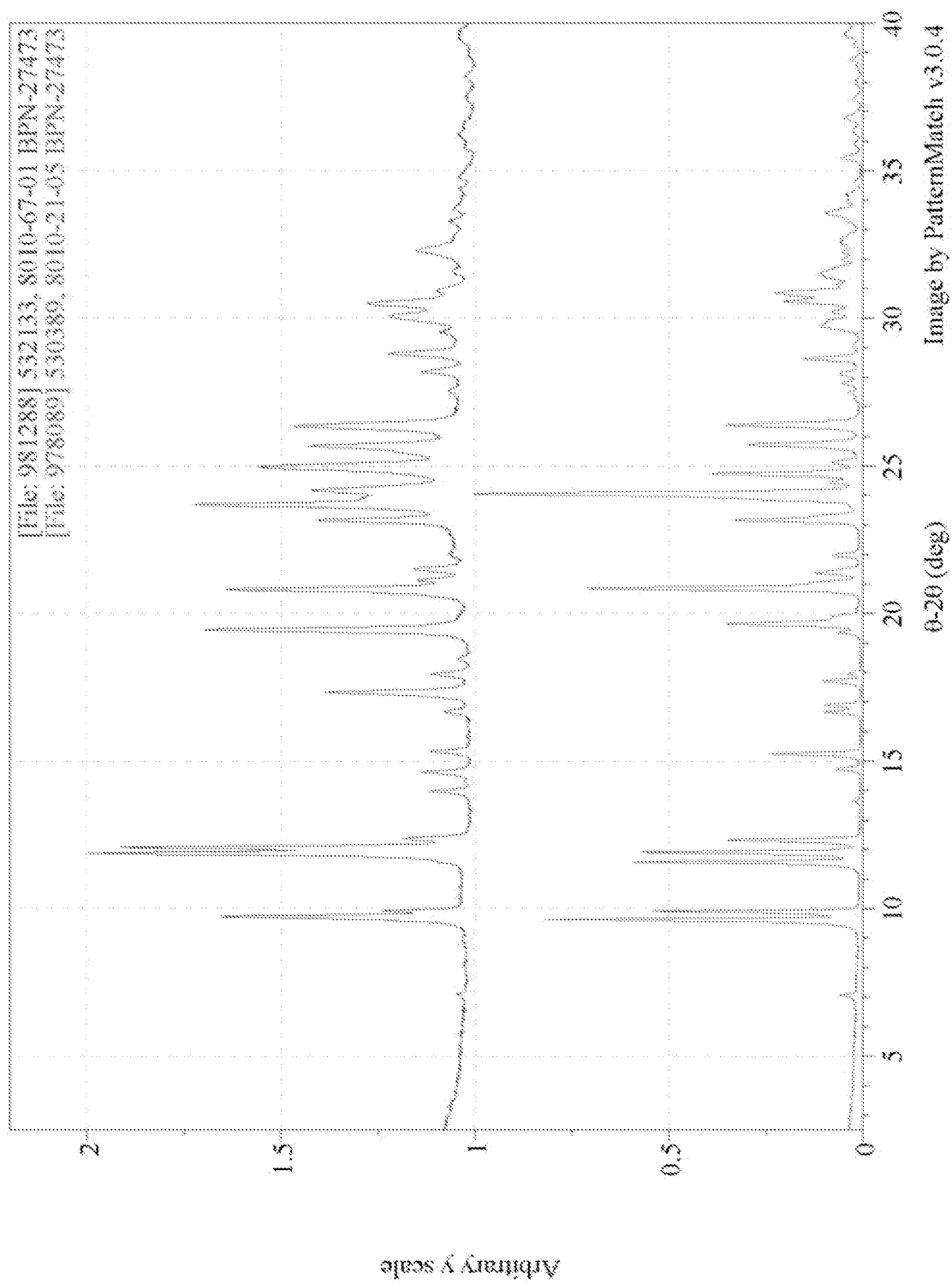
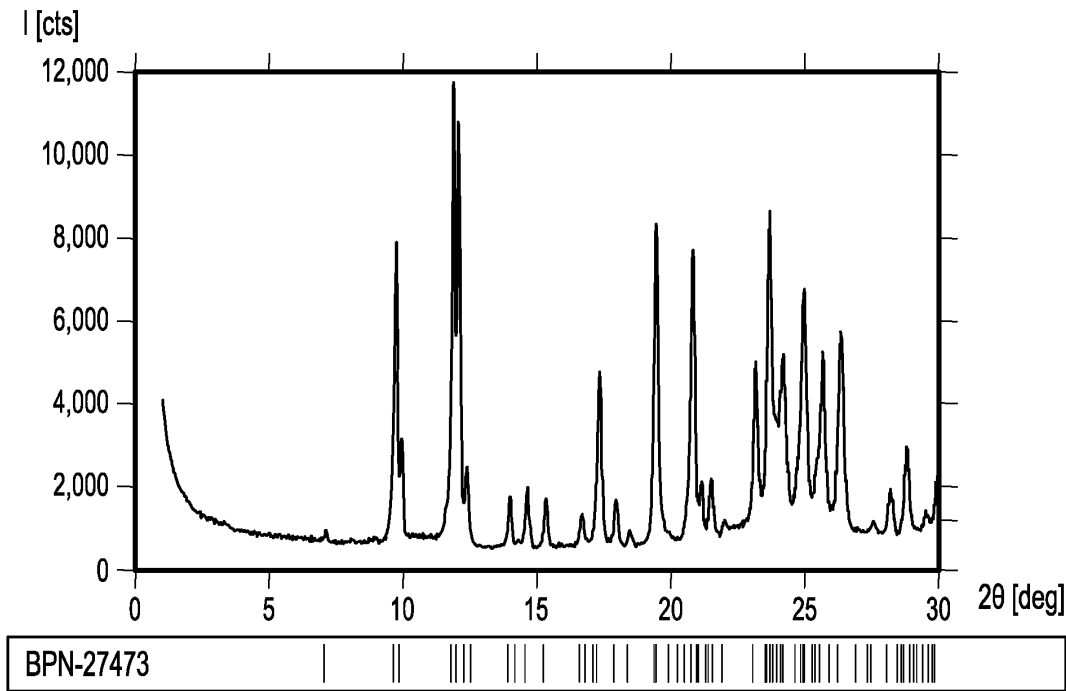


FIG. 37

Image by PatternMatch v3.0.4

Indexing results for XRPD file 981288 collected with Cu-K α radiation.



	BPN-27473
Bravais Type	Triclinic
a [Å]	9.104
b [Å]	9.279
c [Å]	12.416
α [deg]	89.06
β [deg]	86.31
γ [deg]	77.95
Volume [Å ³ /cell]	1,023.6
Chiral Contents?	Not Specified
Extinction Symbol	P -
Space Group(s)	Pc (1), P $\bar{1}$ (2)
Source	Triads Algorithm

Indexing is a non-cGMP activity

FIG. 38

Output Rendered using Triads v2.1.1

FIG. 39A

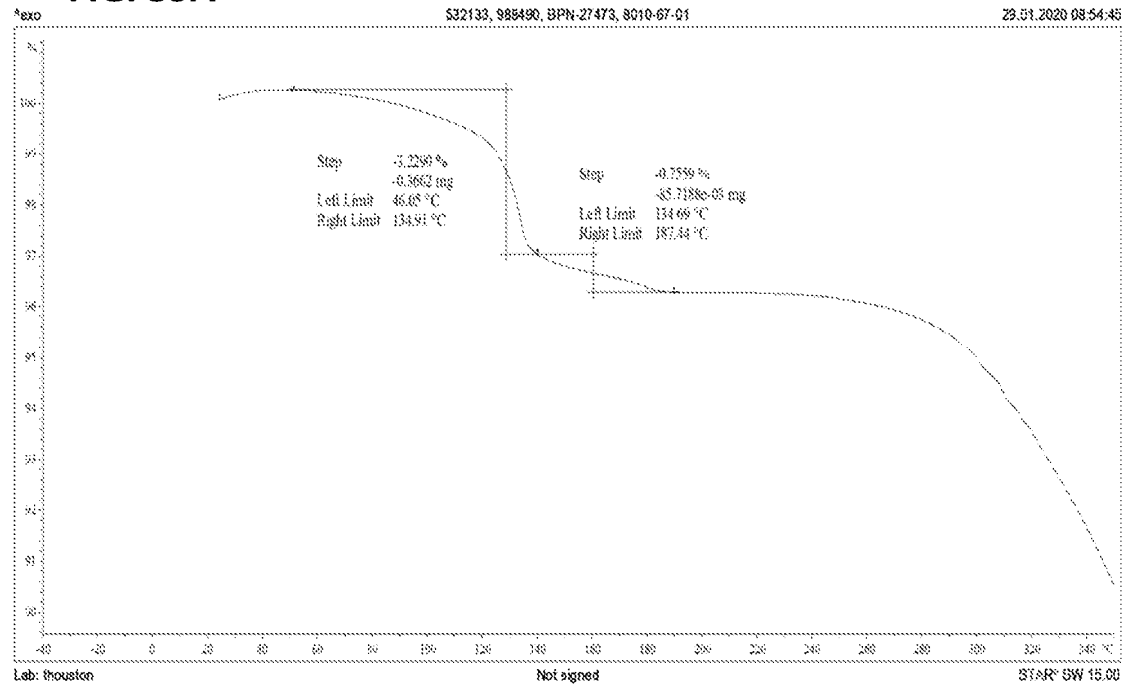
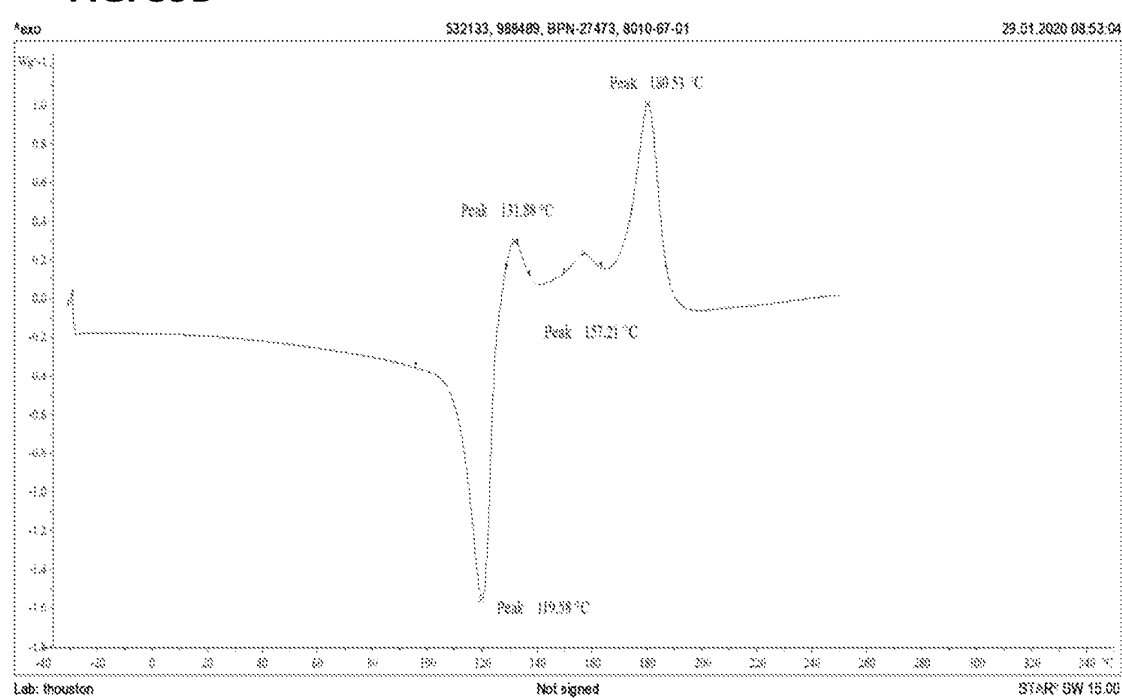


FIG. 39B



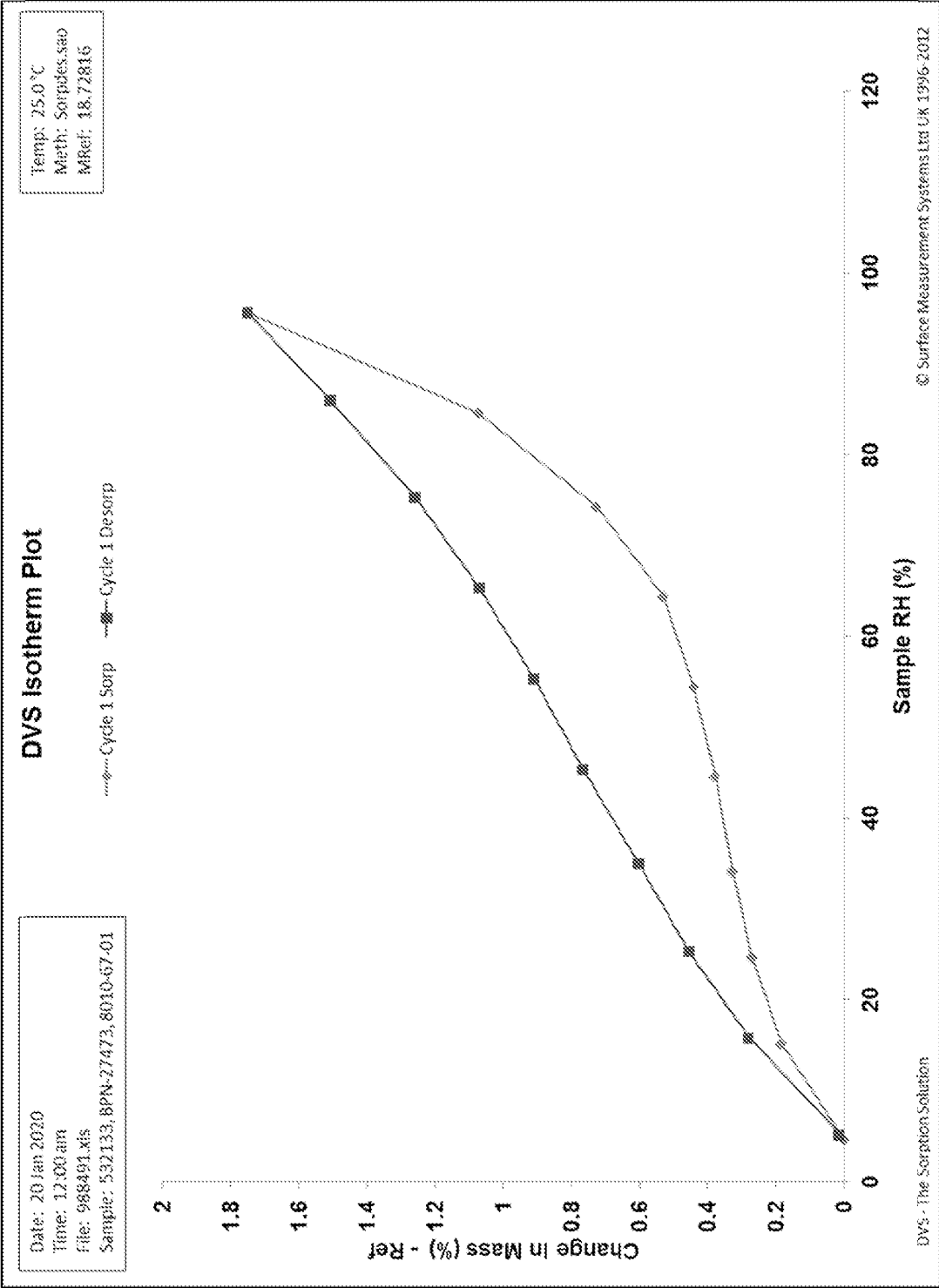


FIG. 40

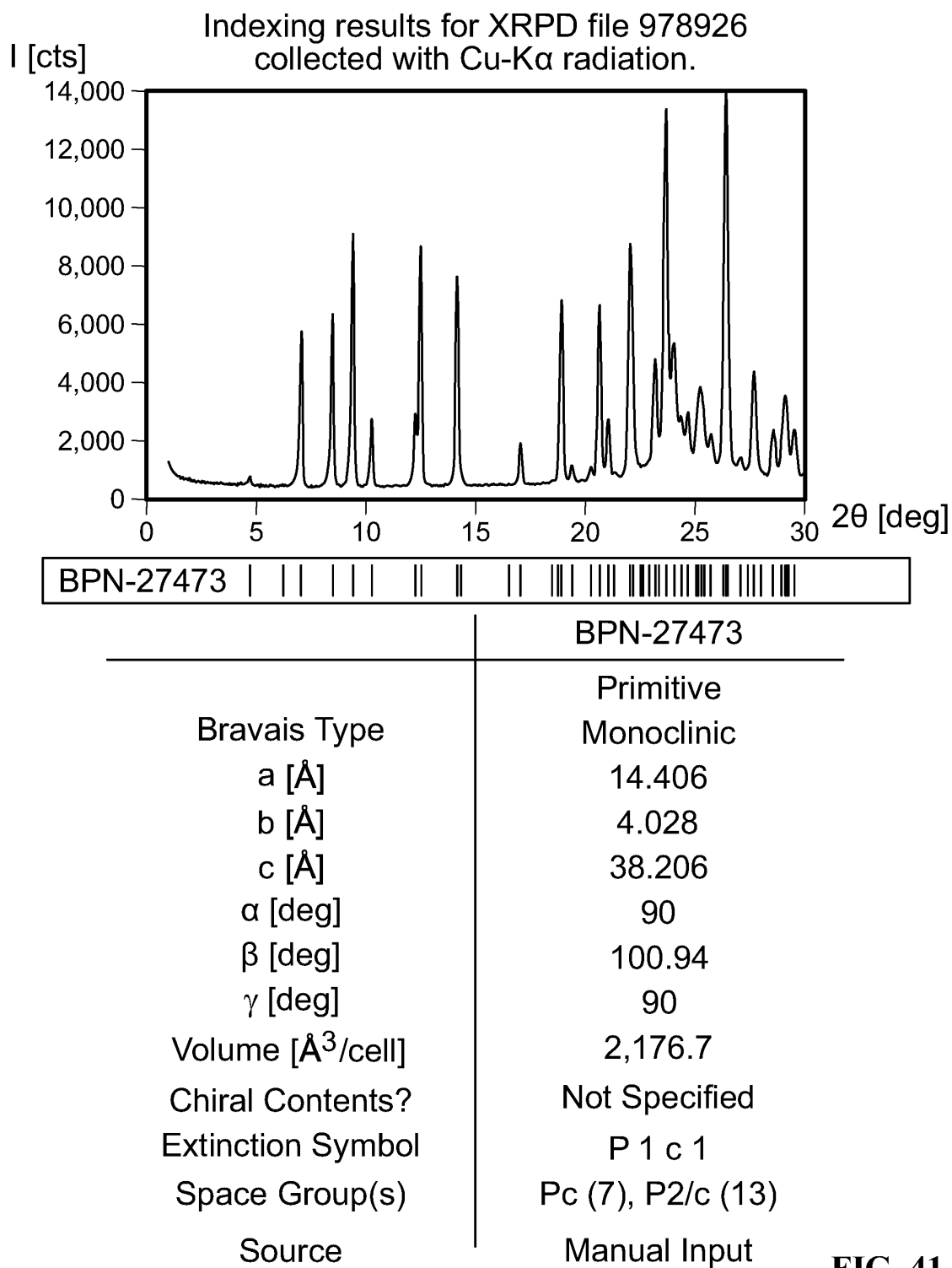


FIG. 41

FIG. 42A

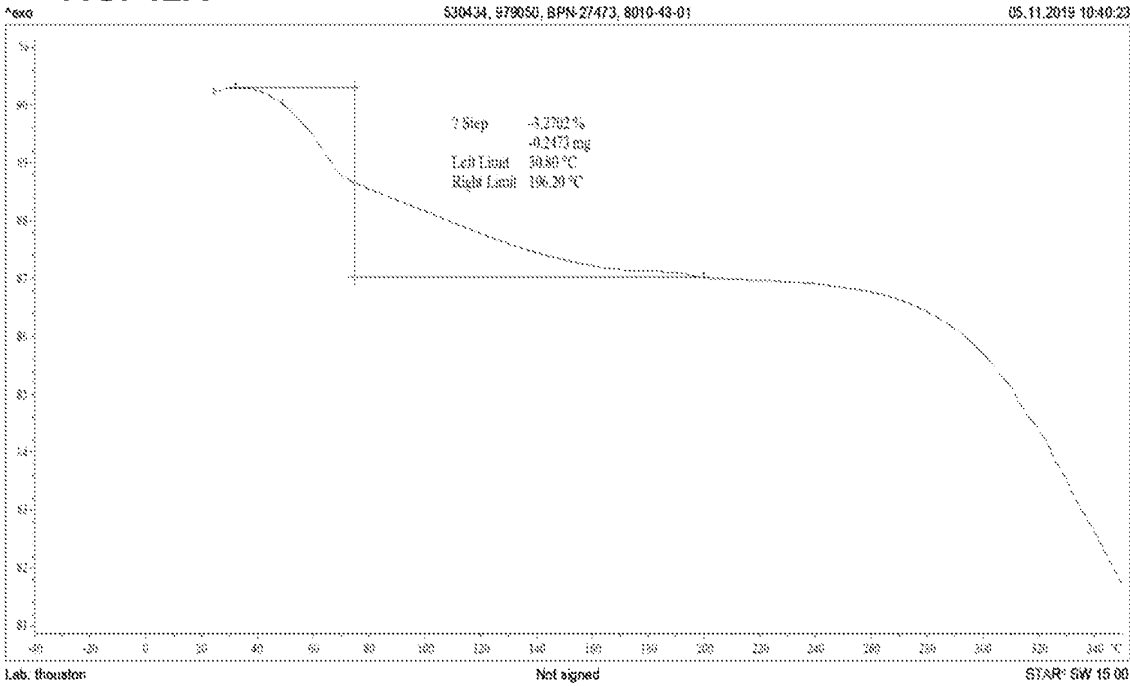
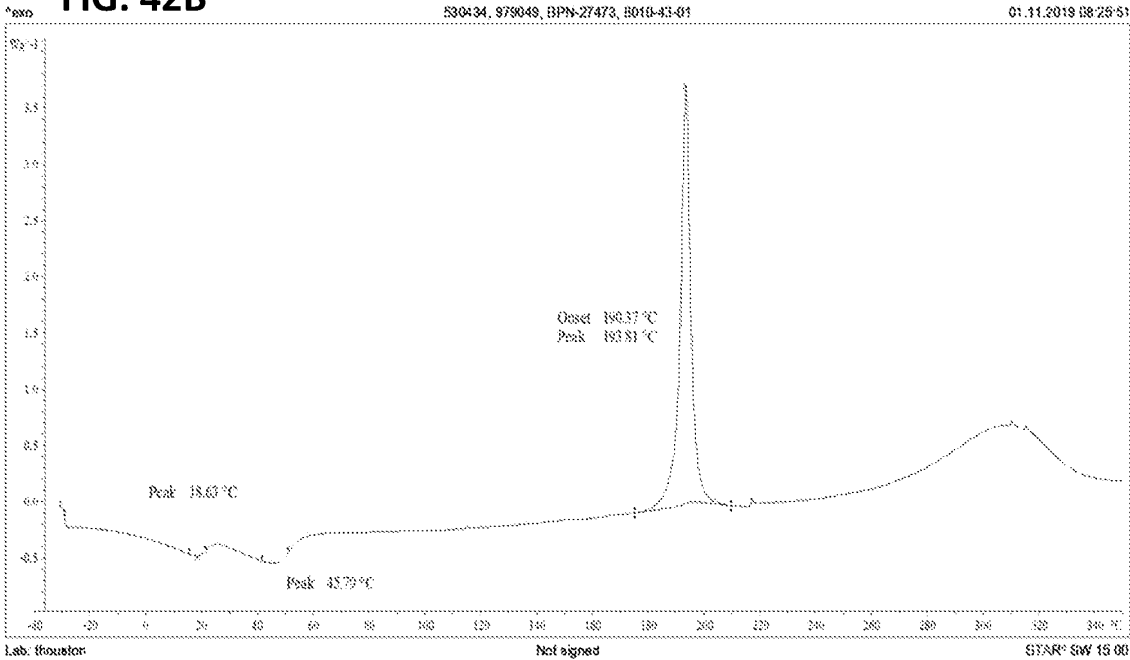


FIG. 42B



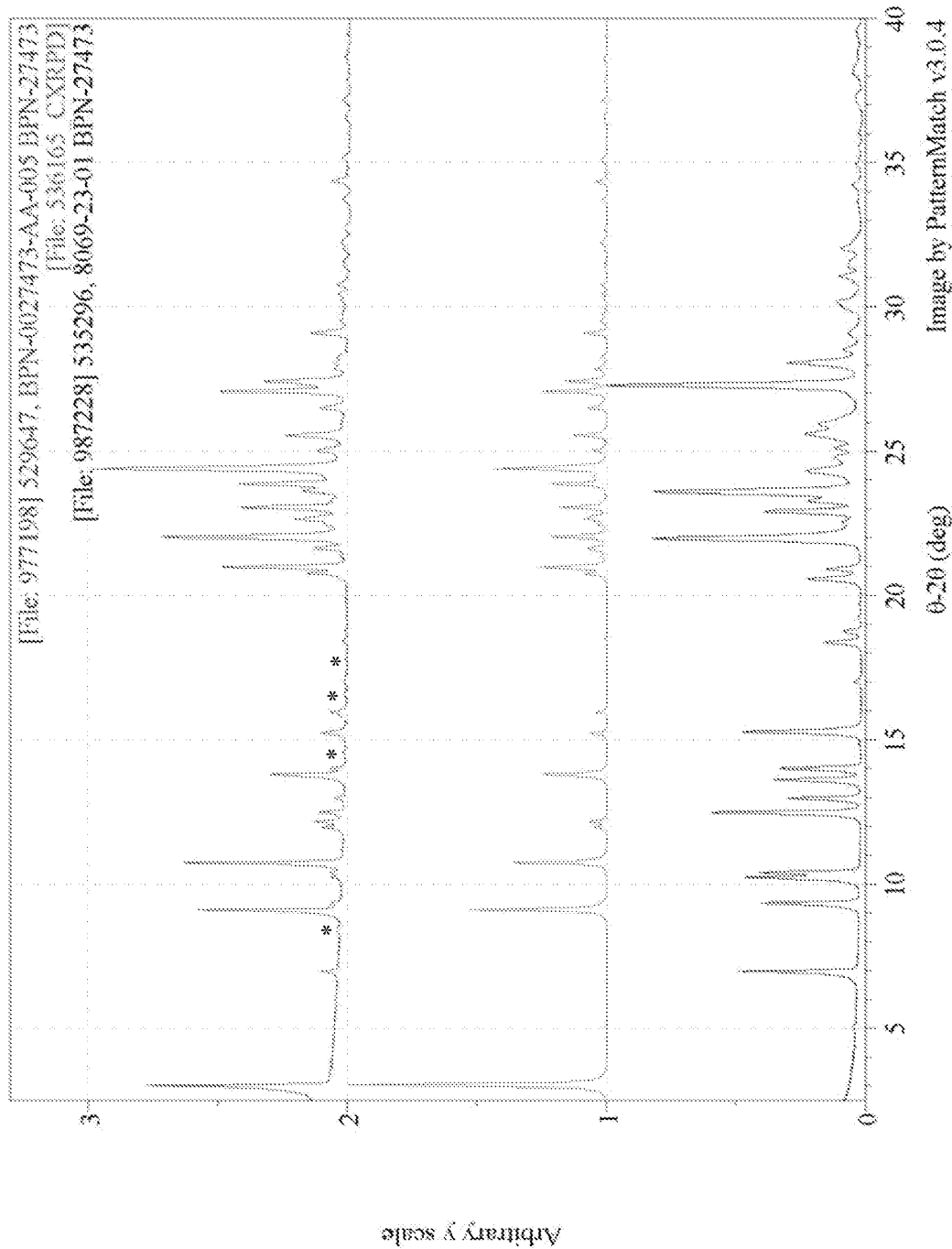


FIG. 43

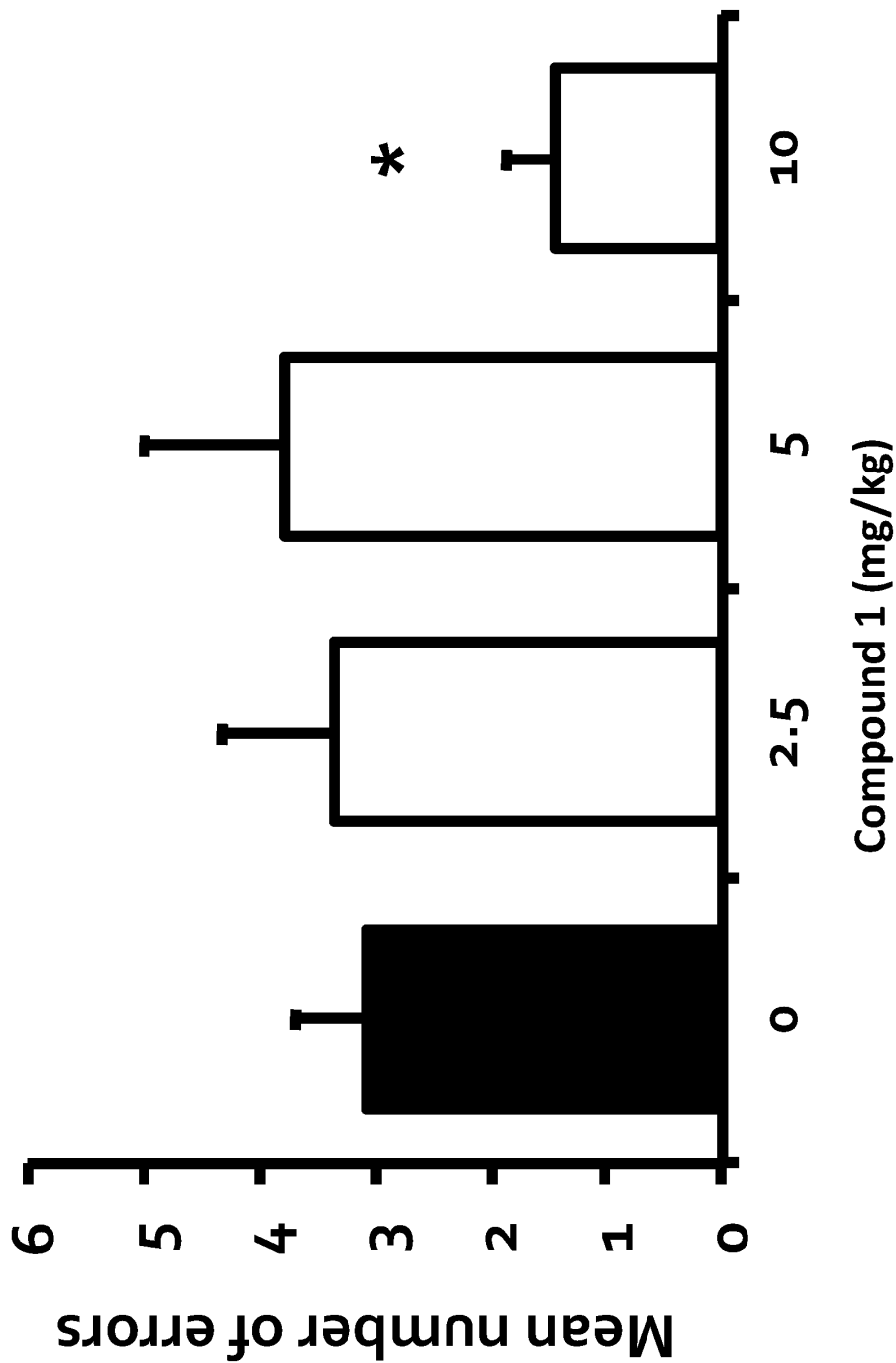


FIG. 44

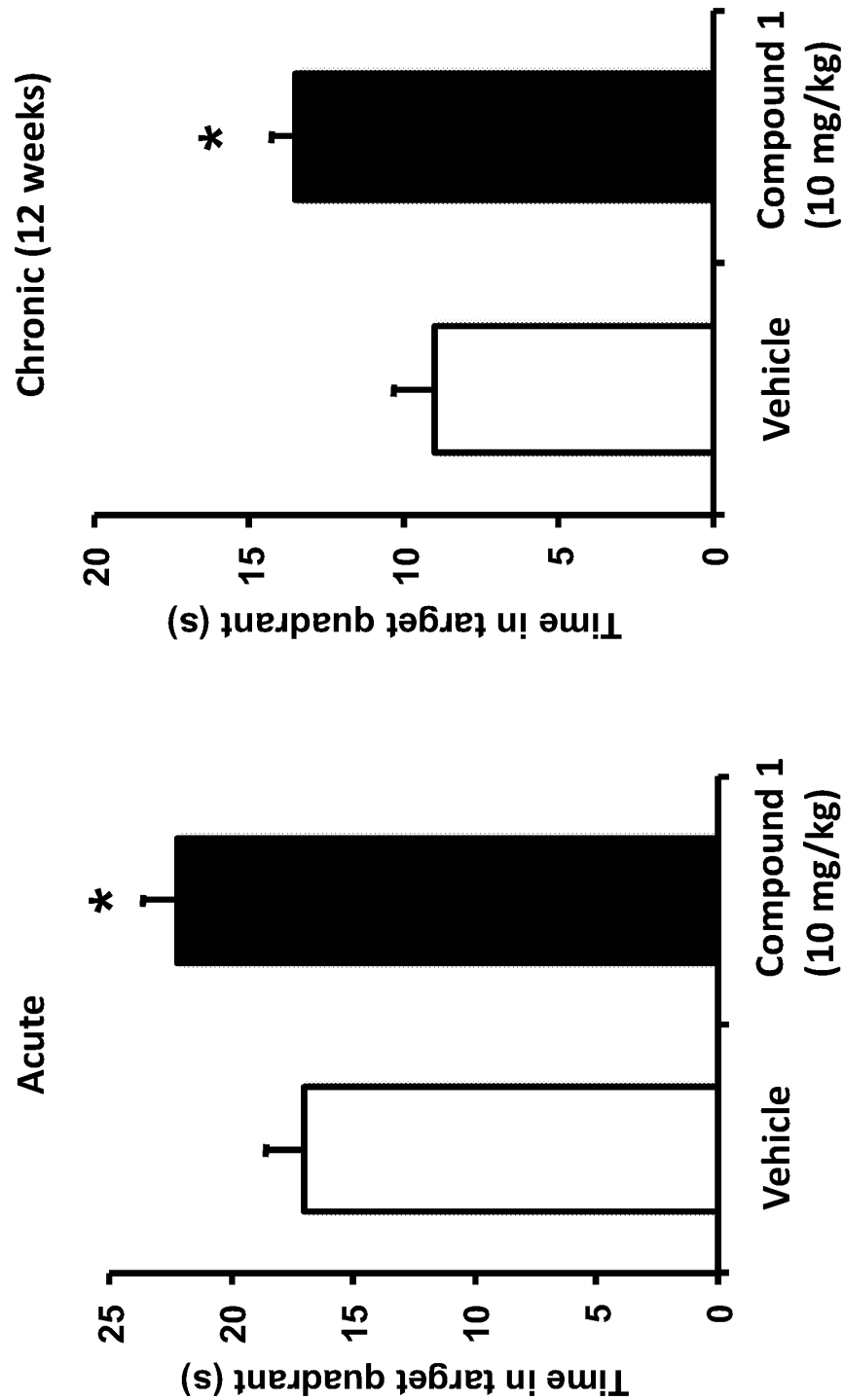


FIG. 45A

FIG. 45B

FIG. 46A

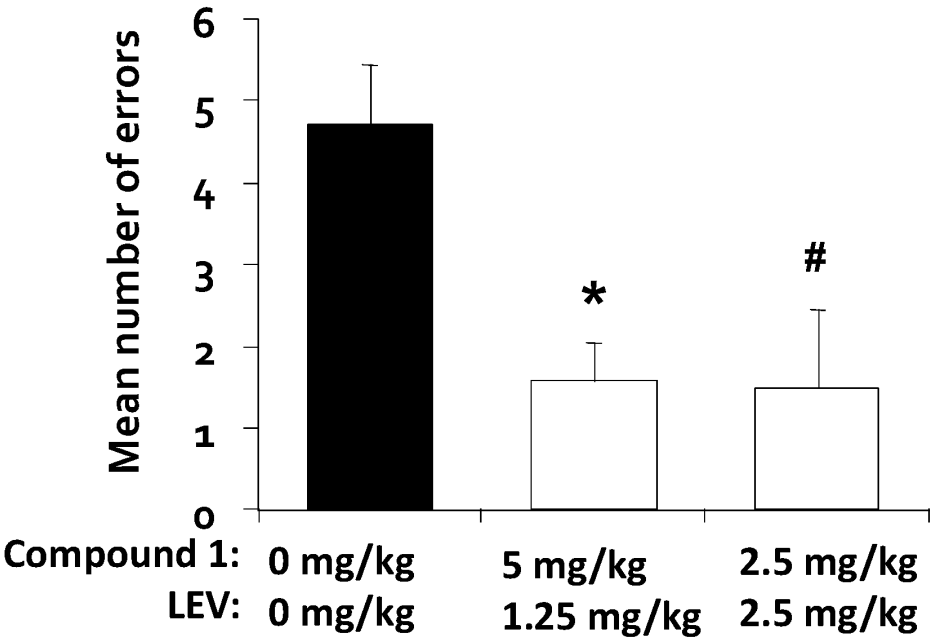


FIG. 46B

