

Part A:

Table S1. Mortality rate and clinical symptoms of experimental animals treated with different doses of lime (*C. aurantifolia*) leaf alkaloid-rich extracts for 14 days.

Dose (mg/kg)	Mortality rate (%)	Symptoms
5	0	None
50	0	None
500	0	None
2000	0	Dullness
5000	0	Lethargy, poor gait

Values represent mean $\pm$ standard deviation (n = 6).

Table S2. Effect of lime leaf alkaloid-rich extracts on escape latency and memory index on day 14.

Groups	Escape latency (sec)	Memory index (%)
1	21.66 ± 0.86 ^a	71.58 ± 1.76 ^a
2	19.28 ± 1.34 ^a	73.15 ± 0.88 ^a
3	18.72 ± 1.22 ^a	74.39 ± 0.64 ^a
4	18.16 ± 0.63 ^a	75.92 ± 1.81 ^a
5	25.14 ± 1.82 ^b	63.76 ± 1.91 ^b
6	36.82 ± 1.63 ^b	56.21 ± 1.58 ^b

Values represent mean ± standard deviation (n = 6). Superscripts with different alphabets along the same row are significantly (P < 0.01) different.

Key

Group 1: control rats received saline water

Group 2: rats treated with 5 mg/kg LLARE (Lime leaf alkaloid-rich extract)

Group 3: rats treated with 50 mg/kg LLARE

Group 4: rats treated with 500 mg/kg LLARE

Group 5: rats treated with 2000 mg/kg LLARE

Group 6: rats treated with 5000 mg/kg LLARE

Table S3. Effect of lime leaf alkaloid-rich extracts on acetylcholinesterase (AChE) and adenosine deaminase (ADA) activities in the brain tissues of experimental animals.

Groups	AChE (umole/min/mg protein)	ADA (mmole/mg protein)
1	1.82 ± 0.61 ^a	0.36 ± 0.15 ^a
2	1.75 ± 0.46 ^a	0.32 ± 0.12 ^a
3	1.38 ± 0.70 ^a	0.28 ± 0.20 ^a
4	2.01 ± 1.02 ^a	0.30 ± 0.13 ^a
5	2.91 ± 1.73 ^a	0.82 ± 0.16 ^b
6	5.79 ± 1.68 ^b	1.28 ± 0.63 ^b

Values represent mean ± standard deviation (n=6). Superscripts with different alphabets along the same row are significantly (P < 0.01) different.

Key

Group 1: control rats received saline water

Group 2: rats treated with 5 mg/kg LLARE (Lime leaf alkaloid-rich extract)

Group 3: rats treated with 50 mg/kg LLARE

Group 4: rats treated with 500 mg/kg LLARE

Group 5: rats treated with 2000 mg/kg LLARE

Group 6: rats treated with 5000 mg/kg LLARE

Table S4. Effect of lime leaf alkaloid-rich extracts on alanine amino transaminase (ALT) and aspartate amino transaminase (AST) activities in the serum of experimental animals.

Groups	ALT (U/L)	AST (U/L)
1	41.86 ± 1.94 ^a	51.48 ± 0.98 ^a
2	40.18 ± 0.96 ^a	51.07 ± 1.65 ^a
3	38.54 ± 1.44 ^a	52.84 ± 1.24 ^a
4	40.64 ± 1.85 ^a	55.27 ± 1.79 ^a
5	48.61 ± 1.72 ^b	68.61 ± 1.42 ^b
6	52.62 ± 1.41 ^b	72.37 ± 1.38 ^b

Values represent mean ± standard deviation (n=6). Superscripts with different alphabets along the same row are significantly (P < 0.01) different.

Key

Group 1: control rats received saline water

Group 2: rats treated with 5 mg/kg LLARE (Lime leaf alkaloid-rich extract)

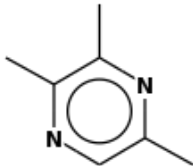
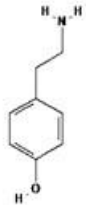
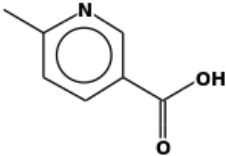
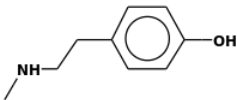
Group 3: rats treated with 50 mg/kg LLARE

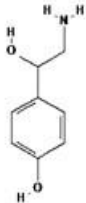
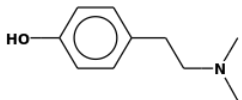
Group 4: rats treated with 500 mg/kg LLARE

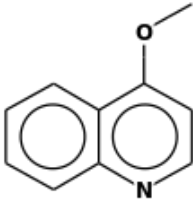
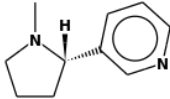
Group 5: rats treated with 2000 mg/kg LLARE

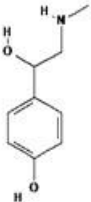
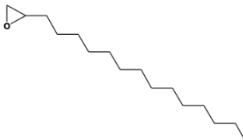
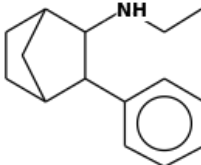
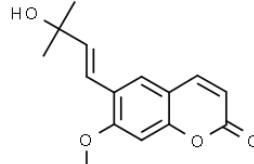
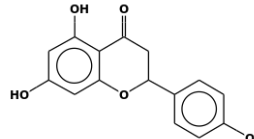
Group 6: rats treated with 5000 mg/kg LLARE

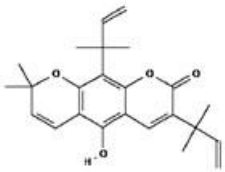
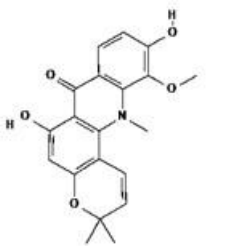
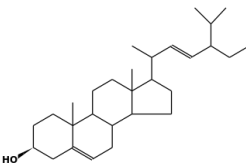
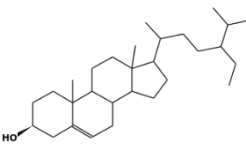
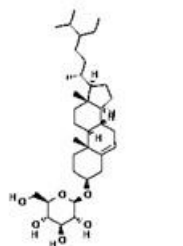
Table S5. Alkaloid compounds in lime leaf alkaloid-rich extract.

Peak #	RT	Compound Detected	Mol. Formula	MW	Peak Area %	Comp (%wt)	m/z	Structures
1	2.00	Pyrazine, trimethyl-	C ₇ H ₁₀ N ₂	122	3.85	4.47	42, 81, 122	
2	5.18	Tyramine	C ₈ H ₁₁ NO	137	5.09	5.24	77, 107, 137	
3	10.00	6-Methylnicotinic acid	C ₇ H ₇ NO ₂	137	7.68	6.13	45, 92, 137	
4	11.49	Phenol, 4-[2-(methylamino)ethyl]-	C ₉ H ₁₃ NO	151	4.85	7.27	44, 71, 151	

5	14.38	Octopamine	$C_8H_{11}NO_2$	153	5.46	3.25	77, 123, 153	
6	15.98	1-Decene, 8-methyl-	$C_{11}H_{22}$	154	5.25	5.15	41, 70, 154	
7	17.00	Hordenine	$C_{10}H_{15}NO$	165	4.24	5.04	42, 58, 165	

8	18.75	Methoxyquinoline	$C_{10}H_9NO$	159	4.95	4.59	50, 116, 159	
9	19.61	Pyridine, 3-(1-methyl-2-pyrrolidinyl)-, (S)	$C_{10}H_{14}N_2$	162	6.66	7.17	42, 84, 162	

10	25.23	Synephrine	$C_9H_{13}NO_2$	267	9.35	12.65	116, 193, 267	
11	26.41	Oxirane, tetradecyl-	$C_{16}H_{32}O$	240	7.67	6.98	47, 82, 240	
12	27.75	2-Norbornanamine, N-ethyl-3-phenyl-	$C_{15}H_{21}N$	215	3.83	2.13	58, 98, 215	
13	29.00	Suberenol	$C_{15}H_{16}$	260	4.44	4.97	42, 58, 260	
14	30.30	Naringenin	$C_{15}H_{12}O_5$	272	7.07	5.95	43, 73, 272	

15	31.00	Clausarin	$C_{24}H_{28}O_4$	380	4.65	3.21	43, 81, 380	
16	35.68	Citracridone I	$C_{20}H_{19}NO_5$	353	6.26	6.20	43, 325, 353	
17	37.00	Stigmasterol	$C_{29}H_{48}O$	412	1.41	2.63	43, 56, 412	
18	38.26	β -Sitosterol	$C_{29}H_{50}O$	414	1.82	2.06	43, 107, 414	
19	40.50	beta-sitosterol-3-O-beta-d-glucoside	$C_{35}H_{60}O_6$	576	5.45	4.90	43, 157, 576	

References

AOAC (2000). Official Methods of Analysis of the Association of Official Analytical Chemists, 17th edn (edited by Horwitz W). Washington, DC.

Part B: Statistics

1 Morris water maze test - Escape Latency

One Way Anova

```
      Df Sum Sq Mean Sq F value Pr(>F)
treatment  6 12865  2144.1   62.37 <2e-16 ***
Residuals 35  1203    34.4
```

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = ECP)

\$treatment

	diff	lwr	upr	p adj
SP-CT	56.3333333	43.5928409	69.073826	0.0000001
T1-CT	10.5000000	-2.2404924	23.240492	0.0529083
T2-CT	2.1666667	-10.5738257	14.907159	0.9948858
T3-CT	11.1666667	-1.5738257	23.907159	0.0329895
T4-CT	19.3333333	6.5928409	32.073826	0.0000358
T5-CT	13.6666667	0.9261743	26.407159	0.0047551
T1-SP	-45.8333333	-58.5738257	-33.092841	0.0000001
T2-SP	-54.1666667	-66.9071591	-41.426174	0.0000003
T3-SP	-45.1666667	-57.9071591	-32.426174	0.00000001
T4-SP	-37.0000000	-49.7404924	-24.259508	0.0000001
T5-SP	-42.6666667	-55.4071591	-29.926174	0.0000002
T2-T1	-8.3333333	-21.0738257	4.407159	0.2044541
T3-T1	0.6666667	-12.0738257	13.407159	0.9999943
T4-T1	8.8333333	-3.9071591	21.573826	0.1540169

T5-T1	3.1666667	-9.5738257	15.907159	0.9639904
T3-T2	9.0000000	-3.7404924	21.740492	0.1395569
T4-T2	17.1666667	4.4261743	29.907159	0.0002420
T5-T2	11.5000000	-1.2404924	24.240492	0.0258405
T4-T3	8.1666667	-4.5738257	20.907159	0.2237237
T5-T3	2.5000000	-10.2404924	15.240492	0.9890430
T5-T4	-5.6666667	-18.4071591	7.073826	0.6369787

Key

CT: Control

SP/SCOP: Scopolamine-induced

T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

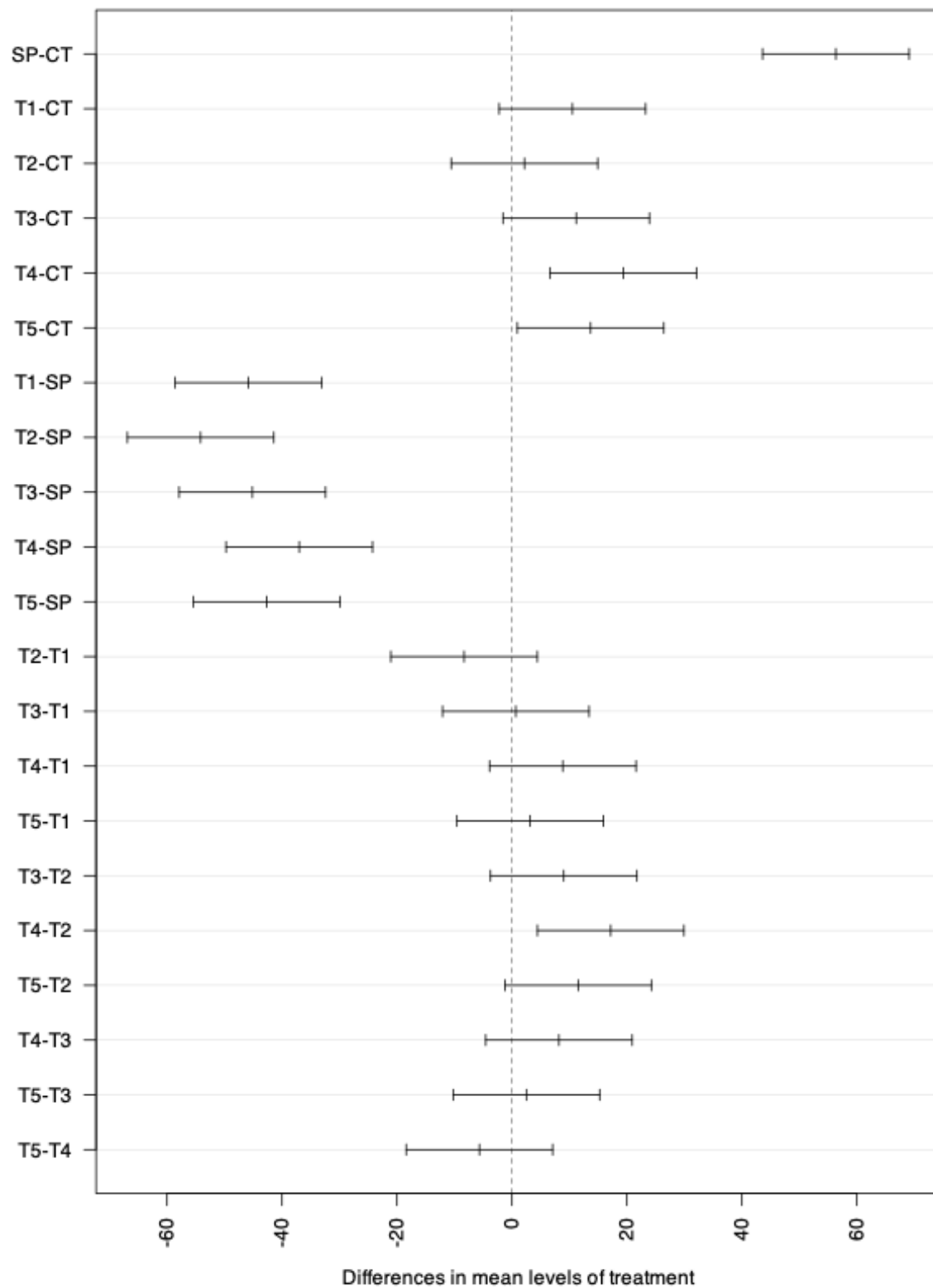
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



2 Y maze test - Memory Index

One Way Anova

```
      Df Sum Sq Mean Sq F value    Pr(>F)
treatment  6  6862  1143.7   53.61 3.37e-16 ***
Residuals 35   747    21.3
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = MI)

```
$treatment
      diff      lwr      upr      p adj
SP-CT -31.333333 -41.3699353 -21.296731 0.0000001
T1-CT  7.000000  -3.0366019  17.036602 0.1493408
T2-CT  9.666667  -0.3699353  19.703269 0.0144238
T3-CT -8.333333 -18.3699353  1.703269 0.0501103
T4-CT -12.666667 -22.7032686  -2.630065 0.0006232
T5-CT -7.333333 -17.3699353  2.703269 0.1156431
T1-SP  38.333333  28.2967314  48.369935 0.0000001
T2-SP  41.000000  30.9633981  51.036602 0.0000007
T3-SP  23.000000  12.9633981  33.036602 0.0000004
T4-SP  18.666667  8.6300647  28.703269 0.0000008
T5-SP  24.000000  13.9633981  34.036602 0.0000001
T2-T1  2.666667  -7.3699353  12.703269 0.9506164
T3-T1 -15.333333 -25.3699353  -5.296731 0.0000319
T4-T1 -19.666667 -29.7032686  -9.630065 0.0000003
T5-T1 -14.333333 -24.3699353  -4.296731 0.0000980
```

T3-T2 -18.000000 -28.0366019 -7.963398 0.0000016
T4-T2 -22.333333 -32.3699353 -12.296731 0.0000001
T5-T2 -17.000000 -27.0366019 -6.963398 0.0000049
T4-T3 -4.333333 -14.3699353 5.703269 0.6676850
T5-T3 1.000000 -9.0366019 11.036602 0.9997483
T5-T4 5.333333 -4.7032686 15.369935 0.4326558

Key

CT: Control

SP/SCOP: Scopolamine-induced

T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

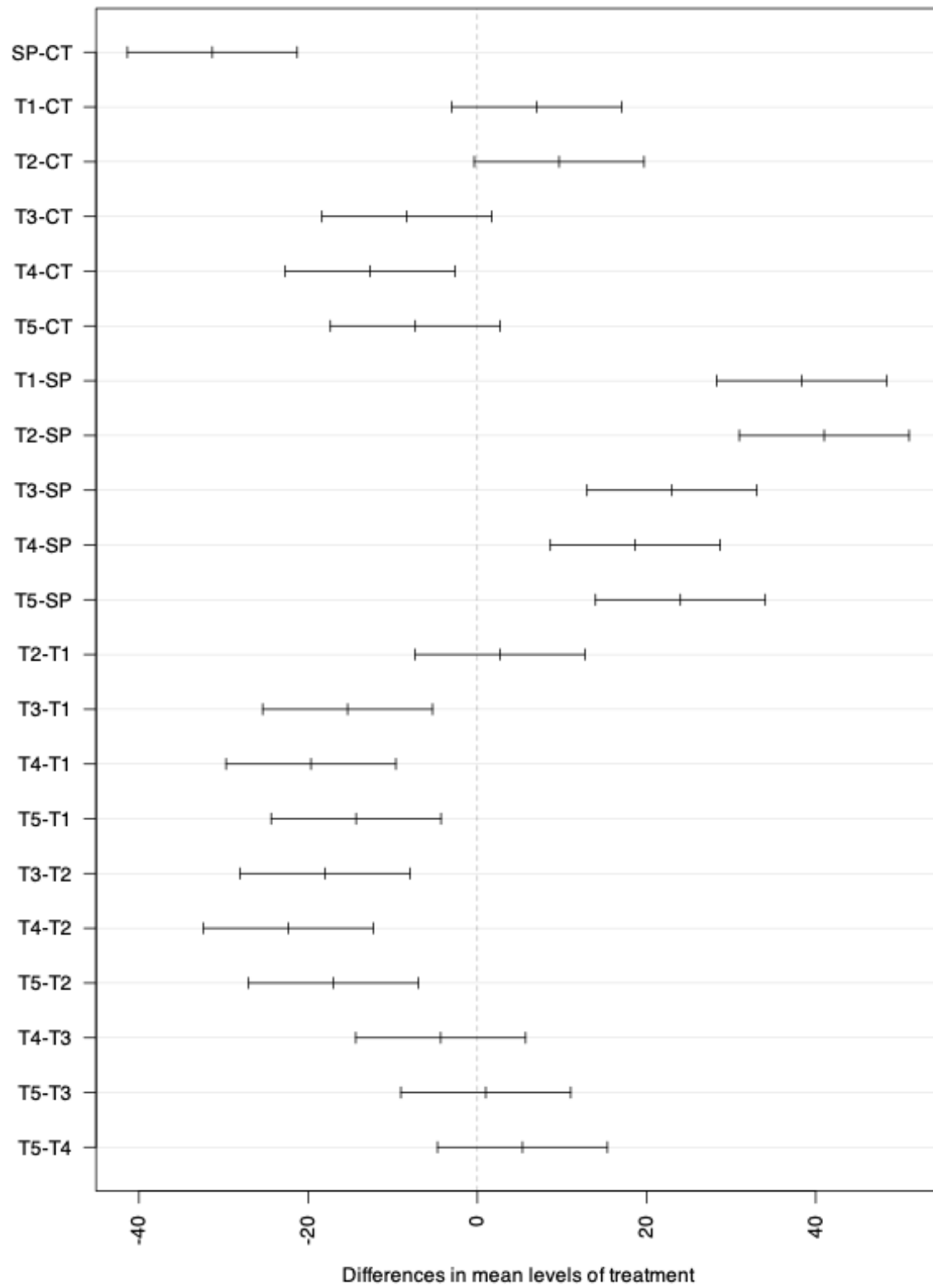
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



3 Open field test - Number of Boxes Crossed

One Way Anova

```
      Df Sum Sq Mean Sq F value Pr(>F)
treatment  6 1359.2   226.5   83.76 <2e-16 ***
Residuals 35   94.7     2.7
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = BC)

```
$treatment
      diff      lwr      upr      p adj
SP-CT -14.6666667 -18.240398 -11.092936 0.0000001
T1-CT  3.0000000  -0.573731  6.573731 0.0461851
T2-CT  2.3333333  -1.240398  5.907064 0.2061267
T3-CT  1.3333333  -2.240398  4.907064 0.7958799
T4-CT -4.6666667  -8.240398 -1.092936 0.0003843
T5-CT -1.6666667  -5.240398  1.907064 0.5853529
T1-SP 17.6666667 14.092936 21.240398 0.0000001
T2-SP 17.0000000 13.426269 20.573731 0.0000003
T3-SP 16.0000000 12.426269 19.573731 0.0000007
T4-SP 10.0000000  6.426269 13.573731 0.0000001
T5-SP 13.0000000  9.426269 16.573731 0.0000004
T2-T1 -0.6666667  -4.240398  2.907064 0.9916046
T3-T1 -1.6666667  -5.240398  1.907064 0.5853529
T4-T1 -7.6666667 -11.240398 -4.092936 0.0000006
T5-T1 -4.6666667  -8.240398 -1.092936 0.0003843
```

T3-T2	-1.0000000	-4.573731	2.573731	0.9373443
T4-T2	-7.0000000	-10.573731	-3.426269	0.0000003
T5-T2	-4.0000000	-7.573731	-0.426269	0.0029167
T4-T3	-6.0000000	-9.573731	-2.426269	0.0000058
T5-T3	-3.0000000	-6.573731	0.573731	0.0461851
T5-T4	3.0000000	-0.573731	6.573731	0.0461851

Key

CT: Control

SP/SCOP: Scopolamine-induced

T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

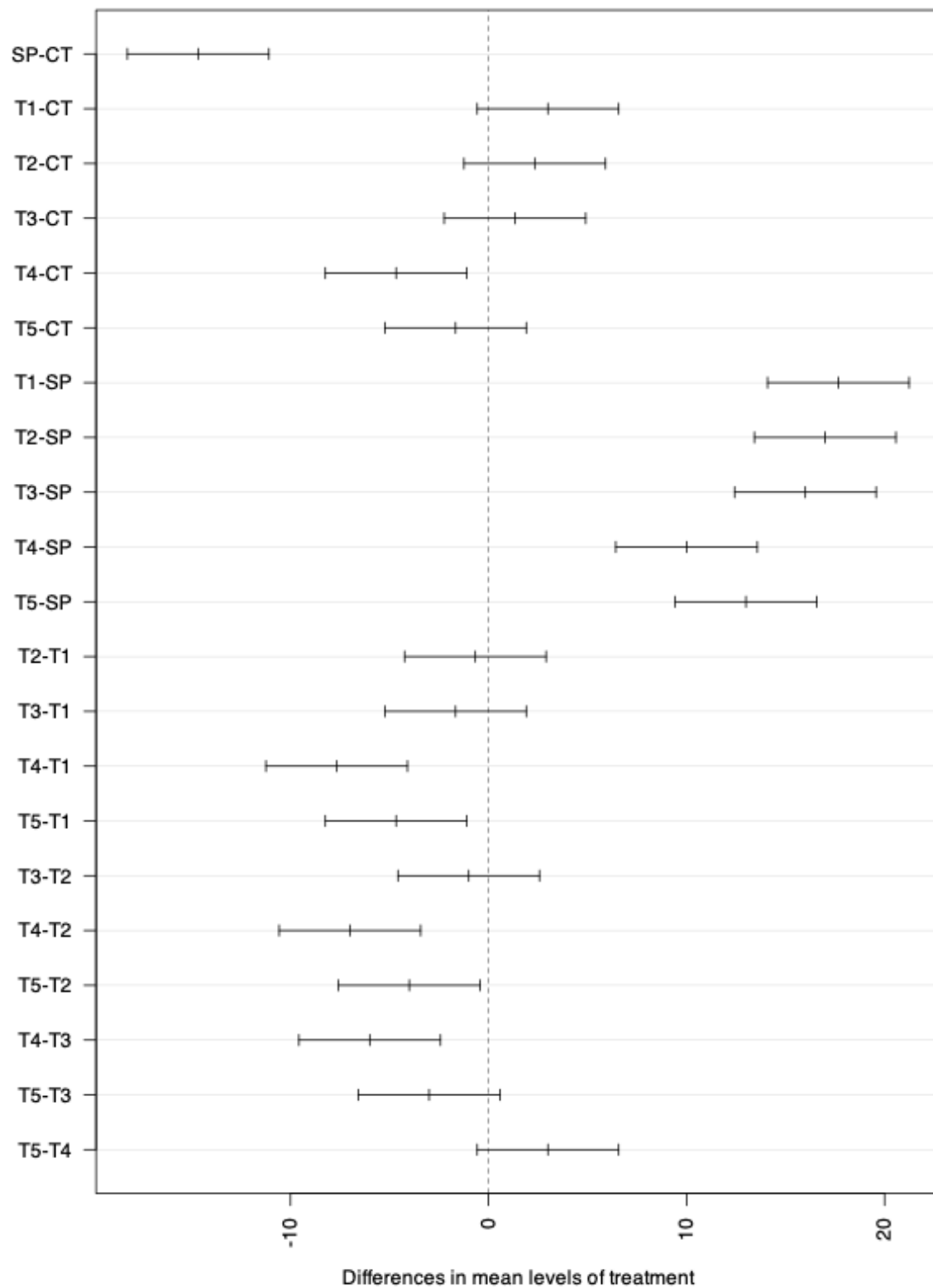
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



4 Open field test - Time Spent in Central Square

One Way Anova

Df Sum Sq Mean Sq F value Pr(>F)

treatment 6 276.54 46.09 110.7 <2e-16 ***

Residuals 35 14.57 0.42

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = TS)

\$treatment

	diff	lwr	upr	p adj
SP-CT	6.666667	5.26481065	8.068523	0.0000001
T1-CT	-0.7000000	-2.10185601	0.701856	0.5066137
T2-CT	-1.0000000	-2.40185601	0.401856	0.1323474
T3-CT	-0.3333333	-1.73518935	1.068523	0.9709606
T4-CT	3.0000000	1.59814399	4.401856	0.0000007
T5-CT	0.3333333	-1.06852268	1.735189	0.9709606
T1-SP	-7.366667	-8.76852268	-5.964811	0.0000002
T2-SP	-7.666667	-9.06852268	-6.264811	0.0000009
T3-SP	-7.0000000	-8.40185601	-5.598144	0.0000001
T4-SP	-3.666667	-5.06852268	-2.264811	0.0000008
T5-SP	-6.3333333	-7.73518935	-4.931477	0.0000001
T2-T1	-0.3000000	-1.70185601	1.101856	0.9828536
T3-T1	0.3666667	-1.03518935	1.768523	0.9541106
T4-T1	3.7000000	2.29814399	5.101856	0.0000004
T5-T1	1.0333333	-0.36852268	2.435189	0.1098746

T3-T2 0.6666667 -0.73518935 2.068523 0.5632861
T4-T2 4.0000000 2.59814399 5.401856 0.0000001
T5-T2 1.3333333 -0.06852268 2.735189 0.0162259
T4-T3 3.3333333 1.93147732 4.735189 0.0000001
T5-T3 0.6666667 -0.73518935 2.068523 0.5632861
T5-T4 -2.6666667 -4.06852268 -1.264811 0.0000005

Key

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T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

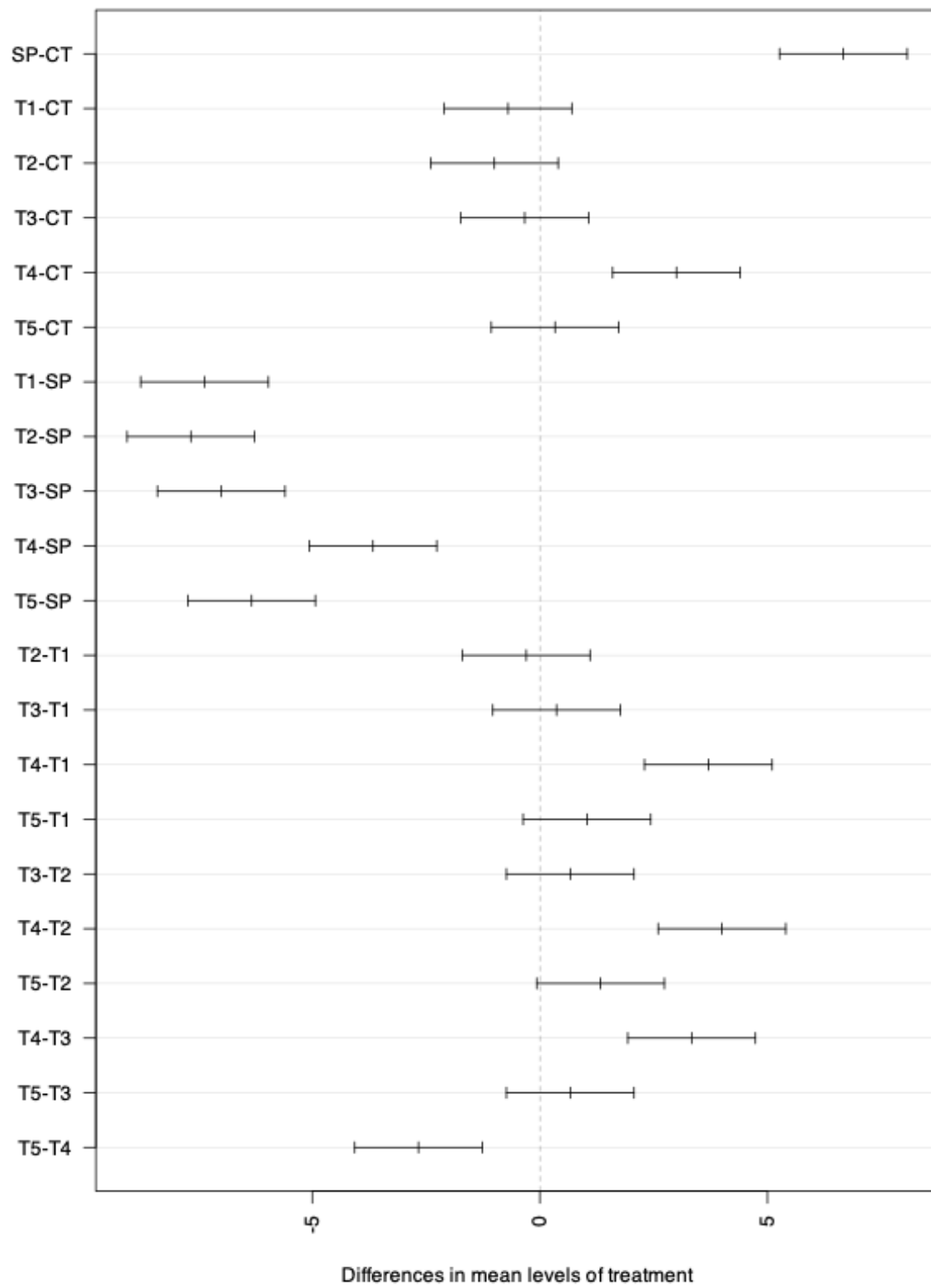
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



5 Acetylcholinesterase activity (Cortex)

One Way Anova

Df Sum Sq Mean Sq F value Pr(>F)

treatment 6 509.5 84.91 306.2 <2e-16 ***

Residuals 35 9.7 0.28

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = ChE)

\$treatment

	diff	lwr	upr	p adj
SP-CT	9.98896800	8.8446169	11.1333191	0.0000001
T1-CT	-0.16078067	-1.3051318	0.9835705	0.9982134
T2-CT	-0.34439267	-1.4887438	0.7999585	0.9134780
T3-CT	-0.06698467	-1.2113358	1.0773665	0.9999889
T4-CT	1.42047833	0.2761272	2.5648295	0.0007826
T5-CT	0.08392600	-1.0604251	1.2282771	0.9999580
T1-SP	-10.14974867	-11.2940998	-9.0053975	0.0000004
T2-SP	-10.33336067	-11.4777118	-9.1890095	0.0000001
T3-SP	-10.05595267	-11.2003038	-8.9116015	0.0000008
T4-SP	-8.56848967	-9.7128408	-7.4241385	0.0000016
T5-SP	-9.90504200	-11.0493931	-8.7606909	0.0000001
T2-T1	-0.18361200	-1.3279631	0.9607391	0.9962739
T3-T1	0.09379600	-1.0505551	1.2381471	0.9999193
T4-T1	1.58125900	0.4369079	2.7256101	0.0001648

T5-T1	0.24470667	-0.8996445	1.3890578	0.9829201
T3-T2	0.27740800	-0.8669431	1.4217591	0.9680907
T4-T2	1.76487100	0.6205199	2.9092221	0.0000271
T5-T2	0.42831867	-0.7160325	1.5726698	0.7935009
T4-T3	1.48746300	0.3431119	2.6318141	0.0004107
T5-T3	0.15091067	-0.9934405	1.2952618	0.9987483
T5-T4	-1.33655233	-2.4809035	-0.1922012	0.0017350

Key

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SP/SCOP: Scopolamine-induced

T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

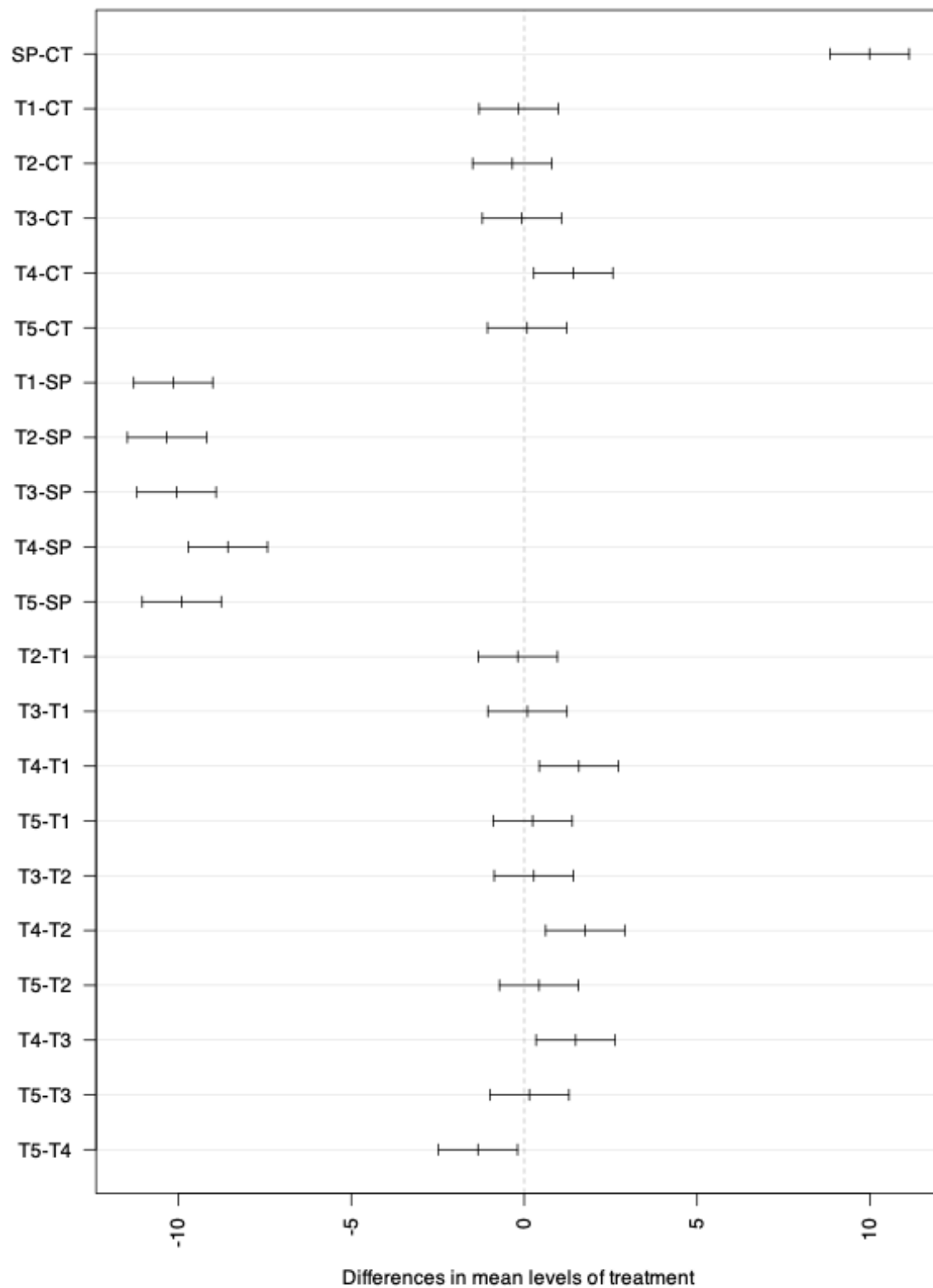
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



6 Acetylcholinesterase activity (Hippocampus)

One Way Anova

Df Sum Sq Mean Sq F value Pr(>F)

treatment 6 437.7 72.96 273.7 <2e-16 ***

Residuals 35 9.3 0.27

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = HCT)

\$treatment

	diff	lwr	upr	p adj
SP-CT	9.76355200	8.64173236	10.8853716	0.0000002
T1-CT	0.88416233	-0.23765731	2.0059820	0.0722208
T2-CT	0.26714133	-0.85467831	1.3889610	0.9707493
T3-CT	0.03301533	-1.08880431	1.1548350	0.9999998
T4-CT	1.53129873	0.40947909	2.6531184	0.0001989
T5-CT	1.40831367	0.28649402	2.5301333	0.0006705
T1-SP	-8.87938967	-10.00120931	-7.7575700	0.0000001
T2-SP	-9.49641067	-10.61823031	-8.3745910	0.0000006
T3-SP	-9.73053667	-10.85235631	-8.6087170	0.0000002
T4-SP	-8.23225327	-9.35407291	-7.1104336	0.0000001
T5-SP	-8.35523833	-9.47705798	-7.2334187	0.0000001
T2-T1	-0.61702100	-1.73884064	0.5047986	0.3917381
T3-T1	-0.85114700	-1.97296664	0.2706726	0.0922930
T4-T1	0.64713640	-0.47468324	1.7689560	0.3362753
T5-T1	0.52415133	-0.59766831	1.6459710	0.5832713

T3-T2	-0.23412600	-1.35594564	0.8876936	0.9849178
T4-T2	1.26415740	0.14233776	2.3859770	0.0026909
T5-T2	1.14117233	0.01935269	2.2629920	0.0084027
T4-T3	1.49828340	0.37646376	2.6201030	0.0002761
T5-T3	1.37529833	0.25347869	2.4971180	0.0009255
T5-T4	-0.12298507	-1.24480471	0.9988346	0.9995631

Key

CT: Control

SP/SCOP: Scopolamine-induced

T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

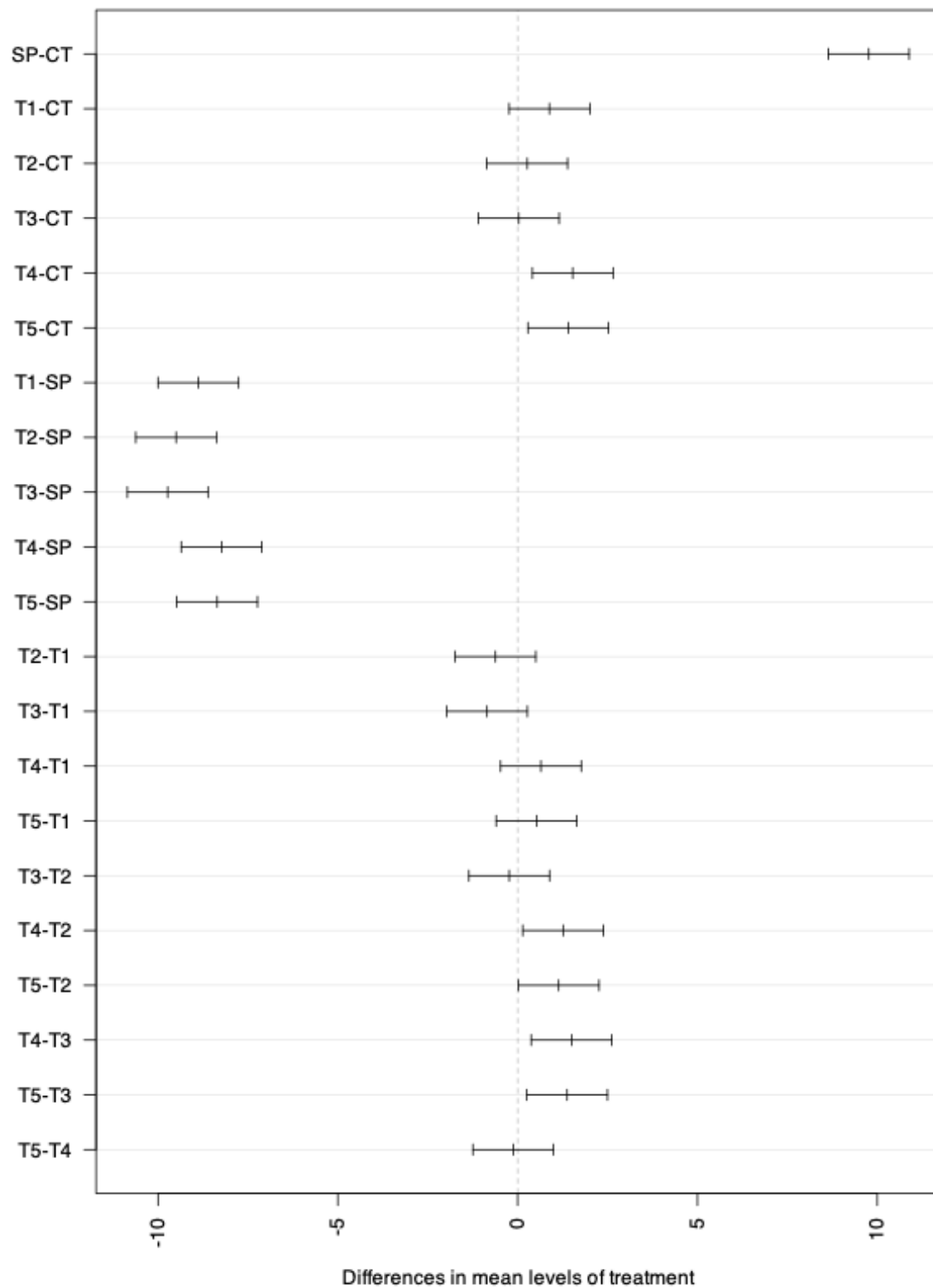
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



7 Adenosine deaminase activity (Cortex)

One Way Anova

Df Sum Sq Mean Sq F value Pr(>F)

treatment 6 1.1114 0.18523 73.13 <2e-16 ***

Residuals 35 0.0887 0.00253

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = CadA)

\$treatment

	diff	lwr	upr	p adj
SP-CT	0.469194000	0.35983261	0.57855539	0.0000005
T1-CT	-0.002408667	-0.11177006	0.10695272	1.0000000
T2-CT	-0.035750000	-0.14511139	0.07361139	0.8774428
T3-CT	0.031756667	-0.07760472	0.14111806	0.9260249
T4-CT	0.052003333	-0.05735806	0.16136472	0.5633864
T5-CT	0.015316667	-0.09404472	0.12467806	0.9982447
T1-SP	-0.471602667	-0.58096406	-0.36224128	0.0000002
T2-SP	-0.504944000	-0.61430539	-0.39558261	0.0000041
T3-SP	-0.437437333	-0.54679872	-0.32807594	0.0000001
T4-SP	-0.417190667	-0.52655206	-0.30782928	0.0000004
T5-SP	-0.453877333	-0.56323872	-0.34451594	0.0000004
T2-T1	-0.033341333	-0.14270272	0.07602006	0.9085063
T3-T1	0.034165333	-0.07519606	0.14352672	0.8984796
T4-T1	0.054412000	-0.05494939	0.16377339	0.5108548
T5-T1	0.017725333	-0.09163606	0.12708672	0.9960622

T3-T2 0.067506667 -0.04185472 0.17686806 0.2618775
T4-T2 0.087753333 -0.02160806 0.19711472 0.0639324
T5-T2 0.051066667 -0.05829472 0.16042806 0.5839430
T4-T3 0.020246667 -0.08911472 0.12960806 0.9919360
T5-T3 -0.016440000 -0.12580139 0.09292139 0.9973973
T5-T4 -0.036686667 -0.14604806 0.07267472 0.8639414

Key

CT: Control

SP/SCOP: Scopolamine-induced

T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

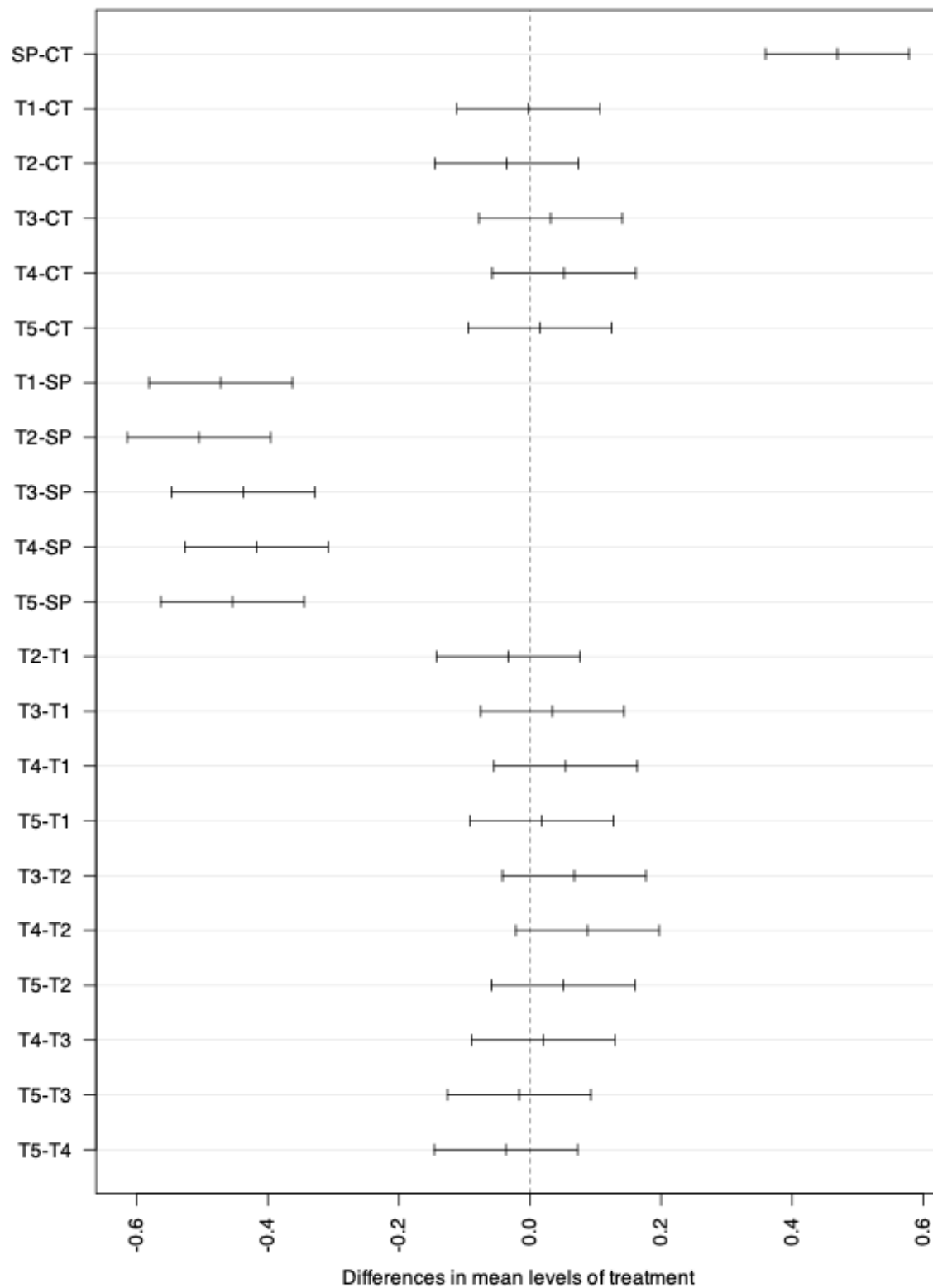
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



8 Adenosine deaminase activity (Hippocampus)

One Way Anova

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
treatment	6	0.6262	0.10436	20.99	2.89e-10 ***
Residuals	35	0.1740	0.00497		

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = HD)

\$treatment

	diff	lwr	upr	p adj
SP-CT	0.10408533	-0.049135681	0.25730635	0.1707840
T1-CT	-0.18243800	-0.335659014	-0.02921699	0.0013578
T2-CT	-0.27893900	-0.432160014	-0.12571799	0.0000012
T3-CT	-0.16470800	-0.317929014	-0.01148699	0.0046439
T4-CT	-0.13350133	-0.286722348	0.01971968	0.0346001
T5-CT	-0.21227000	-0.365491014	-0.05904899	0.0001583
T1-SP	-0.28652333	-0.439744348	-0.13330232	0.0000007
T2-SP	-0.38302433	-0.536245348	-0.22980332	0.0000000
T3-SP	-0.26879333	-0.422014348	-0.11557232	0.0000025
T4-SP	-0.23758667	-0.390807681	-0.08436565	0.0000246
T5-SP	-0.31635533	-0.469576348	-0.16313432	0.0000001
T2-T1	-0.09650100	-0.249722014	0.05672001	0.2411981
T3-T1	0.01773000	-0.135491014	0.17095101	0.9994044
T4-T1	0.04893667	-0.104284348	0.20215768	0.8886346
T5-T1	-0.02983200	-0.183053014	0.12338901	0.9894816

T3-T2 0.11423100 -0.038990014 0.26745201 0.1027211
T4-T2 0.14543767 -0.007783348 0.29865868 0.0165322
T5-T2 0.06666900 -0.086552014 0.21989001 0.6598016
T4-T3 0.03120667 -0.122014348 0.18442768 0.9867005
T5-T3 -0.04756200 -0.200783014 0.10565901 0.9011932
T5-T4 -0.07876867 -0.231989681 0.07445235 0.4721182

Key

CT: Control

SP/SCOP: Scopolamine-induced

T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

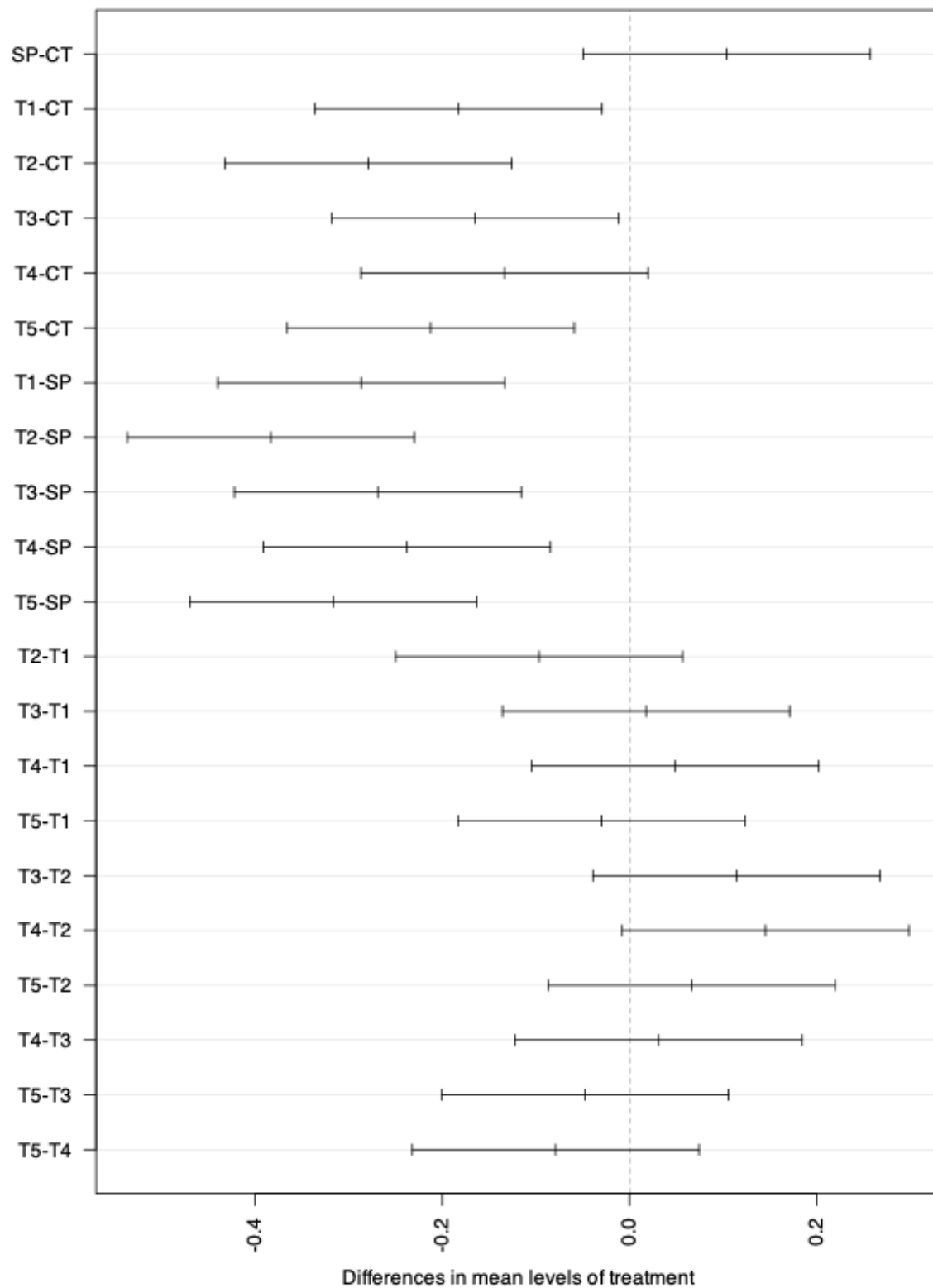
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



9 Monoamine oxidase activity (Cortex)

One Way Anova

```
Df Sum Sq Mean Sq F value Pr(>F)
treatment  6 0.09300 0.015500  43.84 7.5e-15 ***
Residuals 35 0.01237 0.000354
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = Cma)

```
$treatment
      diff      lwr      upr      p adj
SP-CT 0.109306667 0.06844975 0.1501635824 0.0000001
T1-CT 0.001320000 -0.03953692 0.0421769157 0.9999997
T2-CT -0.009166667 -0.05002358 0.0316902491 0.9782272
T3-CT 0.016780000 -0.02407692 0.0576369157 0.7160042
T4-CT 0.101613333 0.06075642 0.1424702491 0.0000008
T5-CT 0.069313333 0.02845642 0.1101702491 0.0000048
T1-SP -0.107986667 -0.14884358 -0.0671297509 0.0000001
T2-SP -0.118473333 -0.15933025 -0.0776164176 0.0000008
T3-SP -0.092526667 -0.13338358 -0.0516697509 0.0000004
T4-SP -0.007693333 -0.04855025 0.0331635824 0.9911785
T5-SP -0.039993333 -0.08085025 0.0008635824 0.0123492
T2-T1 -0.010486667 -0.05134358 0.0303702491 0.9580194
T3-T1 0.015460000 -0.02539692 0.0563169157 0.7852520
T4-T1 0.100293333 0.05943642 0.1411502491 0.0000001
T5-T1 0.067993333 0.02713642 0.1088502491 0.0000068
```

T3-T2	0.025946667	-0.01491025	0.0668035824	0.2328873
T4-T2	0.110780000	0.06992308	0.1516369157	0.0000004
T5-T2	0.078480000	0.03762308	0.1193369157	0.0000004
T4-T3	0.084833333	0.04397642	0.1256902491	0.0000001
T5-T3	0.052533333	0.01167642	0.0933902491	0.0004797
T5-T4	-0.032300000	-0.07315692	0.0085569157	0.0707561

Key

CT: Control

SP/SCOP: Scopolamine-induced

T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

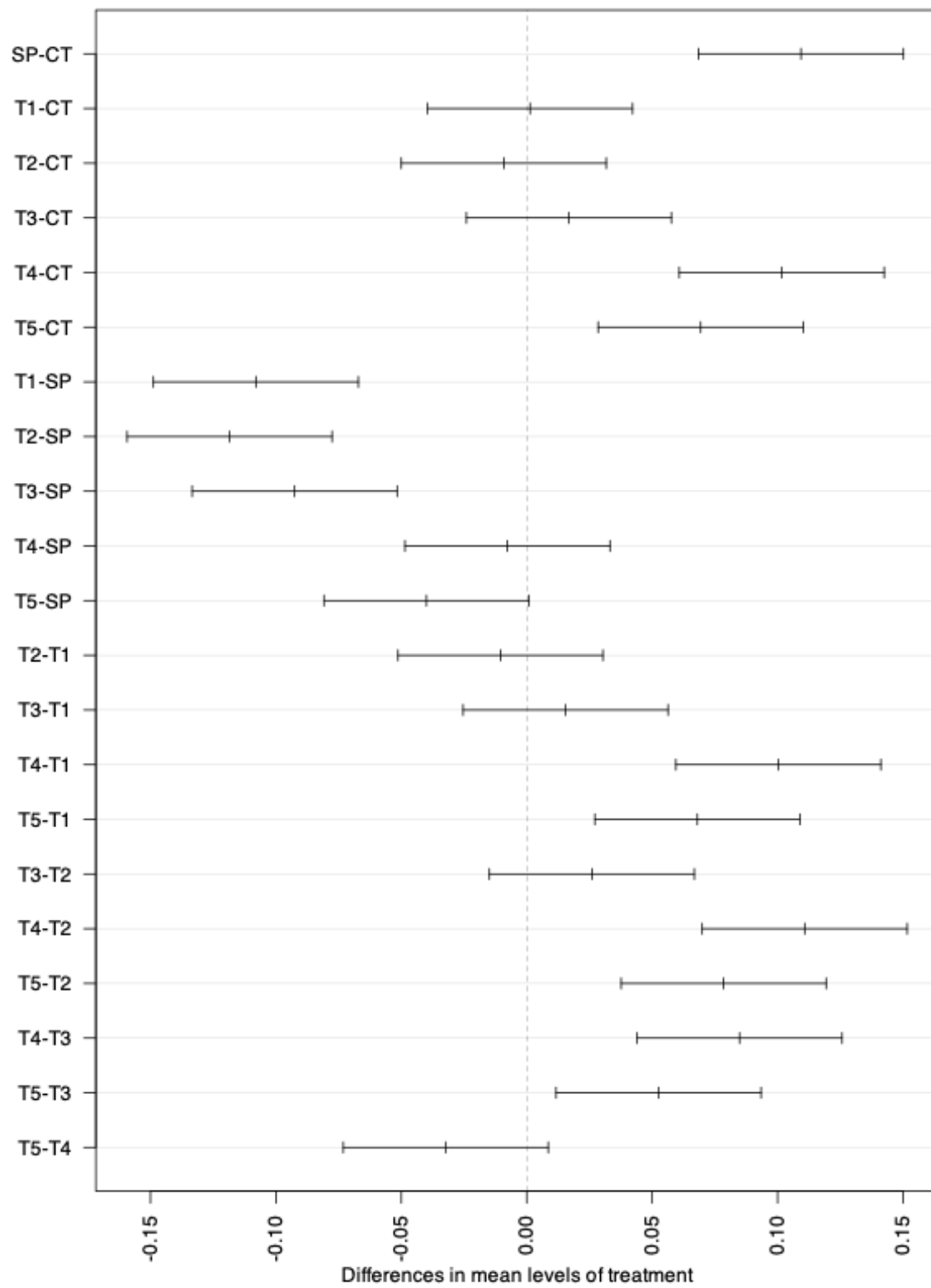
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



10 Monoamine oxidase activity (Hippocampus)

One Way Anova

Df Sum Sq Mean Sq F value Pr(>F)

treatment 6 0.31416 0.05236 368.4 <2e-16 ***

Residuals 35 0.00498 0.00014

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Tukey multiple comparisons of means

99% family-wise confidence level

Fit: aov(formula = score ~ treatment, data = MAo)

\$treatment

	diff	lwr	upr	p adj
SP-CT	0.26993333	0.24402616	0.29584051	0.0000005
T1-CT	0.06775333	0.04184616	0.09366051	0.0000001
T2-CT	0.00558000	-0.02032718	0.03148718	0.9822824
T3-CT	0.06619333	0.04028616	0.09210051	0.0000000
T4-CT	0.13892667	0.11301949	0.16483384	0.0000000
T5-CT	0.05226000	0.02635282	0.07816718	0.0000001
T1-SP	-0.20218000	-0.22808718	-0.17627282	0.0000082
T2-SP	-0.26435333	-0.29026051	-0.23844616	0.0000001
T3-SP	-0.20374000	-0.22964718	-0.17783282	0.0000006
T4-SP	-0.13100667	-0.15691384	-0.10509949	0.0000001
T5-SP	-0.21767333	-0.24358051	-0.19176616	0.0000004
T2-T1	-0.06217333	-0.08808051	-0.03626616	0.0000003
T3-T1	-0.00156000	-0.02746718	0.02434718	0.9999869
T4-T1	0.07117333	0.04526616	0.09708051	0.0000002
T5-T1	-0.01549333	-0.04140051	0.01041384	0.2958659

T3-T2 0.06061333 0.03470616 0.08652051 0.0000006
T4-T2 0.13334667 0.10743949 0.15925384 0.0000002
T5-T2 0.04668000 0.02077282 0.07258718 0.0000015
T4-T3 0.07273333 0.04682616 0.09864051 0.0000001
T5-T3 -0.01393333 -0.03984051 0.01197384 0.4183336
T5-T4 -0.08666667 -0.11257384 -0.06075949 0.0000068

Key

CT: Control

SP/SCOP: Scopolamine-induced

T1: 100 mg/kg LLARE (Lime leaf alkaloid-rich extract)

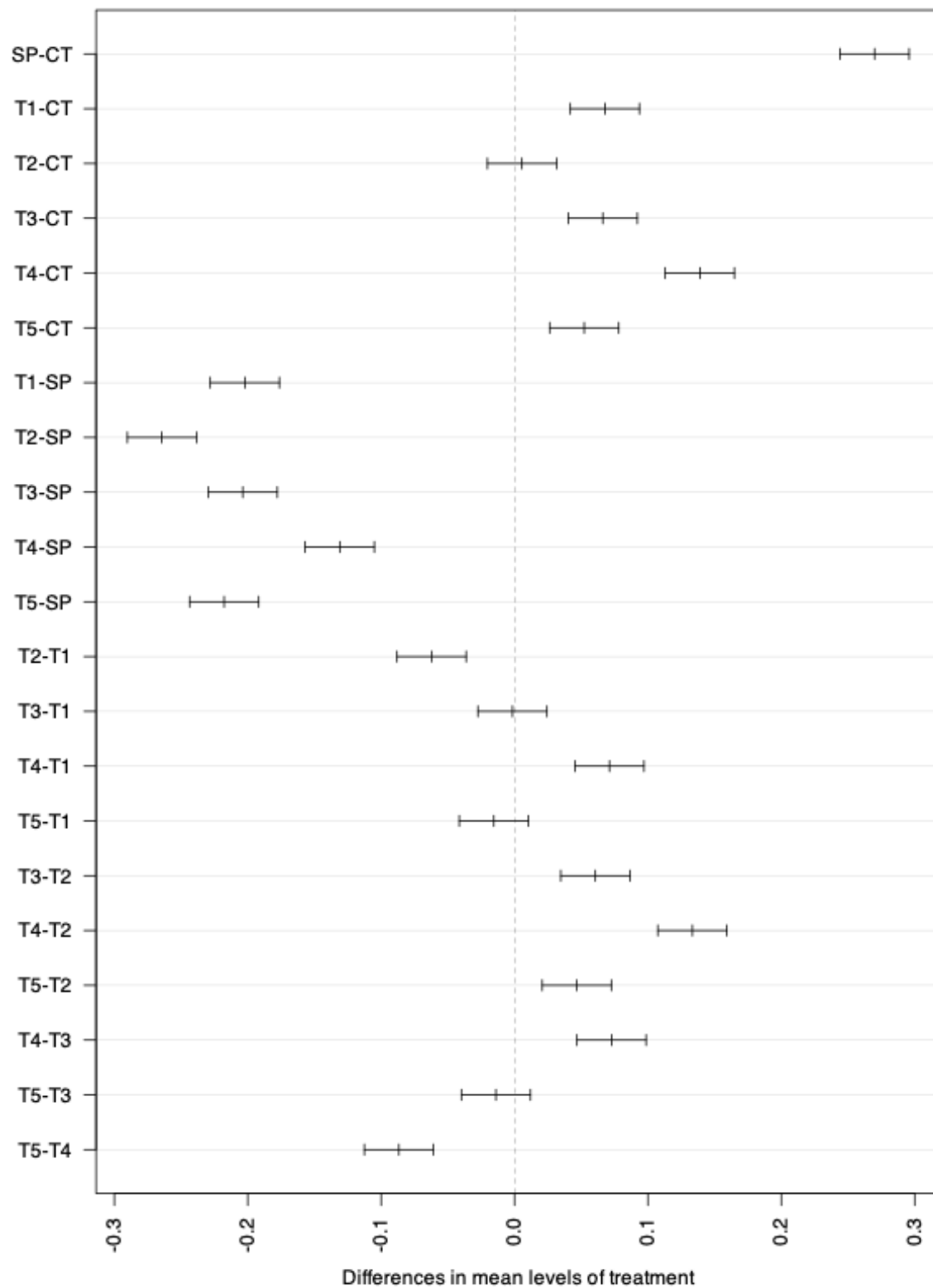
T2: 200 mg/kg LLARE

T3: SCOP + Donepezil

T4: SCOP + 100 mg/kg LLARE

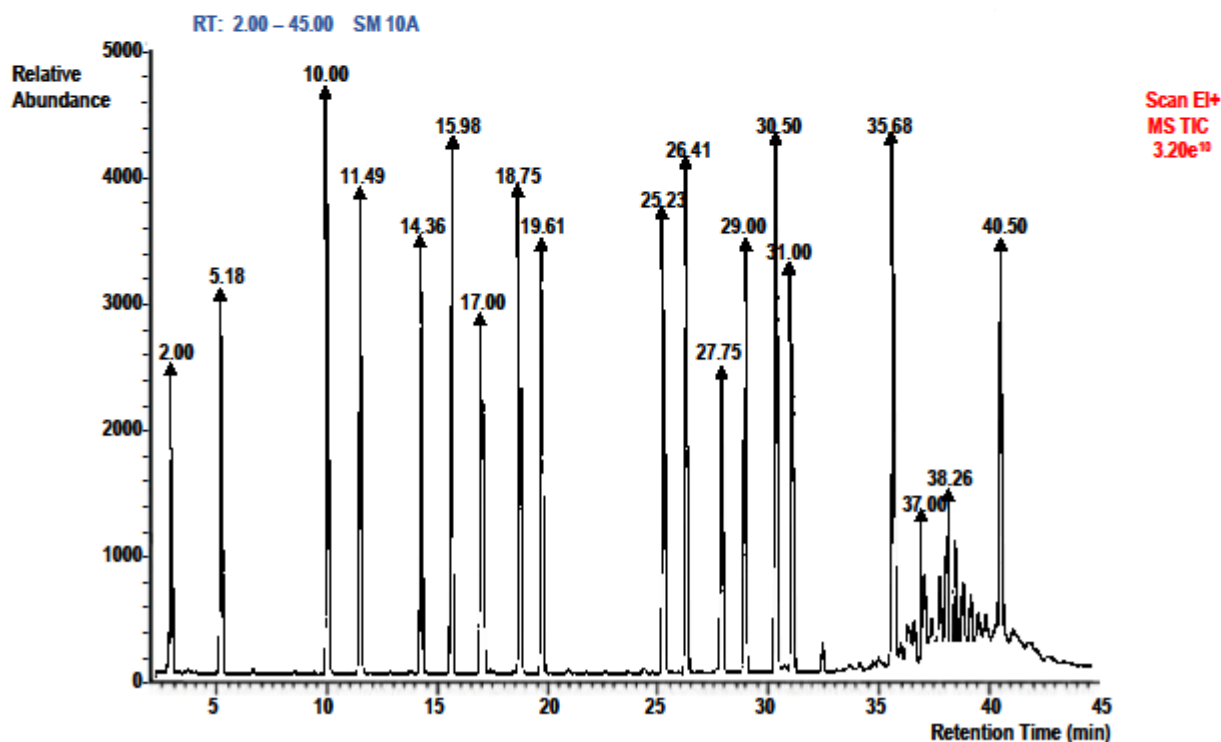
T5: SCOP + 200 mg/kg LLARE

99% family-wise confidence level



Part C: Gas chromatography-mass spectrometry (GC-MS)

Sample ID: DCPE/CAL/GCMS/032024/119811/01 Low Mass (m/z): 40
Operator: Ewere Donatus V.
Data Path: C:\varian\msdchem\data\gcms_sample_01# High Mass (m/z): 800
Run Time: 45.00:00
Instrument Name: GCMS
Sample Name: gcms/data/lime-extract/sample-01# Acquisition Date: 10/03/2024 10:16:03
Comment:
Equipment: Varian 3800/4000 GCMS Client: Consults
ALS Vial: 1 Sample Multiplier: 1
Search Libraries: C:\database\NIST08 Minimum Quality: 10
Column: Agilent MS capillary column
Dimension: 30 m × 0.25 mm i.d.
Carrier Gas: N₂. Flow: 1.0 ml/min
Unknown Spectrum: Apex minus start of peak
Integration Events: ChemStation Integrator.autoint1.e.



Representative gas chromatogram of lime leaf alkaloid-rich extract showing the retention time of its alkaloid compounds.