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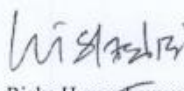

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<https://doi.org/10.1016/J.BRAINRES.2004.11.014>

Enclosure

Enclosure 1. Ethical Clearance Approval Letter

	MEDICAL AND HEALTH RESEARCH ETHICS COMMITTEE (MHREC) FACULTY OF MEDICINE, PUBLIC HEALTH AND NURSING UNIVERSITAS GADJAH MADA – DR. SARDJITO GENERAL HOSPITAL	
ETHICS COMMITTEE APPROVAL		
Ref. No. : KE/FK/1117/EC/2020		
Title of the Research Protocol	: Pengaruh Asam Klorogenat (<i>Chlorogenic Acid</i>) terhadap Perbaikan Disfungsi Memori, Stress Oksidatif, Apoptosis dan Inflamasi pada Otak Tikus Model Diabetes Mellitus	
Document(s) Approved and version	: Study Protocol version 02 2020	
Principle Investigator	: Dr. dr. Dwi Cahyani Ratna Sari, M.Kes., PA(K).	
Participating Investigator(s)	: 1. dr. Nur Arfian, Ph.D. 2. dr. Mawaddah Arrochmah, Ph.D. 3. Wiwit Ananda Wahyu S., S.Keb., M.Sc. 4. Ari Susilowati, S.Si. 5. Satrio Adi Wicaksono 6. Marcello 7. Rafi Irsyad Fakhreza 8. Qintaro Makitsuna M. 9. Fauziyatul Munawaroh	
Date of Approval	: 13 OCT 2020 (Valid for one year beginning from the date of approval)	
Institution(s)/place(s) of research	: Laboratorium Bagian Anatomi FK-KMK UGM	
The Medical and Health Research Ethics Committee (MHREC) states that the document above meets the ethical principle outlined in the International and National Guidelines on ethical standards and procedures for researches involving animal.		
The Medical and Health Research Ethics Committee (MHREC) has the right to monitor the research activities at any time.		
The investigator(s) is/are obliged to submit:		
<input checked="" type="checkbox"/> Progress report as a continuing review (state its due time)		
<input checked="" type="checkbox"/> Report of any serious events		
<input checked="" type="checkbox"/> Final report upon the completion of the study		
	Dr. dr. Eti Nurwening Sholikhah, M.Kes., M.Med.Ed. Panel's vice chairperson	 dr. Rizka Humardewyanita A., Sp.PD-KPTL. Panel's secretary
P.S: This letter uses signature scan of the panel's chairperson and Secretary of the Ethics Committee. The hardcopy official letter with authority's signature will be issued when it is possible and are kept as an archive of the Ethics Committee		Validation number : 5f850235b7cdf (http://komisietik.fk.ugm.ac.id/validasi)
		
Recognized by Forum for Ethical Review Committees in Asia and the Western Pacific (FERCAP) 13-Oct-20		

Enclosure 2. Normality Test of RBG Levels

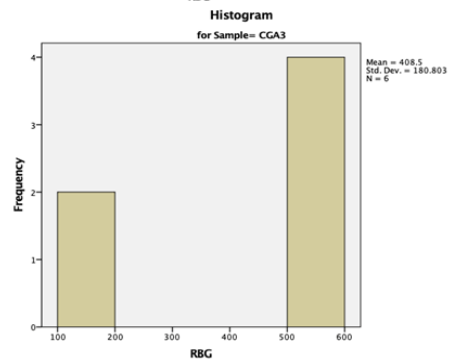
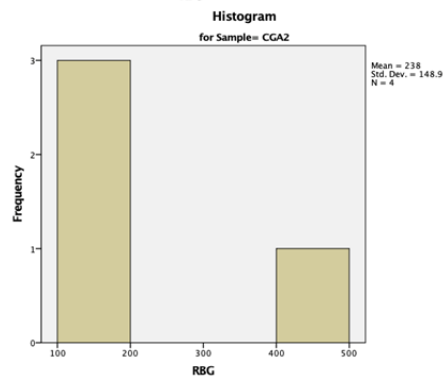
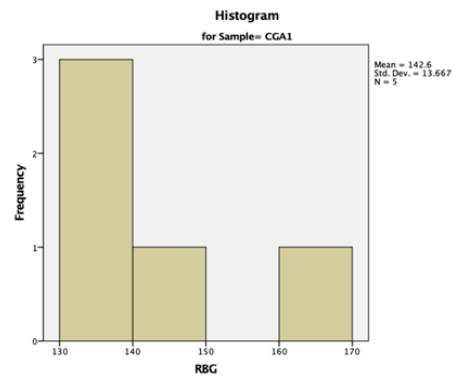
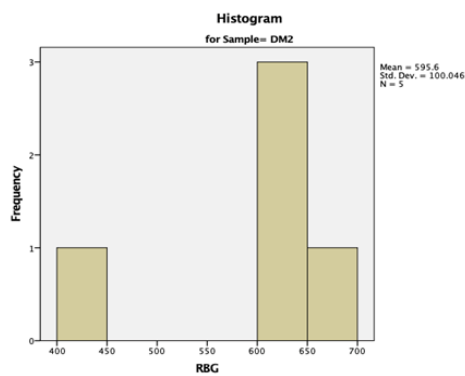
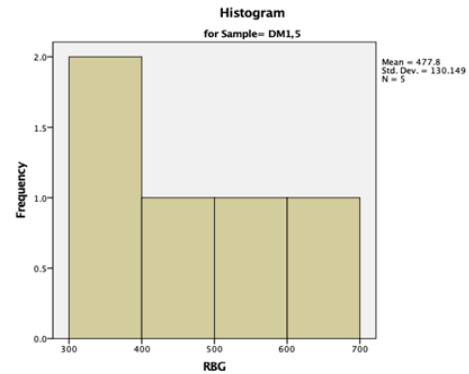
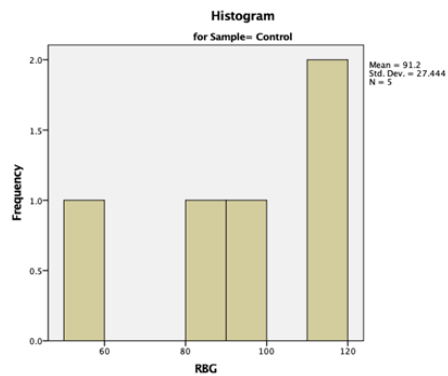
Tests of Normality

Sample	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
RBG Control	.197	5	.200 [*]	.938	5	.652
DM1,5	.208	5	.200 [*]	.912	5	.482
DM2	.318	5	.111	.852	5	.201
CGA1	.318	5	.111	.805	5	.089
CGA2	.424	4	.	.681	4	.007
CGA3	.374	6	.009	.684	6	.004

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Enclosure 3. Normality Test Histogram of RBG Levels



Enclosure 4. Homogeneity Levene Test of RBG Levels

Test of Homogeneity of Variances

RBG

Levene Statistic	df1	df2	Sig.
6.177	5	24	.001

Enclosure 5. Kruskal-Wallis Test of RBG Levels

Kruskal-Wallis Test

Ranks

Sample	N	Mean Rank
RBG Control	5	3.00
DM1,5	5	21.00
DM2	5	26.20
CGA1	5	8.20
CGA2	4	13.50
CGA3	6	19.83
Total	30	

Test Statistics^{a,b}

	RBG
Chi-Square	24.522
df	5
Asymp. Sig.	.000

a. Kruskal Wallis Test

b. Grouping Variable:
Sample

Enclosure 6. Mann-Whitney Test of RBG Levels

Mann-Whitney Test

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG Control	5	3.00	15.00
DM1,5	5	8.00	40.00
Total	10		

Test Statistics^a

	RBG
Mann-Whitney U	.000
Wilcoxon W	15.000
Z	-2.611
Asymp. Sig. (2-tailed)	.009
Exact Sig. [2*(1-tailed Sig.)]	.008 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG Control	5	3.00	15.00
DM2	5	8.00	40.00
Total	10		

Test Statistics^a

	RBG
Mann-Whitney U	.000
Wilcoxon W	15.000
Z	-2.611
Asymp. Sig. (2-tailed)	.009
Exact Sig. [2*(1-tailed Sig.)]	.008 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG Control	5	3.00	15.00
CGA1	5	8.00	40.00
Total	10		

Test Statistics^a

	RBG
Mann-Whitney U	.000
Wilcoxon W	15.000
Z	-2.611
Asymp. Sig. (2-tailed)	.009
Exact Sig. [2*(1-tailed Sig.)]	.008 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG Control	5	3.00	15.00
CGA2	4	7.50	30.00
Total	9		

Test Statistics^a

	RBG
Mann-Whitney U	.000
Wilcoxon W	15.000
Z	-2.449
Asymp. Sig. (2-tailed)	.014
Exact Sig. [2*(1-tailed Sig.)]	.016 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG Control	5	3.00	15.00
CGA3	6	8.50	51.00
Total	11		

Test Statistics^a

	RBG
Mann-Whitney U	.000
Wilcoxon W	15.000
Z	-2.745
Asymp. Sig. (2-tailed)	.006
Exact Sig. [2*(1-tailed Sig.)]	.004 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG DM1,5	5	3.80	19.00
DM2	5	7.20	36.00
Total	10		

Test Statistics^a

	RBG
Mann-Whitney U	4.000
Wilcoxon W	19.000
Z	-1.776
Asymp. Sig. (2-tailed)	.076
Exact Sig. [2*(1-tailed Sig.)]	.095 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG DM1,5	5	8.00	40.00
CGA1	5	3.00	15.00
Total	10		

Test Statistics^a

	RBG
Mann-Whitney U	.000
Wilcoxon W	15.000
Z	-2.611
Asymp. Sig. (2-tailed)	.009
Exact Sig. [2*(1-tailed Sig.)]	.008 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG DM1,5	5	6.60	33.00
CGA2	4	3.00	12.00
Total	9		

Test Statistics^a

	RBG
Mann-Whitney U	2.000
Wilcoxon W	12.000
Z	-1.960
Asymp. Sig. (2-tailed)	.050
Exact Sig. [2*(1-tailed Sig.)]	.063 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG DM1,5	5	6.60	33.00
CGA3	6	5.50	33.00
Total	11		

Test Statistics^a

	RBG
Mann-Whitney U	12.000
Wilcoxon W	33.000
Z	-.549
Asymp. Sig. (2-tailed)	.583
Exact Sig. [2*(1-tailed Sig.)]	.662 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG DM2	5	8.00	40.00
CGA1	5	3.00	15.00
Total	10		

Test Statistics^a

	RBG
Mann-Whitney U	.000
Wilcoxon W	15.000
Z	-2.611
Asymp. Sig. (2-tailed)	.009
Exact Sig. [2*(1-tailed Sig.)]	.008 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG DM2	5	6.80	34.00
CGA2	4	2.75	11.00
Total	9		

Test Statistics^a

	RBG
Mann-Whitney U	1.000
Wilcoxon W	11.000
Z	-2.205
Asymp. Sig. (2-tailed)	.027
Exact Sig. [2*(1-tailed Sig.)]	.032 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG DM2	5	8.20	41.00
CGA3	6	4.17	25.00
Total	11		

Test Statistics^a

	RBG
Mann-Whitney U	4.000
Wilcoxon W	25.000
Z	-2.013
Asymp. Sig. (2-tailed)	.044
Exact Sig. [2*(1-tailed Sig.)]	.052 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG CGA1	5	3.20	16.00
CGA2	4	7.25	29.00
Total	9		

Test Statistics^a

	RBG
Mann-Whitney U	1.000
Wilcoxon W	16.000
Z	-2.205
Asymp. Sig. (2-tailed)	.027
Exact Sig. [2*(1-tailed Sig.)]	.032 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG CGA1	5	3.00	15.00
CGA3	6	8.50	51.00
Total	11		

Test Statistics^a

	RBG
Mann-Whitney U	.000
Wilcoxon W	15.000
Z	-2.745
Asymp. Sig. (2-tailed)	.006
Exact Sig. [2*(1-tailed Sig.)]	.004 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

Ranks

Sample	N	Mean Rank	Sum of Ranks
RBG CGA2	4	3.00	12.00
CGA3	6	7.17	43.00
Total	10		

Test Statistics^a

	RBG
Mann-Whitney U	2.000
Wilcoxon W	12.000
Z	-2.138
Asymp. Sig. (2-tailed)	.032
Exact Sig. [2*(1-tailed Sig.)]	.038 ^b

a. Grouping Variable:
Sample

b. Not corrected for ties.

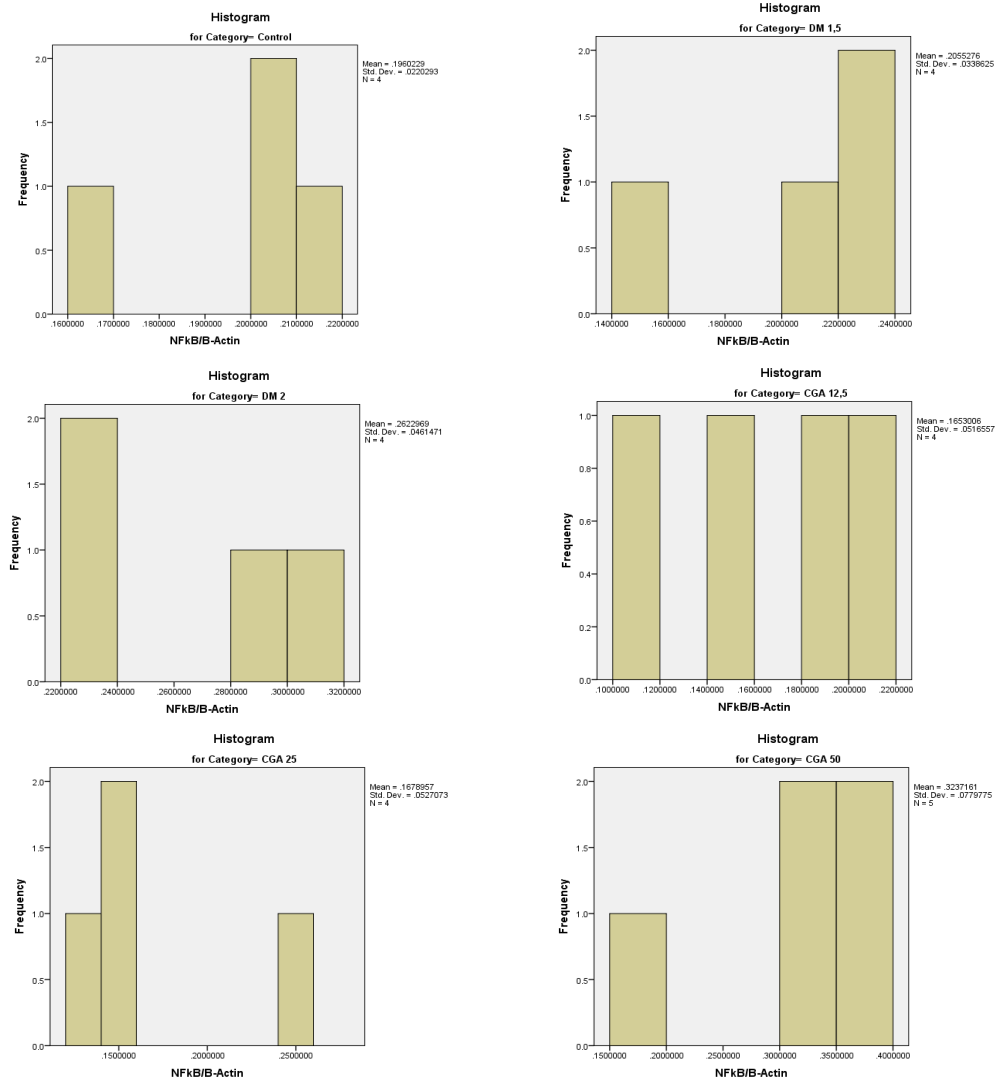
Enclosure 7. Normality Test of NF- κ B mRNA expression

Tests of Normality

Category	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
NF κ B/B-Actin Control	.360	4	.	.811	4	.123
DM 1,5	.274	4	.	.865	4	.278
DM 2	.292	4	.	.856	4	.247
CGA 12,5	.224	4	.	.954	4	.741
CGA 25	.338	4	.	.851	4	.229
CGA 50	.347	5	.048	.817	5	.110

a. Lilliefors Significance Correction

Enclosure 8. Normality Test Histogram of NF- κ B mRNA expression



Enclosure 9. Homogeneity Levene Test of NF- κ B mRNA expression

Test of Homogeneity of Variances

NFkB/B-Actin

Levene Statistic	df1	df2	Sig.
.894	5	19	.505

Enclosure 10. One-way ANOVA Test of NF- κ B mRNA expression

ANOVA

NF κ B/B-Actin

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.086	5	.017	6.324	.001
Within Groups	.052	19	.003		
Total	.138	24			

Enclosure 11. Post-hoc LSD Test of NF- κ B mRNA expression

Multiple Comparisons

Dependent Variable: NF κ B/B-Actin

(I) Category	(J) Category	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval		
					Lower Bound	Upper Bound	
LSD	Control	DM 1,5	-.0095047148	.0369728277	.800	-.086889733	.067880303
		DM 2	-.0662740125	.0369728277	.089	-.143659030	.011111005
		CGA 12,5	.0307223248	.0369728277	.416	-.046662693	.108107343
		CGA 25	.0281272298	.0369728277	.456	-.049257788	.105512248
	CGA 50	-.127693190 [*]	.0350755041	.002	-.201107064	-.054279316	
	DM 1,5	Control	.0095047148	.0369728277	.800	-.067880303	.086889733
		DM 2	-.0567692978	.0369728277	.141	-.134154316	.020615720
		CGA 12,5	.0402270395	.0369728277	.290	-.037157978	.117612057
		CGA 25	.0376319445	.0369728277	.322	-.039753073	.115016962
	CGA 50	-.118188475 [*]	.0350755041	.003	-.191602349	-.044774601	
	DM 2	Control	.0662740125	.0369728277	.089	-.011111005	.143659030
		DM 1,5	.0567692978	.0369728277	.141	-.020615720	.134154316
		CGA 12,5	.0969963373 [*]	.0369728277	.017	.019611319	.174381355
		CGA 25	.0944012423 [*]	.0369728277	.019	.017016224	.171786260
	CGA 50	-.0614191776	.0350755041	.096	-.134833051	.011994696	
	CGA 12,5	Control	-.0307223248	.0369728277	.416	-.108107343	.046662693
		DM 1,5	-.0402270395	.0369728277	.290	-.117612057	.037157978
		DM 2	-.096996337 [*]	.0369728277	.017	-.174381355	-.019611319
		CGA 25	-.0025950950	.0369728277	.945	-.079980113	.074789923
	CGA 50	-.158415515 [*]	.0350755041	.000	-.231829389	-.085001641	
CGA 25	Control	-.0281272298	.0369728277	.456	-.105512248	.049257788	
	DM 1,5	-.0376319445	.0369728277	.322	-.115016962	.039753073	
	DM 2	-.094401242 [*]	.0369728277	.019	-.171786260	-.017016224	
	CGA 12,5	.0025950950	.0369728277	.945	-.074789923	.079980113	
CGA 50	-.155820420 [*]	.0350755041	.000	-.229234294	-.082406546		
CGA 50	Control	.1276931901 [*]	.0350755041	.002	.054279316	.201107064	
	DM 1,5	.1181884754 [*]	.0350755041	.003	.044774601	.191602349	
	DM 2	.0614191776	.0350755041	.096	-.011994696	.134833051	
	CGA 12,5	.1584155149 [*]	.0350755041	.000	.085001641	.231829389	
CGA 25	.1558204199 [*]	.0350755041	.000	.082406546	.229234294		

*. The mean difference is significant at the 0.05 level.

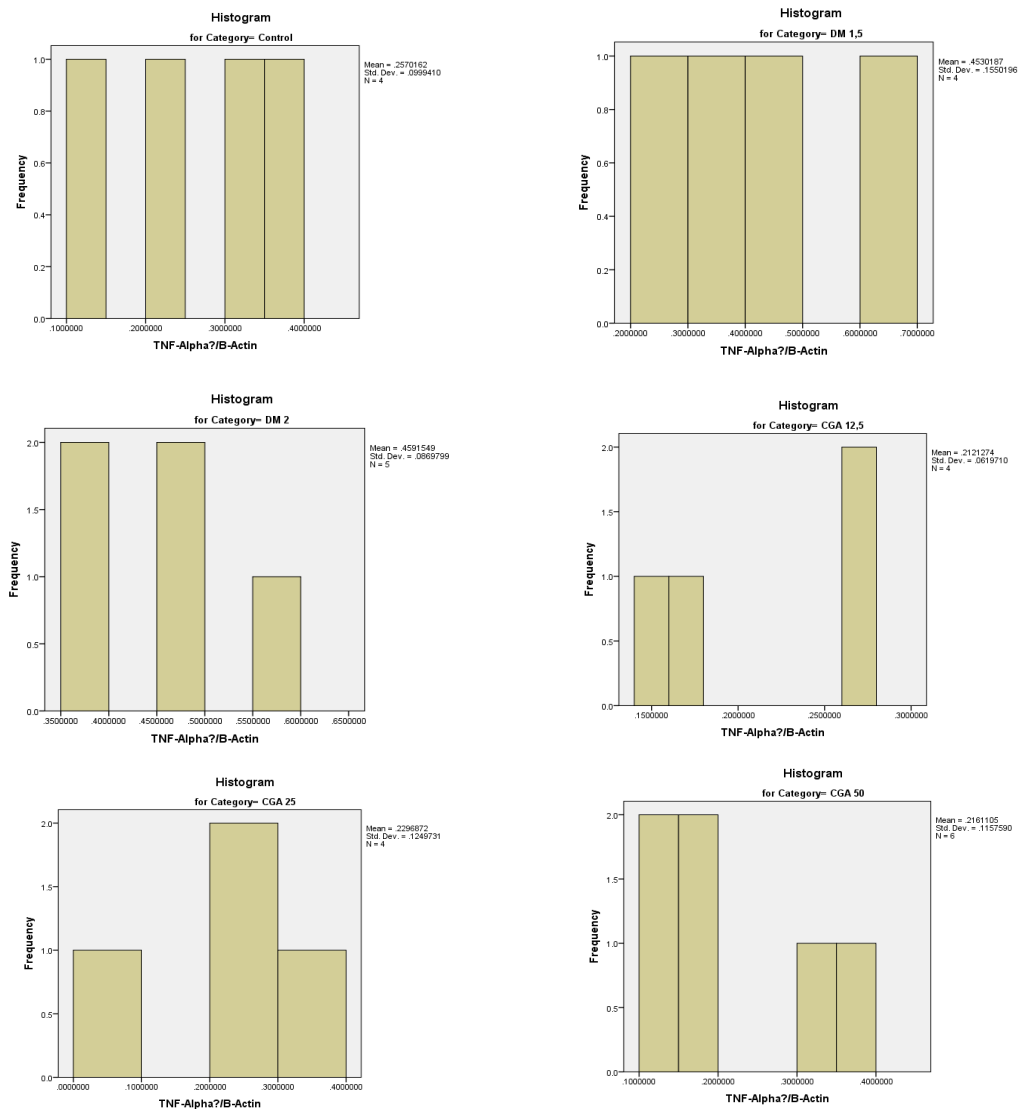
Enclosure 12. Normality Test of TNF- α mRNA expression

		Kolmogorov-Smirnov ^a			Shapiro-Wilk		
Category		Statistic	df	Sig.	Statistic	df	Sig.
TNF-Alpha?/B-Actin	Control	.213	4	.	.960	4	.778
	DM 1,5	.172	4	.	.987	4	.940
	DM 2	.214	5	.200 [*]	.911	5	.473
	CGA 12,5	.294	4	.	.817	4	.137
	CGA 25	.298	4	.	.919	4	.531
	CGA 50	.339	6	.030	.820	6	.089

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Enclosure 13. Normality Test Histogram of TNF- α mRNA expression



Enclosure 14. Homogeneity Levene Test of TNF- α mRNA expression

Test of Homogeneity of Variances

TNF-Alpha α /B-Actin

Levene Statistic	df1	df2	Sig.
.726	5	21	.612

Enclosure 15. One-way ANOVA of TNF- α mRNA expression

ANOVA

TNF-Alpha α /B-Actin

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.320	5	.064	5.219	.003
Within Groups	.258	21	.012		
Total	.578	26			

Enclosure 16. Post-hoc LSD Test of TNF- α mRNA expression

Multiple Comparisons

Dependent Variable: TNF-Alpha/B-Actin

(I) Category	(J) Category	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval		
					Lower Bound	Upper Bound	
LSD	Control	DM 1,5	-.196002488 [*]	.0783302952	.021	-.358899255	-.033105722
		DM 2	-.202138694 [*]	.0743106427	.013	-.356676135	-.047601252
		CGA 12,5	.0448887800	.0783302952	.573	-.118007986	.207785546
		CGA 25	.0273290570	.0783302952	.731	-.135567709	.190225823
		CGA 50	.0409056787	.0715054493	.573	-.107798044	.189609401
	DM 1,5	Control	.1960024883 [*]	.0783302952	.021	.033105722	.358899255
		DM 2	-.0061362055	.0743106427	.935	-.160673647	.148401236
		CGA 12,5	.2408912683 [*]	.0783302952	.006	.077994502	.403788035
		CGA 25	.2233315453 [*]	.0783302952	.010	.060434779	.386228312
		CGA 50	.2369081669 [*]	.0715054493	.003	.088204445	.385611889
	DM 2	Control	.2021386938 [*]	.0743106427	.013	.047601252	.356676135
		DM 1,5	.0061362055	.0743106427	.935	-.148401236	.160673647
		CGA 12,5	.2470274738 [*]	.0743106427	.003	.092490032	.401564915
		CGA 25	.2294677508 [*]	.0743106427	.006	.074930309	.384005192
		CGA 50	.2430443725 [*]	.0670780573	.002	.103547916	.382540829
	CGA 12,5	Control	-.0448887800	.0783302952	.573	-.207785546	.118007986
		DM 1,5	-.240891268 [*]	.0783302952	.006	-.403788035	-.077994502
		DM 2	-.247027474 [*]	.0743106427	.003	-.401564915	-.092490032
		CGA 25	-.0175597230	.0783302952	.825	-.180456489	.145337043
		CGA 50	-.0039831013	.0715054493	.956	-.152686824	.144720621
	CGA 25	Control	-.0273290570	.0783302952	.731	-.190225823	.135567709
		DM 1,5	-.223331545 [*]	.0783302952	.010	-.386228312	-.060434779
		DM 2	-.229467751 [*]	.0743106427	.006	-.384005192	-.074930309
		CGA 12,5	.0175597230	.0783302952	.825	-.145337043	.180456489
		CGA 50	.0135766217	.0715054493	.851	-.135127101	.162280344
CGA 50	Control	-.0409056787	.0715054493	.573	-.189609401	.107798044	
	DM 1,5	-.236908167 [*]	.0715054493	.003	-.385611889	-.088204445	
	DM 2	-.243044372 [*]	.0670780573	.002	-.382540829	-.103547916	
	CGA 12,5	.0039831013	.0715054493	.956	-.144720621	.152686824	
	CGA 25	-.0135766217	.0715054493	.851	-.162280344	.135127101	

*. The mean difference is significant at the 0.05 level.