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Short Communication

Effect of $GABA_B$ Receptor Antagonist (CGP55845) on the Hematological and Serum Biochemical Profile of Adult Male Albino Mice

Rabia Qurashi, Qurat ul Ane Gillani* and Furhan Iqbal*

Institute of Pure and Applied Biology, Zoology Division, Bahauddin Zakariya University, Multan 60800, Pakistan

Rabia Qurashi and Qurat ul Ane Gillani contributed equally to the manuscript.

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Authors' Contributions
FI designed the study and revised the manuscript. RQ and QUAG conducted the lab experiments, analyzed the data and wrote the article.

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ABSTRACT

Present study was conducted to report the effect of 1mg / ml of solvent / Kg body weight $GABA_B$ receptor antagonist (CGP55845; 3-N [1-(S)-(3,4- dichlorophenyl) ethyl] amino-2-(S)- hydroxypropyl-P-benzyl-phosphinic acid), intraperitoneally injected for 12 days, on hematological and serum biochemical profile of 6 week old male albino mice. Blood samples from male albino mice (CGP55845 treated N = 14 and saline treated N = 16) were collected directly by cardiac puncture and used for estimation of hematological and some serum biochemical parameters. The hematological parameters did not show any significant variation between the two groups. From amongst serum biochemical parameters triglycerides (P = 0.02) in CGP55845 treated mice showed significant increase compared to the control mice. All other studied parameters remained unaffected indicating that CGP55845 can be injected intraperitonially for the treatment of neurological ailments.

Gama-amino butyric acid (GABA) is widely distributed in mammalian nervous system act as inhibitory neurotransmitter which maintain overall balance between neuronal excitation and inhibition that is essential for normal brain function (Gillani *et al*., 2015). Dysfunction of GABAergic transmission is associated with many neurological disorders including schizophrenia, epilepsy, depression and autism spectrum disorder (Luscher *et al*., 2011).

$GABA_B$ receptors play significant role in treatment of many neurologic and psychiatric disorders such as anxiety, depression, pain, epilepsy and drug addiction (Bowery, 2006). $GABA_B$ receptors can affect the regulation of memory related neuronal plasticity and they are also known to be associated with the mechanism of epileptogenesis (Iqbal and Gillani, 2016). $GABA_B$ receptor antagonist show wide range of memory enhancing effects in many learning processes, such as learning of passive avoidance test in mice, active and passive avoidance test in aged rats and social recognition in rats (Hernandez *et al*., 2006). CGP55845 act via decreasing the GABAergic tone in the basal forebrain, most prominently occupying the $GABA_B$ receptor on postsynaptic neuron thus preventing the action of GABA at the synapse (Mayse, 2009).

Recently we had reported that intraperitoneal injection of CGP 55845 (@1 mg/ml solvent/Kg body weight) to female albino mice did not affected the blood chemistry and can be used for pharmacological purposes (Aslam *et al*., 2015). The present also shows that CGP 55845 injected intraperitoneally (i.p.) in adult male albino mice does not give different results and hence this drug can be safely used for the treatment of neurological disorders in mammals.

Materials and methods

Adult male (6 week old) albino mice (n = 30; 16 control and 14 treated with CGP55845), obtained from Zoology Department, Punjab University, Lahore, were housed in individual cages (22±1°C) during experiment and provided with standard mouse diet and water. Ethical committee of Zoology Department (Bahaudin Zakarya University Multan) had approved this experimental protocols and animal handling procedure.

Treated group received dose of $GABA_B$ receptor antagonist CGP55845 (1mg/kg body weight) for 12 days by injecting intraperitoneally while the control mice received saline solution for 12 days in parallel. The blood was obtained through retro orbital sinus or by cardiac

* Corresponding authors: anneegillani@gmail.com; furhan.iqbal@bzu.edu.pk
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puncture of mice and used for estimation of hematological parameters such as total white (TWBC) and red blood cells (TRBC), blood glucose level, packed cell volume (PCV) and mean corpuscular volume (MCV) and serum biochemical parameters such as alanine transaminase (ALT), aspartate transaminase (AST), total protein, cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides using Hitachi 902 automatic analyzer (Japan) following Khadim *et al*. (2014).

To analyze the data, statistical package Minitab (version 16, Pennsylvania) was used. Data was expressed in Mean ± standard deviation. Comparison of various hematological and studied serum biochemical parameters between two treatments was carried out by applying two sample t-test.

Table I.- Comparison of various hematological and biochemical parameters between $GABA_B$ receptor antagonist (CGP55845) and saline treated (control) male albino mice. Data is expressed as Mean ± Standard deviation. Ranges of values are given below the Means. P-value indicates the results of 2 sample t-test.

Parameters	Control (n = 16) (Range)	CGP55845 treated (n = 14) (Range)
Hematological profile		
Glucose (mg/dl)	209.7 ± 17.8 (74 – 293)	185.2 ± 3.72 (118 -218)
PVC (%)	41.5 ± 3.3 (28 – 56)	39.22 ± 0.91 (30 – 52)
TRBC ($x10^3$)	24.48 ± 0.64 (12.1 - 34)	21.9 ± 0.97 (13.1 – 40.5)
TWBC ($x10^3$)	10.72 ± 0.25 (6 – 15.5)	10.43 ± 0.20 (7.75 – 13.4)
MCV (fp)	1.85 ± 0.26 (1.06 – 4.13)	2.10 ± 0.11 (0.81 – 3.90)
Serum biochemical profile		
Total Protein (g/dl)	5.65 ± 0.16 (2.07 – 9.03)	6.40 ± 0.18 (3.36 – 9.47)
Cholesterol (mg/dl)	162.4 ± 4.6 (57 – 292)	136.2 ± 4.36 (64 – 258)
Triglycerides (mg/dl)	191 ± 8.4 (73 – 381)	335 ± 14* (78 – 644)
HDL (mg/dl)	39.1 ± 1.35 (25 – 61)	35 ± 1.85 (13 – 63)
LDL (mg/dl)	92.2 ± 4.31 (32 – 188)	52.6 ± 5.53 (7.2 – 169)
ASAT (U/l)	198 ± 18 (0.2 – 270)	180 ± 14 (0.1 – 393)
ALAT (U/l)	265 ± 16 (61 – 508)	182 ± 20 (31 – 342)

P > 0.05, non-significant; *P < 0.05, least significant. PCV, packed cell volume; TRBC, total red blood cell count; TWBC, total white blood cell count; MCV, mean corpuscular volume; HDL, high density lipoprotein; LDL, low density lipoprotein; ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase.

Results and discussion

Table I shows the various hematological and serum biochemical parameters of CGP55845 treated and untreated albino mice. All the parameters studied did not show any significant difference between the two groups, except for triglycerides which was significantly higher in treated group.

GABA is a four carbon non-protein amino acid which acts as a major inhibitory neurotransmitter in the central nervous system (Huang *et al*., 2007) and it play controlling role in balancing the excitability and inhibitory state in cortex and hippocampus (Paulsen and Moser, 1998). Our results are in agreement with a recent study conducted by Aslam *et al*. (2015) who showed that CGP 55845 can be supplemented in both male and female albino mice without affecting the cell counts at any stage of their adult life.

Butyrate is known for its weight loss effects by effecting triglycerides and lipoproteins is the conjugate base of butyric acid (Masud *et al.,* 2016). It has been reported that higher concentrations of triglyceride in serum leads to lower high density lipoproteins (HDL) concentrations (Aslam *et al*., 2015). This correlation was also observed during present studies as triglyceride level was significantly higher and HDL value was lower in CGP55845 treated mice indicating a normal blood chemistry and physiology following CGP 55845 application (Table I).

Conclusion

Our results indicated that $GABA_B$ receptor antagonist, CGP55845, has no effect on the studied hematological and most of the serum biochemical parameters of male albino mice as all these parameters had non-significant (P > 0.05) variations when compared between saline and CGP55845 treated male albino mice, indicating normal blood chemistry and physiology. So it is recommended that CGP 55845 may be administrated intravenously in subjects for the treatment of neurological ailments, where required.

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Statement of conflict of interest

Authors have declared no conflict of interest.

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