Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 2621-2628 | ISSN:2251-6727

Aqueous Extracts of Glycyrrhiza Glabra Linn and Diosmetin Effect on Ambulatory and Behavioral Functioning in Wistar Rats with Ethanol-Induced Cognitive Impairment.

Dr. Sasikumar Arumugam[1], Dr. Subamalani S[2*], Dr. Balaji Arumugam[3], Dr. Jamunarani Srirangaramasamy[4]

[1]Associate Professor, Department of Physiology, Arunai Medical College and Hospital, Tiruvannamalai, Tamilnadu, India.606603.

[2]Associate Professor, Department of Physiology, Tagore Medical College and Hospital, Chennai, India.600127.

[3*]Professor & Head, Department of Community Medicine, Arunai Medical College and Hospital, Tiruvannamalai, Tamilnadu, India.606603.

[4]Professor & Head, Department of Pathology, Bhaarath Medical College Hospital, BIHER, Selaiyur, Chennai 600073

***Corresponding Author:**Dr. Subamalani S

*Associate Professor, Department of Physiology, Tagore Medical College and Hospital, Chennai, India.600127.

KEYWORDS

Diosmetin; Glycyrrhiza Glabra behavioural function; cognitive impairment

ABSTRACT

The aging process, exposure to various chemicals, radiation, and stressful situations can contribute to the degeneration of nerve cells in the brain, leading to cognitive decline. Alcohol-induced mild cognitive impairment (MCI) is a growing concern among middle-aged adults, affecting emotional response, memory, and learning processes. The hippocampal region, a crucial component of the limbic system, plays a primary role in memory and learning. Alcohol-induced MCI is associated with oxidative stress, cholinergic system damage, and inhibition of key receptors in various brain regions. Ethanol alters processes dependent on glutamatergic and dopaminergic inputs, resulting in cognitive impairment. Younger individuals may be more susceptible to ethanol's effects on motor and cognitive functions. This study explores the potential therapeutic benefits of natural products in mitigating ethanol-induced neurotoxicity, focusing on the aqueous extract of GGL (AqGg) and Diosmetin (Dm). AqGg, a herbal extract frequently used in the Indian medical system, is known for its memory and learning-enhancing properties. Diosmetin, a well-known antioxidant molecule, has shown promise in improving working memory and spatial learning. The research aims to investigate the antioxidant properties of AqGg and Dm in protecting against cognitive and ambulatory impairment induced by ethanol. The study includes an assessment of the impact on declarative and episodic memory, considering corticostriatal and limbic system-hippocampus connections

INTRODUCTION:

The nerve cells in the brain may die off as a person ages, is exposed to different chemicals or physical agents, is exposed to radiation, or experiences stressful situations. Due to excessive alcohol intake, alcohol-induced mild cognitive impairment (MCI) is a growing social issue among middle-aged adults. The ability to act on emotional experiences, remember past information, and identify new information is known as cognition. One of the limbic system's components and the primary area for memory and learning is the hippocampal region. The creation, storage, and retrieval of declarative and episodic/declarative memory at corticostriatal and limbic system-hippocampus connections depend on glutamatergic and dopaminergic inputs(Calabresi et al, 2016). Alcohol-induced MCI is brought on by oxidative stress, damage to the cholinergic system, and inhibition of the α-

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 2621-2628 | ISSN:2251-6727

amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) and N-methyl-D-aspartate receptor (NMDAR) in several brain regions (Wills et al, 2013). These processes are changed by ethanol, which results in cognitive impairment. Younger mice were shown to be more susceptible to the effects of ethanol on their motor and cognitive functions than older ones (Novier et al., 2013). A small amount of ethanol damages the hippocampal region and causes learning memory impairment. However, a high dose of ethanol—at least 3g/kg—was necessary for other areas like the frontal cortex, nucleus accumbens, and amygdala. The drug development area took into consideration the therapeutic benefits of natural products in an effort to identify a better molecule for neurological illnesses. One such herbal extract that is frequently utilized in the Indian medical system to improve memory and learning is aqueous extract of GGL (AqGg) (Chakkaravarthi et al, 2013). At 833.3 mg/kg body weight, the fatal dose (LD50) was noted. The protective effect against neurotoxicity is attributed to Dm, a well-known antioxidant molecule (Villa et al, 1992). According to Daniela et al. (2014), Dm improved working memory and spatial learning and shows promise as a therapeutic method for treating cognitive deficiencies in people with neurocognitive disorders. Thus this study was aimed to investigate the antioxidant properties of AqGg and Dm on cognitive and ambulatory impairment against ethanol-induced neurotoxicity.

Materials and methods:

Experimental animals:

A total of 36 adult Wistar albino rats (*Rattus norvegicus*), with 200 to 250 g body weight were purchased from Center for laboratory animal research, department of research development, Saveetha Institute of Medical And Technical Sciences, Chennai. IAEC Reference number - (SU/CLAR/RD/038/2017) dated 25/08/17. The rats were housed in polypropylene cages with paddy husk bedding, standard food pellets and drinking water *ad libitum*, and 12hr light and 12hr dark schedule in 23°C ± 2°C.

Chemicals and Drugs: Ethanol(95%, Nanda, Inc), normal saline, Dm (Sigma, Inc), Acetylcholinesterase(Sigma, Inc) and BDNF assay kit (Bosterbio, USA), dimethyl sulfoxide (DMSO), Ki67, GFAP, CD68 and calretinin antibodies (BIOSB, USA), DCX(Cell Signalling, USA) and other laboratory chemicals (Labthi,Inc), were purchased for this experiment.

Plant material and extract preparation: The roots of GGL was purchased from a local herbal market in Chennai and authenticated by medical botanist, department of medicinal chemistry, National Institute of Siddha, Tambaram sanatorium, Tamilnadu. The specimen was deposited for future reference and the authentication number is NIAS 1502015. The roots were powdered and mixed with distilled water in sohxlet apparatus for aqueous extract preparation. The filtrate was collected and evaporated using reduced pressure evaporator and the extract yield was collected for the study

Experimental groups: Animals were grouped into

Group I (DMSO control) group received DMSO for 21 days

Group II (ETOH) group received ethanol (1.75g/kg/d) for 21 days,

Group III (AqGg) received aqueous extract of GGL (150mg/kg/d) along with DMSO for 21 days,

Group IV (Dm) received Dm (4mg/kg/d) along with DMSO for 21 days

Group V (AqGg +EtOH) group received aqueous extract of GGL (150mg/kg/d) along with ethanol (1.75g/kg/d) for 21 days.

Group VI (Dm +EtOH) received Dm (4mg/kg/d) along with ethanol (1.75g/kg/d) for 21 days.

Standardization of behavioural tests:

All animals were transferred to an experimental room from the quarantine room, after acclimatization behavioural training was given for one week. In this period the animals were familiarized with apparatus and test procedures. During behavioural training period standardisation of the experimental procedure was done. Behavioral assessments were studied using Open field test, eight arm radial maze and narrow beam test. Behavioural studies were conducted on 1st, 10th and 21st day of the experiment for six groups.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 2621-2628 | ISSN:2251-6727

Eight arm radial maze (EARM): EARM is to test spatial learning and memory .It is designed to evaluate working and reference memory. The radial arm maze consists of eight arms, numbered from 1 to 8 arms of 48x 3x 12 cm, extending radially from a central platform (40 cm in diameter), with a 5 cm edge around the apparatus. Each Radial arm was equally spaced and contained food cups at the end. Removable blocks of 9x3x13 cm were used to block the selected arm of the maze. The maze was elevated 40cm from the ground or floor. The following variables; Number of reference memory errors (entry of animal into the non-baited arm), Number of working memory errors (re-entry of animal into already visited baited arm), and time taken to visit all four baited arm (Latency) were scored for 5min and recorded.

Open field test (OFT): OFT is a measure of the emotional behaviour in an animal. It is a systematic assessment of new environment exploration, locomotor activity and anxiety related behaviors in rats. The OFT apparatus is made of a large square shaped arena of 80 cm×80 cm with 40 cm high walls. The floor is marked into 25 equal square segments to allow quantification of locomotor activity. Each rat was placed at the centre of the arena and observations were made reading: the, Time spent in the periphery of the arena, time spent in the center of the arena, Number of times crossing the squares (NSC) by the animals and number of fecal pellets passed.

Elevated plus maze (EPM): It is a Simple method to assess anxiety- like behaviour in rats. The apparatus is made of wood, two open arm (50x10x2cm) and two closed arm (50x10x40cm) opposite to each other elevated 45cm from the ground. The animal was placed in the center of the maze and let to explore the maze for 5minutes.We have observed Time spent in open arm with all 4 paws, Number of time animal crossed over open arm, Total number of arm crossed (both close & open), Number of fecal pellet and Number of rearing. (Cruz et al, 1994)

Narrow beam test: The rats were trained to walk on a 10-20mm wide wooden beam elevated 100 cm above the floor. After training, traversing time through beam to reach safe platform (100 mm distance) and number of slips (NOS) were quantified. (Shear et al., 2010)

Statistical analysis:

The data were expressed as Mean ± SEM and analysed using one way analysis of variance followed by post-hoc student Newman Keuls test (SNK) test for multiple comparison of groups. All statistical analysis and graph plotting was carried out using Sigma Plot software version13.0 (Systat, USA).

Results:

4.5.1 Effect of AEGGL and Dm on EARM:

Behavioral tests were conducted on the 1st, 10th, and 21st day of the experiment, four hours after ethanol administration. Table 1 illustrates a progressive reduction in spatial memory in the EtOH (ethanol) group, evidenced by a decreased latency period and increased working memory errors (WME) and reference memory errors (RME) in the Ethanol-Associated Memory (EARM) test. On the first day, EtOH exhibited significantly increased WME (7.5±1), indicating acute ethanol-induced effects.

Over the 21-day period, AqGg+EtOH and Dm+EtOH groups demonstrated a notable improvement in spatial memory compared to the EtOH group. SNK post hoc analysis on the 21st day revealed statistically significant differences in WME ($F= 20.429$, $P< 0.001$), RME ($F= 20.078$, $P< 0.001$), and latency period ($F= 27.889$, $P< 0.001$) between groups. AqGg and Dm groups, without ethanol, showed lower WME, RME, and increased latency period compared to the control group after 21 days ($F= 2.543$, $P< 0.049$). Specifically, AqGg demonstrated significant effects on EtOH-induced Mild Cognitive Impairment (MCI) rats compared to Dm after 10 and 21 days. FTable 1 indicated increased WME and RME in the EtOH group, suggesting spatial memory impairment, which improved in the Dm group ($p<0.001$). Latency period significantly decreased in the Dm group and Dm+EtOH group compared to the EtOH group (Fig.1.C), indicating the beneficial effects of Dm on ethanol-induced cognitive impairment.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 2621-2628 | ISSN:2251-6727

4.5.2 Effect of AEGGL and Dm on EPM:

The Elevated Plus Maze (EPM) test evaluated the behavioral performance of Wistar rats with ethanol-induced cognitive impairment. Table 2 presented variables such as the number of entries in the open and closed arms, number of rearing, and fecal pellets. On the 1st day, acute effects of ethanol on anxiety were observed, but no significant differences were found between groups. On the 10th and 21st days, the EtOH group exhibited increased anxiety, as evidenced by decreased open arm entries, which was prevented in AqGg+EtOH and Dm+EtOH groups. Closed arm entries were significantly higher in the EtOH group, indicating ethanol-induced anxiety. AqGg demonstrated an immediate effect on ethanol induction, while Dm showed significance on subsequent days. Rearing behavior showed no significant differences on the 21st day. Fecal pellet analysis suggested fewer effects on passing fecal pellets in EPM.

4.5.3 Effect of AEGGL and Dm on Open Field Exploration:

The Open Field Test (OFT) assessed anxious behavior, with results shown in Table 3. AqGg+EtOH and Dm+EtOH groups spent more time in the center of the arena than the EtOH group, indicating a preventive effect of drugs on ethanol-induced anxiety. Time spent near the periphery was significantly different between control and EtOH groups. The number of squares crossed (NSqC) was significantly different between groups on the 21st day, indicating the drugs' efficiency in ambulation and open field exploration. Fecal pellet analysis showed significance on the 10th and 21st days only for the AqGg group.

4.5.4 Effect of AQGG and Dm on Ambulation:

Table 4 demonstrated the effects of AqGg and Dm on latency to cross the narrow beam and the number of slips (NOS) during traverse. The motor activity was affected in the EtOH group, with AqGg and Dm protecting motor functions. NOS were 70% increase from the control group, but AqGg and Dm-treated groups showed 5% fewer NOS than the control group on the 21st day. Latency to cross and NOS were statistically significant between AqGg+EtOH and Dm+EtOH groups and the EtOH group throughout the days, indicating the drugs' protective effects on motor functions.

Table 1: Results of Eight Arm Radial Maze test on Wistar rats with ethanol induced cognitive impairment.

DAY 1			
GROUPS	Working Memory Error	Reference Memory Error	LATENCY
Control	7.5±1	6±0.7	393±9
EtOH	11±0.6	11±1	461±18
AqGg	7±1	9±0.6	409±22
Dm	8±1	8.3±1	404±15
AqGg+EtOH	8±1	8.6±0.6	420±13
Dm+EtOH	9±1	9±1	469±6
DAY 10			
Control	6±0.4	5±0.7	368±8
EtOH	12±1	12±1	473±12
AqGg	5.5±1	8.5±0.7	364±14
Dm	5.5±1	7±1	356±11*
AqGg+EtOH	9±1	10.6±1	421±10*
Dm+EtOH	9±1	10±1.3	452±8*
DAY 21			
Control	5±0.3	4±0.2	334±8
EtOH	13±1	14±0.6	481±4
AqGg	5±0.5	6±0.3	332±14

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 2621-2628 | ISSN:2251-6727

Dm	5±1	6±0.8	330±13*
AqGg+EtOH	12±1	10.5±1	412±5
Dm+EtOH	12±1.3	9.3±1	424±6.5*

EtOH-ethanol; AqGg- aqueous extract of Glycyrrhiza glabra; Dm-Diosmetin
The data were expressed as mean ± SE and analysed by one way analysis of variance followed by student-Newman-Keuls test for multiple comparison and Statistical significant.

Table 2: Results of elevated plus maze test on Wistar rats with ethanol induced cognitive impairment.

DAY 1				
GROUPS	Number of open arm entry	Number of closed arm entry	Rearing	Fecal pellet
Control	10.5 ± 1.23	25.0 ± 2.7	9.67 ± 0.33	5 ± 0.25
EtOH	8.2 ± 1.67	43.16 ± 1.04	8.0 ± 0.73	9 ± 0.6
AqGg	12.5 ± 1.08	35.0 ± 3.29	12.5 ± 1.0	6 ± 0.3
Dm	10.8 ± 1.5	39.0 ± 3.95	11.5 ± 1.0	6 ± 0.74
AqGg+EtOH	8.5 ± 1.20	29.0 ± 3.24	9.5 ± 1.0	9 ± 0.76*
Dm+EtOH	10 ± 1.35	37.33 ± 2.53	9.5 ± 1.0	9 ± 1.1*
DAY 10				
Control	17.7 ± 1.32	17.33 ± 1.76	12.33 ± 0.9	5.5 ± 0.5
EtOH	8.0 ± 0.73	57.0 ± 2.73	7.83 ± 0.6	9 ± 0.7
AqGg	20.33 ± 2.3	18.16 ± 1.24	14.0 ± 1.06	6.5 ± 1.2
Dm	22.5 ± 1.9	21.0 ± 2.26	13.5 ± 1.08	6.5 ± 1.1
AqGg+EtOH	9.83 ± 0.74	42.16 ± 5.14	7.33 ± 0.84	8.5 ± 1.4*
Dm+EtOH	11.2 ± 0.60	40.83 ± 3.3	9.0 ± 1.21	10 ± 1.3*
DAY 21				
Control	21.67 ± 1.4	14.20 ± 1.07	11.5 ± 0.7	6 ± 0.44
EtOH	12.67 ± 1.0	32.2 ± 2.0	11.5 ± 1.25	8 ± 0.51
AqGg	23.33 ± 1.5	23.33 ± 3.0	9.0 ± 1.44	6.5 ± 0.70
Dm	25.0 ± 2.7	19.0 ± 2.3	8.0 ± 0.77	6.5 ± 1.0
AqGg+EtOH	9.83 ± 0.74	47.0 ± 3.7	12.0 ± 0.79	10.5 ± 1.17*
Dm+EtOH	11.2 ± 0.65	43.5 ± 2.68	11.0 ± 0.88	10 ± 1.3*

EtOH-ethanol; AqGg- aqueous extract of Glycyrrhiza glabra; Dm-Diosmetin
The data were expressed as mean ± SEM and analysed by one way analysis of variance followed by student-Newman-Keuls test for multiple comparison and Statistical significant.

Table 3: Results of open field exploration test on Wistar rats with ethanol induced cognitive impairment.

DAY 1				
GROUPS	Time spent in centre	Time spent in periphery	Number of square crossed	Fecal pellet
Control	80.5 ± 3.8	220 ± 4	34 ± 1.7	7 ± 0.5
EtOH	53.3 ± 5.0	250 ± 5	22.5 ± 1.4	9 ± 0.4
AqGg	81.3 ± 4.3	219 ± 4.3	26 ± 1.5	7 ± 0.6*
Dm	81.1 ± 5.0	219 ± 4.5	25 ± 2	8 ± 0.4*
AqGg+EtOH	70 ± 7.0	224 ± 6	27 ± 2	8 ± 0.6**
Dm+EtOH	65 ± 6.0	229 ± 5	29 ± 2.2	8 ± 0.3**
DAY 10				
Control	58 ± 3.2	242 ± 3.2	43 ± 2	5 ± 0.6

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 2621-2628 | ISSN:2251-6727

EtOH	41.6 ± 3.0	258 ± 3.0	17 ± 1	9 ± 1**
AqGg	64.5 ± 4.0	235 ± 4.0	47 ± 2	5 ± 0.7**
Dm	77.5 ± 4.2	223 ± 4.2	50 ± 3	6 ± 0.7**
AqGg+EtOH	51.3 ± 4.1	249 ± 4.1	33 ± 2	8 ± 1**
Dm+EtOH	46.3 ± 3.8	254 ± 4.0	33 ± 3	8 ± 1**
DAY 21				
Control	67 ± 3.3	233 ± 3.3	48 ± 2	5 ± 0.5
EtOH	39 ± 4.0	261 ± 4	13 ± 0.5	10 ± 1**
AqGg	71 ± 4.0	229 ± 4	52 ± 2	5 ± 0.4*
Dm	82 ± 3.1	218 ± 3	54 ± 2	5 ± 0.6*
AqGg+EtOH	44 ± 3.4	256 ± 3.4	29 ± 2	9 ± 0.6**
Dm+EtOH	43 ± 4.3	257 ± 4.3	28 ± 3	9 ± 1**
EtOH-ethanol; AqGg- aqueous extract of Glycyrrhiza glabra; Dm-Diosmetin The data were expressed as mean ± SE and analysed by one way analysis of variance followed by student-Newman-Keuls test for multiple comparison and Statistical significant.				

Table 4: Results of narrow beam walk test on Wistar rats with ethanol induced cognitive impairment.

DAY 1		
GROUPS	Number of slips	Latency (Sec)
Control	3.33 ± 0.21	4.33 ± 0.21
EtOH	9.16 ± 0.65	17.33 ± 1.54**
AqGg	3.33 ± 0.21	5.0 ± 0.37
Dm	3.83 ± 0.48	4.83 ± 0.40
AqGg+EtOH	6.33 ± 0.33	18.16 ± 1.3**
Dm+EtOH	8.0 ± 0.26	19.0 ± 1.77**
DAY 10		
Control	3.33 ± 0.21	4.5 ± 0.22
EtOH	9.67 ± 0.61	31.0 ± 1.21**
AqGg	3.50 ± 0.22	4.5 ± 0.22
Dm	3.50 ± 0.22	4.67 ± 0.33
AqGg+EtOH	7.33 ± 0.33	36.67 ± 2.3**
Dm+EtOH	7.33 ± 0.56	28.66 ± 3.51**
DAY 21		
Control	3.83 ± 0.31	5.0 ± 0.36
EtOH	9.83 ± 0.31	20.5 ± 1.18**
AqGg	4.0 ± 0.37	5.0 ± 0.37
Dm	3.67 ± 0.33	5.16 ± 0.48*
AqGg+EtOH	7.33 ± 0.80	20.83 ± 1.51**
Dm+EtOH	8.5 ± 0.85	21.33 ± 1.76**
EtOH-ethanol; AqGg- aqueous extract of Glycyrrhiza glabra; Dm-Diosmetin The data were expressed as mean ± SE and analysed by one way analysis of variance followed by student-Newman-Keuls test for multiple comparison and Statistical significant.		

Discussion:

Substantial support from neuroinflammatory cascade of ethanol brain damage also derives from studies exhibiting protection against ethanol induced-brain damage with flavonoids. Collin's work explained that neuroinflammation as a process of brain damage (Collins et al, 1998); Hamelink established that flavonoids protect against ethanol induced brain damage. (Hamelink et al, 2005) we have also found that administration of AqGg and Dm protect the cognitive abilities from 21 days of ethanol neurotoxicity. In brief rats were trained to navigate the

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 2621-2628 | ISSN:2251-6727

EARM, OFT and narrow beam test for 1 week then 1.75mg/kg EtOH given to the concern group from day1 followed by drugs. Alcohol act through both central nervous system and systemic mechanisms stimulates a neuroinflammatory cascade and leads to neurotoxicity (Crews et al, 2008) Reversal of Spatial memory impairment was induced by cerebral ischemia in rats assessed by EARM suggest that it is an ideal tool to confirm the cognitive functions specifically after impairment (Pu et al, 2007). We have observed the results clearly that the rats with ethanol induced MCI advocate impaired spatial memory and locomotion. These results agreed with Daniela et al, that Dm resulted in significant retention of memory. (Daniela et al, 2014). EtOH group have shown increased number of entries into the baited arm (WME) and unbaited arm (RME) after 10 days of ethanol exposure, which might be acute effects EtOH. This may contribute to increased impulsivity and poor decision making associated with sub inducing levels of ethanol (de Wit et al. 2000; Dougherty et al. 2008). AqGg and Dm were compensated the effects of EtOH and protects the cognitive abilities that might be enhanced by inhibition of AChE and activation of nicotinic and muscarinic cholinergic receptors. This activation enhances hippocampal excitatory input from entorhinal cortex and from dentate gyrus.

Open field test may be sensitive to hippocampal sub regions pathways (Lim et al, 2001) and therefore increased open field activity has been used as an index of locomotor, anxiety and exploratory activity in ethanol induced rats. There was significant difference exist among groups in time spending in the center of the arena, rearing and grooming behaviors of the test field. This might be due to the NMDARs in the hippocampus might be inhibited by ethanol and may enhance long term depression (LTD) especially in CA1 region (Hendricson et al, 2002). Alteration in the ion channels, enzymes and receptors contributes into change in the synaptic functions by EtOH. AqGg and Dm might be act on receptor and ion channels at molecular level to protect from chronic ethanolic effects. However the cognitive skills were enhanced by AqGg and Dm, motor activity didn't much affect after 21 days which is shown in narrow beam test, compared with EtOH induced groups. Only acute effects of ethanol could be seen in the results. The concentration of consuming ethanol, duration of consumption, age and other factors may disturb the locomotion. In this study dosage of ethanol may cause only cognitive impairment not motor disturbances. (Gawel et al, 2016). The results clearly advocate that the induction of ethanol has produced cognitive impairment in rats. Even in assessing the spatial learning and memory by EARM the drugs from phytochemicals have reversed the ethanol induced mild cognitive impairment. The numbers of reference memory, working memory error were significantly reduced when comparing in between groups. The data's were analyzed by one way ANOVA followed by post host SNK test was done for comparison between groups and the results are found to be statistically significant $P < 0.001$).

The elevated plus maze test was conducted to assess the anxiety related behavior of the animals. In this study, the animal spent more time in closed arm indicated increased anxiety after alcohol intoxication (Wei et al, 2007). Also, the animals entry into the open arm was very much restricted reflect decline in general locomotor activity. Glabridin from extract of Glycyrrhiza glabra significantly antagonize the amnesia and improved the performance in elevated plus maze. (Cui et al 2007) Effects of AqGg might be the presence of glabridin a major flavonoid from Glycyrrhiza glabra reversed the learning and memory deficits (Hasanein et al,2004). Glycyrrhiza glabra and its extracts were inhibited the apoptosis pathway by endogenous antioxidant mechanism and exhibit the neurocognitive effects on in vivo and in vitro cerebral injury models (Yu et al, 2008). Our results also coincided with Yu et al. The ethological parameters of decline rearing activity also showed decrease emotional behavior in alcohol treated rats. The defecation rate was increased though not significantly also supports that increase anxiety level exist in chronic alcoholic animals. This result of the present study was in agreement with previous studies. 1.75mg/kg of ethanol treatment produced only cognitive impairment did not affect the motor dysfunctions (Gawel et al, 2016) and it is not agreed with narrow beam walking test results. NOS and latency periods were affected in EtOH and retrieved by AqGg and Dm. Our findings indicated that AqGg and Dm alleviate the cognitive dysfunction and motor skills. Spatial memory, navigation, learning and motor functions significantly improved after ethanol induction

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 2621-2628 | ISSN:2251-6727

(Lalonde, 2002). We have observed that AqGg and Dm prevent the EtOH induced cognitive impairment in Wistar rats. Molecular level studies are required to enlighten the exact mechanism of being neurocognitive agent against alcohol related disorders. AqGg and Dm could be used as precursor material to derive potential drug molecule for treating ethanol induced cognitive impairment. In conclusion, both Aqueous Extract of GGL (AqGg) and Diosmetin (Dm) demonstrated efficacy in ameliorating ethanol-induced spatial memory deficits. AqGg, in particular, exhibited promising potential in mitigating ethanol-induced cognitive impairment, providing valuable insights into their therapeutic benefits for addressing cognitive decline associated with alcohol-induced mild cognitive impairment.

References:

1. Calabresi P, Picconi B, Tozzi A, Ghiglieri V (2016). Interaction between basal ganglia and limbic circuits in learning and memory processes. Parkinsonism & related disorders, 22, S65-S68.
2. Novier A, Skike CE, Diaz-Granados JL, Mittleman G, Matthews DB (2013). Acute alcohol produces ataxia and cognitive impairments in aged animals: a comparison between young adult and aged rats. Alcoholism: Clinical and Experimental Research, 37(8), 1317-1324
3. Chakkravarthi KK, Avadhani R (2013). Beneficial effect of aqueous root extract of Glycyrrhiza glabra on learning and memory using different behavioral models: An experimental study. Journal of natural science, biology, and medicine, 4(2), 420.
4. Villa P. Dario C, DeFrancesco L, Amalia G. Raffaella P(1992);Protective effect of diosmetin on in vitro cell membrane damage and oxidative stress in cultured rat hepatocytes.Toxicology
5. Daniela R, Cláudia RZ, Renan G, Gizelda M, Rêgo,JM and Cerutti et al (2014); Flavones from Erythrina falcata are modulators of fear memory.BMC Complementary and Alternative Medicine.1-17
6. Collins MA, Zou JY, Neafsey EJ (1998). Brain damage due to episodic alcohol exposure in vivo and in vitro: furosemide neuroprotection implicates edema-based mechanism. The FASEB Journal, 12(2), 221-230.
7. Hamelink C, Hampson A, Wink DA et al. (2005) Comparison of cannabidiol, antioxidants, and diuretics in reversing binge ethanolinduced neurotoxicity. J Pharmacol Exp Ther 314:780–8.
8. Crews FT, Nixon K (2008). Mechanisms of neurodegeneration and regeneration in alcoholism. Alcohol & Alcoholism, 44(2), 115-127.
9. Gawel K, Krzysztof L, EwaGibula B, MalgorzataJenda, Marta, et al (2016); Cholinesterase inhibitors, donepezil and rivastigmine, attenuatespatial memory and cognitive flexibility impairment inducedby acute ethanol in the Barnes maze task in rats.Naunyn-Schmiedeberg's Arch Pharmacol. 389:1059–1071
10. Wei XY, Yang JY, Wang CF, Wu, (2007); “Anxiolytic effect of saponins from Panax quinquefolium in mice,” Journal of Ethnopharmacology. 111(3): 613–618.
11. Cui YM, Ao MZ, Li W, Yu LJ (2008); Effect of glabridin from Glycyrrhiza glabra on learning and memory in mice. Planta Med. 2008 Mar;74(4):377-80.
12. Hasanein P (2011); Glabridin as a major active isoflavan from Glycyrrhiza glabra (licorice) reverses learning and memory deficits in diabetic rats. ActaPhysiol Hung. 98(2):221-30.
13. Yu X, Xue CC, Zhou ZW, Li CG, Du YM, Liang J et al (2008); In vitro and in vivo neuroprotective effect and mechanisms of glabridin, a major active isoflavan from Glycyrrhiza glabra (licorice).Planta Med.74(4):377-80.
14. Lalonde R (2002).The neurobiological basis of spontaneous alternation. NeurosciBiobehav Rev 26:91–104.