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Behavioral Effect of Fructus Psoralea on Ethanol Induced Neurodegeneration of Hippocampus in Wistar Albino Rat

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Abstract

The behavioral effect of Fructus Psoraleae (FP) was investigated in the rat by using maze apparatus. Ethanol was found to increase the ambulatory, rearing and grooming behaviors in the open-field test. In animal studies, FP increase the number of cholinergic neurons in the basal forebrain which in turn leads to increased hippocampal function, a structure heavily implicated in behavioral activity and memory consolidation. In addition, FP blocked plasma elevated cortisol level, an indicator of the hypothalamic–pituitary–adrenal (HPA) axis. People with extensive hippocampal damage may experience amnesia, learning and memory disabilities. Hence the herb FP may be used as an adjuvant to treat the above neurological disorders.

Introduction

Alcohol causes 1.8 million deaths (3.2% of total) and a loss of 58.3 million (34% of total) of Disability-Adjusted Life Years (DALY) (WHO, 2004), while neurological condition account for 40% of the 58.3 million DALYs. Ethanol, the active drug in alcoholic beverages, has a number of effects in humans (White AM *et al.*, 2000).

- Short term effects include: intoxication, dehydration, alcohol poisoning (Which can be fatal) and memory loss.
- Longer term alcohol affects heart function, liver metabolism and brain function. (White AM *et al.*, 2000).

In human beings, persistent intake of alcohol can result in damage to cortical and sub-cortical structures of the brain, can lead to brain shrinkage, neurotransmitter impairments, inhibition of frontal cortex functioning, reduced hippocampal function (4-7). It significantly inhibits neuronal activity in the CA1 and CA3 pyramidal cell layers of the hippocampus (White AM *et al.*, 2000) (10). Animal studies has revealed that alcohol has been found to reduce the number of cholinergic neurons in the basal forebrain leading to reduced hippocampal function, a structure heavily implicated in memory consolidation (4). It also affects N-methyl-D-aspartate (NMDA) receptors by inhibiting the ion current induced by (NMDA), a glutamate receptor agonist (3). This prevents excitatory synaptic transmissions from occurring, affecting synaptic plasticity and in turn, memory and learning.

The hippocampus is a major component of the brain of human beings and other mammals. The hippocampal formation consists of the hippocampus proper (cornu ammonis literally "Amun's horns", abbreviated CA), the area dentata, and the subicular complex (Lorente de No *et al*., 1934). It belongs to the limbic system and plays important roles in the learning, memory & behavioural activity. The hippocampus as a whole has the shape of a curved tube, which has been analogized variously to a seahorse, a ram's horn (*Cornu Ammonis*, hence the subdivisions CA1, CA2, CA3 & CA4), or a banana (Amaral et al., 2006).

Dry fruit of leguminous plant *Psoralea corylifolia* Linn. (syn: *Cullen corylifolium* Linn.) is one of the most popular Traditional Chinese Medicine and officially listed in Chinese Pharmacopoeia (Qiao CF *et al*., 2006). Bakuchi has earned the name Kusthanasini as it is one of the best herbs, used in the treatment of various skin disorders (Qiao CF *et al*., 2006 & Sah P *et al*., 2006). The main chemical constituents are

- Coumarin derivatives include psoralen, isopsoralen methoxypsoralen (Yang yishan *et al.,*1983, Zhao Jianhin *et al.,* 1990 and Lu Zehua *et al.,* 1987).
- Flavones includes coryfolin, corylifolinin, bavachinin, isobavachin, neobavaisoflavne, bavachromene, corylin, bavachalcone, neobavachalcone (Lui Daiquah *et al.,* 2006).
- Mono-terpane-phenol includes bakuchiol (Lui Daiquah *et al.,* 2006).

Fructus Psoraleae possessed estrogen-like effects (Shen Li-xial et al., 2009). The estrogen also has direct effect over hippocampus (Gabriele Flugge *et al*., 1986) but the possible mechanism is unknown. However, reports of the effect and mechanism of Fructus Psoralea on the neurons on the Hippocampus are rare. In this experiment, Behavioral studies of Fructus Psoralea on ethanol induced neurodegeneration of Hippocampus in Wistar Albino Rat were studied.

Research Design

This study was conducted according to the ethical norms approved by Ministry of Social Justices and Empowerment, Government of India and by Institutional Animal Ethics Committee (IAEC) Guidelines of Saveetha University (IAEC No.Anat.002/2009). All animal procedures were performed according to the internationally approved principles & protocols for laboratory animal use and care and in accordance with the recommendations for the proper care and use of laboratory animals.

Experimental groups

Animals were divided in to four groups with six animals in each group.

- Group I : Control Group
- Group II : Animals orally treated with Fructus Psoralea in a daily dose of 25mg/kg (100 mg/kg body weight) orally by gavage for 2 months
- Group III : Animals induced with Ethyl Alcohol (5%) for 2 months daily
- Group IV: Animals induced with Ethyl Alcohol and orally treated with Fructus Psoralea 25mg/kg (100 mg/kg body weight) by gavage method) for 2 months (gauge needle size of 16, length of 11 cm and the diameter of 3).

Number of days each animal will be housed: 2 – 4 months

Preparation of plant extract

Fresh seeds of P. corylifolia were dried in an incubator for 2 days at 40 degree C, crushed separately in an electric grinder and then pulverized. This powder was extracted three times with petroleum ether (w/v, 1: 2) kept in incubator at 37 degree C for 36 h. The slurry was stirred intermittently for 2 h and left overnight. The mixture was then filtered and filtrate was dried by low pressure. Dark brown residues (somraji) were collected. The residue was suspended in water in a fixed dose and used for treatment (41).

Methods Adopted

I. Behavioral Studies

Behavioural maze studies (D'Hooge and De Deyn 2001, Burwell *et al.* 2004, Harker and Whishaw 2004 and Dash *et al.* 2004) are used to study spatial learning and memory in rats. Maze studies helped uncover general principles about learning that can be applied to many species, including humans. They are

Behavioral studies

- The classic maze
- The T-maze
- The multiple T-maze
- The Y-maze
- The radial arm maze
- The Morris water maze

Results

I. Behavioral Studies

Data analysis & findings

:

S.No.	BEHAVIOUR	G I	G II	G III	G IV
1.	Abnormal active avoidance behavior	1469	1032	2803	1432
2.	Abnormal conditioned taste aversion behavior	1454	1122	2799	1457
3.	Abnormal contextual conditioning	1432	1069	2800	1469
4.	Abnormal cued conditioning behavior	1001	1454	3156	1454
5.	Abnormal food preference	1469	1032	2410	1832
6.	Abnormal long-term recognition memory	1454	801	2730	1801
7.	Abnormal olfactory -discrimination memory	1460	799	4156	1650
8.	Abnormal operant conditional behavior	2803	1800	3410	2903
9.	Abnormal passive avoidance behavior	2799	2156	3730	2799
10.	Abnormal short-term recognition memory	2800	1410	5307	2860
11.	Head bobbing	1410	1307	1810	1510
12.	Head shaking	2730	2599	2730	2730
13.	Head tossing	2307	1800	3307	2507
14.	Increased exploration in new environment	2799	2999	1415	2730
15.	Negative geotaxis	5156	5156	5356	5156
16.	Reduced exploration in new environment	1410	1410	1417	1410
17.	Retropulsion	2797	1357	3797	2997
18.	Thigmotaxis	5420	5797	3420	5620
19.	Walking backwards	3064	5420	3064	3064
20.	Decreased coping response	3063	3064	3063	3063
21.	Increased coping response	1395	3063	1395	1395
22.	Bi-directional circling	2156	1395	5156	3156
23.	Hyperactivity	1402	1629	1402	1402
24.	Hypoactivity	2597	2402	2797	2797
25.	Increased vertical activity	2797	3574	2597	2767
26.	Lethargy	2420	2202	3420	2620
27.	No spontaneous movement	3064	1404	3064	3064
28.	Reduced vertical activity	3063	2757	3063	3063
29.	Unidirectional circling	1395	1396	1395	1395
30.	Decreased anxiety	2156	2364	3156	2560
31.	Increased anxiety	2629	1363	3629	2669

Classification of behavioural response (Borchelt P.L. et al., 1982)

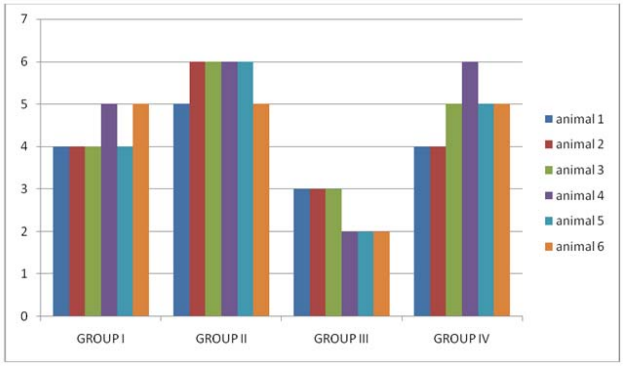
S.NO	POSITIVE RESPONSE	NEGATIVE RESPONSE
1.	Increased exploration in new environment	Abnormal active avoidance behavior
2.	Negative geotaxis	Abnormal conditioned taste aversion behavior
3.	Reduced exploration in new environment	Abnormal contextual conditioning
4.	Retropulsion	Abnormal cued conditioning behavior
5.	Thigmotaxis	Abnormal food preference
6.	Walking backwards	Abnormal long-term recognition memory
7.	Increased coping response	Decreased coping response
8.	Bi-directional circling	Abnormal passive avoidance behavior
9.	Hyperactivity	Hypoactivity
10.	Increased vertical activity	Head bobbing, shaking &tossing
11.	No spontaneous movement	Abnormal short-term recognition memory
12.	Unidirectional circling	Lethargy
13.	Decreased anxiety	Increased anxiety
14.	Reduced vertical activity	Abnormal operant conditional behavior

Grading of Animal Behaviour (Rondeau DB *et al*., 1978 & J Murphy *et al*., 2009)

- Grade I - no activity
- Grade II - very dull
- Grade III - dull
- Grade IV – minimal activity
- Grade V – less brisk
- Grade VI- brisk
- Grade VII – very brisk
- Grade VIII- hyper active

S.NO	POSITIVE RESPONSE	NEGATIVE RESPONSE	GRADE
1	0 - 1000	6000 - 7000	Grade I - no activity
2	1000 - 2000	5000 - 6000	Grade II - very dull
3	2000 - 3000	4000 - 5000	Grade III - dull
4	3000 - 4000	3000 - 4000	Grade IV – minimal activity
5	4000 - 5000	2000 - 3000	Grade V – less brisk
6	5000 - 6000	1000 - 2000	Grade VI- brisk
7	6000 - 7000	0 - 1000	Grade VII – very brisk

Following histogram shows the grading t-of the behavioural activities of the rat



Results

- Behavioral activities of the rat were found to be diminished. (Group III)
- In group II, behavioral activities improved more than control group.
- In group IV, behavioral activities are closed to control group.

Conclusion

- In my experiment, 24 Wistar albino rats were used to study the behavioural study of Fructus Psoraleae on ethanol induced neurodegeneration of Hippocampus in Wistar Albino Rat.
- The herb Fructus Psoralea is more efficient in producing neuroprotective effects in ethanol induced hippocampus of Wistar albino rats. Fructus Psoralea protects especially the more sensitive cells of CA1 & CA 3 region of hippocampus increasing their packed cell density. Finally, in both the regions, Fructus Psoralea is the herb of choice to treat illness in cornu ammonis region. As ethanol affects most of the neurons in cornu ammonis region of hippocampus, the herb Fructus Psoralea may be used as a supplement to alleviate the harmful effects of ethanol, there by improve the behavioral activity and memory.
- Hippocampus is one of the first regions in brain to suffer in Alzheimer's disease, encephalitis, medial temporal lobe epilepsy. People with extensive hippocampal damage may experience amnesia, learning and memory disabilities. Hence the herb fructus psoraleae may be used as an adjuvant to treat the above neurological disorders.

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