Antidepressant activity of *Cucumis melo* Fruit Extract in Stress Induced Rats

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ABSTRACT

Cucumis melo (Cucurbitaceae), from many centuries have been used in Indian traditional medicinal system for the treatment of various disorders such as cardioprotective aid and in obesity. The present study was to investigate the possible antidepressant activity of *Cucumis melo* (CM) fruit extract in stress induced rats. Hydroethanolic extract of CM was quantified for phenolic content by Folin-Ciocalteau's method. CUMS protocol was employed to induce stress in rats. CM (50 and 100mg/kg,bw) and Fluoxetine (20mg/kg,bw) was administered during 21day stress exposure period. Antidepressant activities were assessed by Forced Swimming Test (FST). The results conclude that CM possesses anti-stress and moderate anxiolytic activity which may be due, in part, to its antioxidant effect.

Keywords: *Cucumis melo*, antidepressant activity, antioxidant effect.

INTRODUCTION

Depression is the common mental disorder that presents with depressed mood, loss of interest or pleasure, feeling of guilt. Depression can lead to suicide [1] (WHO, 2012). Brain Derived Neurotrophic Factor (BDNF) exerts direct antidepressant activity in animal models of depression. Other studies demonstrate that chronic antidepressant treatment increase the rate of neurogenesis in the adult hippocampus [2, 3]. The studies also show that antidepressants upregulate the cAMP and neurotrophin signalling involved in plasticity and survival. BDNF are the key mediators of therapeutic response to antidepressants [4]. The body has developed several endogenous antioxidant defence mechanisms that include several enzymes like SOD, CAT, GPx, GR and non-enzymatic defence like GSH, vitamin E & C. The activities of these enzymatic and non-enzymatic antioxidants are used as oxidative stress relievers.

MATERIALS AND METHODS

Preparation of Plant extract

The hydro-ethanolic extract of the chosen fruit *Cucumis melo* (CM) was prepared [5]. The hydro-ethanolic extract was prepared at large scale. It was filtered and the filtrate was then concentrated to dryness under controlled temperature in a microwave oven. The extract yielded was brown, hygroscopic and it was stored air tight in desiccators for further use.

Procurement of Animal

Young male Albino rats of Wistar strain (120±20g) was procured from laboratory animal house, Thrissur, Kerala. The ethical clearance for handling of experimental animals was obtained from Institutional Animal Ethics Committee (IAEC), Ministry of Social justice and Empowerment, Government of India (IAEC No: 257/2014/IAEC). The animals were maintained

under constant room temperature 22^0C with 12 hours day and night cycle.

Induction of Depression

Depression was induced by Chronic Unpredictable Mild Stress (CUMS) protocol in albino rats. The status of depression was diagnosed by Forced Swimming Test (FST) on the seventh day of induction, third and seventh day of treatment.

Experimental design

The experimental rats were divided into 5 groups of six animals in each and were fed with single dose of plant extract and drug per day with the following concentrations.

***Group I*:** Normal Control

***Group II*:** Depression control

Group III: Depressed rats which were orally administered with standard drug Fluoxetine (20mg/kg, body weight) for 7days

Group IV: Depressed rats which were orally administered with low dosage of hydroethanolic extract of CM (50mg/kg, body weight) for 7days

***Group V*:** Depressed rats which were orally administered with high dosage of hydroethanolic extract of CM (100mg/kg, body weight) for 7days

Collection of serum and tissue

After the end of experimental treatment period, the animals were sacrificed by cervical dislocation under mild chloroform anaesthesia. Blood was collected by cardiac puncture and serum was separated by centrifugation at 2500 rpm.

Biochemical analysis

The amount of protein, total cholesterol, enzymic and non-enzymic antioxidants (Superoxide Dismutase, Catalase, Glutathione peroxidase and Lipid peroxidation) were analysed in experimental rats.

Statistical analysis

All the results were expressed as Mean ± SD. Statistical analysis was done using R statistical package.

RESULTS AND DISCUSSION

Preliminary Phytochemical analysis of CM was done and the results showed the presence of rich alkaloids, flavonoids, saponins, carbohydrates, phenols, glycosides, tannins and to lesser extent proteins.

Forced Swimming Test (FST):

Depressed animals stayed immobile for longer time during the final 4 minutes of analysis and immobility time decreased significantly after 7 days of treatment with the plant extract (Table 1).

Biochemical analysis

In this study, levels of protein & total cholesterol were low in depressed rats and they were found to be enhanced after treatment with the plant extract. They also enhance the antioxidant activity (Table 2).

Table 1

Forced Swimming Test (FST)

Groups	Before treatment (min:sec:msec)	After treatment (min:sec:msec)	
		3rd day	7th day
Group I	00:32:10	00:35:02	00:30:18
Group II	01:40:09	01:42:35	00:52:00
Group III	01:44:52	01:22:08	00:21:94
Group IV	01:56:76	01:08:01	00:30:31
Group V	01:58:21	01:49:90	00:39:58

Table 2

Estimation of protein and total cholesterol

Groups	Protein (µg)	Serum cholesterol (µg)	Triglyceride (mg/dl)
Group I	111 ± 3.65	300 ± 4.04	98 ± 3.68
Group II	59 ± 3.86 a*	120 ± 4.20 a*	126 ± 4.07 a*
Group III	75 ± 4.10b*	30 ± 4.04 b*	120 ± 4.40 b*
Group IV	99 ± 4.03 b*	190 ± 4.28 b*	117 ± 3.96 b*
Group V	110 ± 4.50 b*	190 ± 4.48 b*	115.3 ± 3.79*

Data are expressed as Mean *SEM*, n=6, using student t-test. * $P<0.05$, ns denotes "no significant change". a , b denote comparison a. between group I and Group II and between group II and Groups III, IV and V respectively.

Table 3

Estimation of enzymic and non-enzymic antioxidants

Groups	SOD	CAT	GPx	LPO	Vit. C
Group I	0.80 ± 0.05	4.0 ± 3.27	200 ± 4.0	0.30 ± 0.03	3.8 ± 1.3
Group II	0.05 ± 0.02 a*	4.0 ± 3.50ns	300 ± 4.17 a*	0.15 ± 0.03 a*	4.8 ± 1.37 a*
Group III	0.70 ± 0.15 b*	5.2 ± 3.54 b*	300 ± 3.96ns	0.40 ± 0.04 b*	5 ± 2.02ns
Group IV	0.43 ± 0.14 b*	5.2 ± 4.3 b*	300 ± 3.78ns	0.58 ± 0.03 b*	4.3 ± 1.45 b*
Group V	0.60 ± 0.13 b*	6.4 ± 4.0 b*	200 ± 3.87 b*	0.40 ± 0.03 b*	4 ± 1.40 b*

Data are expressed as Mean *SEM*, n=6, using student t-test. * $P<0.05$, Group II (Depressed Controls), ns denotes "not significant change". a , b denote comparison between group I and Group II

The total protein content decreases in case of depression [6]. The protein concentration in the brain tissue was low in depression when compared to other groups which indicated reduced transcription and translational mechanism. The serum cholesterol and the triglyceride levels were found to be reduced and increased respectively in depressed groups and the levels were seem to return towards normal levels in treated groups (Table 2).

Antioxidant studies (enzymic and non-enzymic) were analysed as the oxidative stress has major influence on depression. The activity of SOD is decreased in depression but elevated levels were found in normal and treated groups (Table 3).

On the contrary, activity of CAT did not differ significantly in both depression and normal control groups. The drug and plant extract have reducing effect towards LPO. Vitamin C level was found to be normal and it is hypothesised that it has no role in depression (Table 3).

Statistical analysis revealed that protein, serum cholesterol and GPx showed significant difference between 'normal and depressed groups' and between 'depressed and higher dosage of hydroethanolic extract of CM (100mg/kg, bw) treated groups'. CAT & vitamin C showed no significant difference between 'normal controls and depressed groups' and 'depressed and Flouxetine treated groups' respectively.

Depression

Low levels of potassium can aggravate anxiety, irritability and mood swings and the subjects with mild symptoms of depression showed improvement in moods when their intake of potassium-rich foods was increased. Potassium is an important mineral for mental health and brain function due to the role it plays in maintaining the electrical conductivity of the brain and nerve transmissions. Potassium is also central to the transportation of serotonin, a neurotransmitter that promotes feelings of well-being and happiness. The normal Potassium content in the *Cucumis melo* is said to be 593 to 44,000 ppm making it one of the favourite fruits of very high potassium content [7].

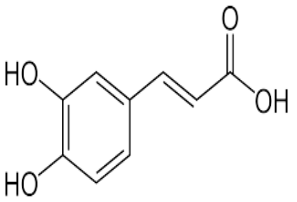

Figure 1. Structure of Caffeic acid

Cucumis melo was reported to have up to 3,300 and 4,370 ppm of Magnesium and Ascorbic acid respectively besides having copious amounts of Caffeic acid which contains both phenolic and acrylic functional groups, antioxidant *in vitro* and also *in vivo* [8].

CONCLUSION

Cucumis melo fruit extract showed moderate anxiolytic and high propensity to improve the antioxidant status in rats. Hence it may be considered as one of the cardinal herb in reducing depression and further work can be aimed at identifying and extracting the active principle that may have antidepressant activity.

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