The Protective Effects of *Gingko biloba* on Adrenal Gland Function in Met-Amphetamine Receiving Rats

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***Abstract*—**Studies show that gingko extract has improving effects on several body system including endocrine glands . The aim of this study was to investigate the effects of gingko leaf extract on serum levels of ACTH and cortisol in met-amphetamine receiving male rats**.** In this laboratory experimental study, male Wistar rats were randomly divided to control group, and normal saline1, met-amphetamine (4mg/kg) and "met-amphetamine (4mg/kg) + gingko leaf extract (50 mg/kg)" receiving rats. The injections were carried out once a week. After 6 weeks, blood samples were collected using cardiac puncture method and following serum collection, the levels of ACTH and cortisol were measured by radioimmunoassay method. The data were statically analyzed using ANOVA. The results of the present study show that there was no significant difference in serum levels of ACTH and cortisol in rats receiving normal saline compared with control animals. However, serum levels of ACTH and cortisol significantly increased in rats receiving met-amphetamine compared to control group ($P<0.01$, $P<0.001$, respectively). Serum levels of ACTH and cortisol did not significantly change in rats receiving amphetamine + gingko leaf extract compared to control group. The findings suggest that gingko extract has protective effects against increased adrenal gland function in met-amphetamine receiving rats **.**

***Index Terms*—** Met-Amphetamine, Gingko, ACTH, Cortisol, Rat.

I. INTRODUCTION

Ginkgo (*Ginkgo biloba)*, is a unique species of tree and is the only extant taxon in the division Ginkgophyta. It has various uses in traditional medicine and as a source of food. Ginkgo is marketed in dietary supplement form with claims it can enhance cognitive function in people without known cognitive problems, but such claims are unfounded because it has no effect on memory or attention in healthy people [1].

Ginkgo biloba extract , made from the dried leaves of the Ginkgo tree, is one of the top sellers within the growing market for herbal remedies in many European countries as well as in the USA [2].

Ginkgo biloba is among the most favourite and best explored herbal drugs. Recent investigations show that significant levels of Ginkgo biloba flavonoids cross the blood-brain barrier and enter the CNS of rats after oral application of GBE [3]. Ginkgo biloba extract protects brain from ischemia/reperfusion injuries [4]. Ginkgo biloba has also improving effects on Alzheimer's disease [5]. The studies show that Ginkgo biloba can be used as an adjuvant therapy for progressive normal and high tension glaucoma [6]. Ginkgo is used in the treatment of peripheral vascular disease and cerebral insufficiency [7]. Ginkgo may have undesirable effects, especially for individuals with blood circulation disorders and those taking anticoagulants such as aspirin or warfarin, although recent studies have found ginkgo has little or no effect on the anticoagulant properties or pharmacodynamics of warfarin in healthy subjects [8].

Methamphetamine (METH), a potent and addictive synthetic derivative of amphetamine, is currently one of the most widely abused illegal stimulants in the United States and worldwide [9]. Methamphetamine (METH) is an increasing popular and highly addictive stimulant associated with autonomic nervous system (ANS) dysfunction, cardiovascular pathology and neurotoxicity [10]. Methamphetamine also influences adrenal gland function [11].

The aim of this study was to investigate the effects of gingko leaf extract on serum levels of ACTH and cortisol in met-amphetamine receiving male rats.

II. MATERIAL AND METHODS

A. Animals

Adult Wistar rats weighting 200±30g were purchased and raised in our colony from an original stock of Pasteur institute (Tehran, Iran).The temperature was at 23±2 ^{0}C and animals kept under a schedule of 12h light:12h darkness (light on at: 08: 00 a.m.) with free access to water and standard laboratory chow. Care was taken to examine the animals for general pathological symptoms. Food was withheld for 12-14h before death**.**

B. Protocol of Study

In this laboratory experimental study, male Wistar rats were randomly divided to control group, and normal saline1, met-amphetamine (4mg/kg) and "met-amphetamine (4mg/kg) + gingko leaf extract (50 mg/kg)" receiving rats.

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The injections were carried out once a week. After 6 weeks, blood samples were collected using cardiac puncture method and following serum collection, the levels of ACTH and cortisol were measured by radioimmunoassay method. All animal experiments were carried out in accordance with the guidelines of Institutational Animals Ethics Committee.

C. *Statistical Analysis*

All values are presented as mean ± SD. Statistical significance was evaluated by one-way analysis of variance (ANOVA) using SPSS 19. Significance was measured using Fisher's least significant for the exact P values and significant differences are noted in the results. Differences with $P<0.05$ were considered significant

III. Results

Figure I shows serum levels of ACTH in male rats.

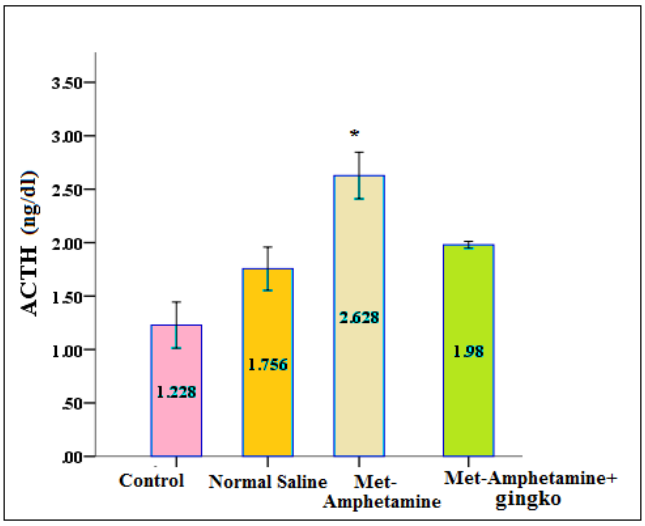

Fig I. Serum levels of ACTH in male rats. * indicates significant difference compared to control group

Figure II shows serum levels of cortisol in male rats

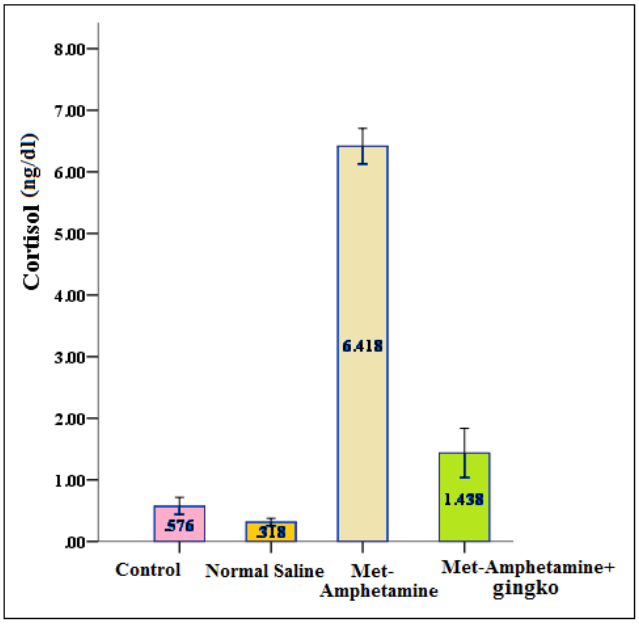

Fig II. Serum levels of cortisol in male rats. * indicates significant difference compared to control group

The results of the present study show that there was no significant difference in serum levels of ACTH and cortisol in rats receiving normal saline compared with control animals. However, serum levels of ACTH and cortisol significantly increased in rats receiving met-amphetamine compared to control group ($P<0.01$, $P<0.001$, respectively). Serum levels of ACTH and cortisol did not significantly change in rats receiving amphetamine + gingko leaf extract compared to control group.

IV. Discussion

Our study indicated that serum ACTH and cortisol levels increased in met-amphetamine receiving rats, however, administration of gingko leaf extract withstand against this increase in ACTH and cortisol levels. In line with our findings there are other studies showing that chronically using met-amphetamine may destroy the regulatory function of the HPA axis, especially the feedback regulation of cortisol to ACTH [12]. On the other hand, it has also been shown that the extract of Ginkgo biloba possess significant anti-stress properties [13], by which may possess protective effects on adrenal gland. In recent studies it has also been demonstrated that repeated treatment of rats with the standardized extract of Ginkgo biloba leaves, EGb 761, and its bioactive component ginkgolide B (GKB), specifically reduces the ligand binding, and protein and messenger RNA expression of the adrenal mitochondrial peripheral benzodiazepine receptor (PBR), a key element in the regulation of cholesterol transport, resulting in decreased circulating corticosterone levels [14]. Treatment of rats and adrenocortical cells with ginkgolide B (GKB), a purified component of Ginkgo biloba leaf extracts, leads to decreased corticosteroid synthesis 15].

V. Conclusion

The findings suggest that gingko extract has protective effects against increased adrenal gland function in met-amphetamine receiving rats .

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