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STRESS-PROTECTIVE ACTIVITY OF THE EXTRACT *FORNICIUM UNIFLORUM* L.

ABSTRACT

The results of studies on the adaptogenic properties of *Fornicium uniflorum* L. extracts has been given in the present article. The aim of the study was to evaluate stress-protective activity of extracts from *Fornicium uniflorum* L. at immobilization stress in white rats. The dry extract from *Fornicium uniflorum* rhizomes has stress protective properties in 18-hour immobilization stress simulated in white rats. It has been revealed that the given plant remedy prevents from the development of the "Selye's triad" signs: hypertrophy of renal glands, involution of immune competent organs (thymus and spleen), as well it prevents heavy destructions in the stomach mucosa.

Keywords: adaptogens, phytoecdysteroids, *Fornicium uniflorum* L., immobilization stress, antioxidant activity.

INTRODUCTION

At the present stage of the social development, there is a growing incidence rate of so called "civilization diseases"; there are recorded new, previously unknown nosological entities and syndromes caused by the depression of adaptive mechanisms, especially in people living in unfavorable environmental conditions. In the Extreme North conditions, a human body is mostly subjected to the influence of the whole complex of unfavorable factors which exhaust the adaptive resources, affect the health and bring about diseases. In this connection, the increase of the non-specific resistance of the body by pharmacological remedies – adaptogens is regarded as a priority. For this purpose, the development of the remedies of plant origin seems to be the direction with

good prospects, as they are free from the main disadvantages of chemotherapeutic drugs such as drug habituation, toxicity, the development of side reactions during chronic administration of the drug.

The group of the plant adaptogenes is rather numerous, many of which were anciently used in the folk medicine as tonics and health improving means. A mechanism of their effect remained unknown for a long time. In the modern concept, the biologically active substances responsible for the pharmacological effect of the plant adaptogenes are conditionally divided into three groups: phenolic compounds, tetracyclic triterpenoids (triterpenoid glycosides) and oxylipins. These compounds are kin to endogenic mediators and hormones of the central stress-realizing systems of the body, namely, sympathoadrenal

and hypothalamic-pituitary-adrenal ones.

However, these mechanisms are not by far solitary ones; there are many other biologically active substances contributing to adaptogenic properties of a plant [15]. Phytoecdysteroids fall into the group of such substances; they are polyhydroxylated sterins, structurally identical or kin to true molting hormones. They are practically contained in all plants but the difference in their concentration reaches to 8-9 orders [8]. Physiologically, the phytoecdysteroids influence the body of a human and warm-blooded animal in a variety of ways: they regulate metabolism being ligands for endocellular and membrane receptors; they are capable to change homeostasis of the body; have an effect on the growth, differentiation and scheduled cell death; they have psychostimulant, adaptogenic,

stimulating, immunomodulating and other effects [1, 5, 6, 10, 13]. Unfortunately, in spite of the high biological activity of ecdysteroids, at present, there is only one officinal ecdysteroid-containing plant – *Leuzea carthamoides*, various medicinal forms of which are used in the clinical practice. In this connection a search of new natural sources of phytoecdysteroids and the study of their composition and properties is a promising direction of the modern pharmacological science.

We have developed a method for preparing the dry extract from the rhizomes of *Fornicium uniflorum* L. – another ecdysteroid-containing plant; besides it contains flavonoids, amino acids, vitamins and polysaccharides [4].

The aim of the present work was to evaluate the stress-protective activity of the *Fornicium uniflorum* dry extract in immobilization stress induced in rats.

MATERIALS AND METHODS

Experiments were carried out on the male and female Wistar rats weighing 180-200 g observing the rules of the “European Convention for the protection of vertebrate animals used for experimental and other scientific purposes” (Strasburg, 1986) and the order of the RF Health Ministry N 267 concerning the GLP rules (19.06.2003). The animals were divided into 4 groups: intact group, control group, the first and second experimental groups of animals. The rats of the first experimental group received intragastrically the aqueous solution of the *Fornicium uniflorum* extract at a dose of 10 ml/kg for 7 days, preventively before exposure to stress (once a day, 30 min. before feeding). The rats of the second experimental group received a preparation of comparison – dealcoholized extract from *Leuzea carthamoides* at a dose of 5.0 ml/kg. The animals of the control group received the distilled water in the same volume and according to the analogous scheme. On the 7th day of the experiment the animals of the control and experimental groups were exposed to immobilization stress. The immobilization stress was simulated by fixing the animals in supine position for 18 hours [11]. After the experiment, the animals were decapitated under ether narcosis; the blood was taken for biochemical analyses, the organs (adrenal glands, thymus, spleen, stomach) were removed; then the evidence of alterations in the organs after stress was estimated; the intensity of destructive injuries in the stomach mucosa was evaluated by calculating the Pauls' index

[2]. The intensity of free radical oxidation processes was evaluated taking into account the accumulation of malonic dialdehyde (MDA) in the blood serum [7]. The state of the antioxidant system was judged by the activity of catalase [3] and superoxide dismutase (SOD) and the content of the reduced glutathione [12]. The statistical processing was carried out by the standard method with the use of the Student's t-criterion.

RESULTS AND DISCUSSION

The studies have revealed that the 18-hour immobilization stress in rats is followed by the development of the classic “Selye's triad”: the hypertrophy of adrenal glands, involution of immune competent organs and injury of the stomach wall mucosa (Tables 1 and 2). In the rats receiving the *F. uniflorum* extract, there was noted a reduction in the severity of the “Selye's triad” signs: the mass of adrenal glands was 30% lower, the mass of thymus and spleen was 48 and 41% higher respectively, as compared to the same indices in the rats of the control group. The immobilization stress in the rats of the control group caused the injuries in the stomach wall mucosa in the form of droplet hemorrhages, erosions and stripe-like ulcers. In the rats receiving the *F. uniflorum* extract, stress-induced injuries in the stomach wall mucosa were less expressed. No erosions of the stomach wall mucosa in the rats of the first experimental group were noted as distinct from the animals of the second experimental group. Deep injuries in the stomach wall mucosa in the form of stripe-like ulcers neither were noted in the both experimental groups. Thus, the administration of the tested remedy to the rats rendered the marked gastro-protective effect in exposure to stress.

The preventive introduction of the *F. uniflorum* extract had the marked antioxidant effect: the MDA concentration was 27% lower; the catalase and SOD activities were higher by 32% and 70% respectively, and the reduced glutathione was 23% higher as compared with the same indices in the animals of the control group (Table 3). The indices of the antioxidant activity in the rats receiving the tested remedy were comparable with those in the rats receiving *L. carthamoides*.

The findings of the studies demonstrate that the *F. uniflorum* extract has the marked stress-protective property and prevents the development of the stress-induced reaction, namely, the hypertrophy

of adrenal glands, involution of immune-competent organs and destructions in the stomach wall mucosa in rats exposed to immobilization stress. It is known that the activation of free radical oxidation plays an important role in the development of stress-induced injuries in the organs; it results in the impairment of the structural integrity in the lipid layer of cell membranes and decreased activity of membrane-bound enzymes. The many-hours-long immobilization is followed by extensive production of free radicals and intensification of the LPO processes, as evidenced by the increase of the MDA content in the blood serum and decrease in the activity of the antioxidant protection enzymes in the rats of the control group. The stress-protective effect of the tested remedy is associated with its inhibiting influence on the FRO and LPO processes. Besides the substances of the phenolic nature, the phytoecdysteroids, presumably, also contribute to the realization of the antioxidant activity of the *F. uniflorum* extract, as they have direct antiradical properties and are capable to increase the level of the endogenic antioxidant protective system in animals [14].

CONCLUSION

The *F. uniflorum* extract has the marked stress-protective property in the 18-h immobilization stress induced in rats. The tested remedy protects from the development of the classic “Selye's triad”: the hypertrophy of adrenal glands, involution of immune competent organs and prevents the development of destructive processes in the stomach wall mucosa. The stress-protective effect of the *F. uniflorum* extract is due to the marked antioxidant activity of phenolic compounds and phytoecdysteroids contained in the plant. The antioxidant effects of the given substances are due to the direct antiradical effect, as well to their indirect influence in the free radical processes and their capability to increase the level of the endogenic antioxidant protective system. The effect of ecdysteroids is not limited to antioxidant properties; they also have hypolipidemic, anti-sclerotic and anti-diabetic properties; they promote the functions of the liver, kidneys and modulate the activity of the immune system. The stress-protective effect of *F. uniflorum* is due to its capacity to regulate mechanisms of adaptation in the body at stress. The findings of the research testify the applicability of the *F. uniflorum* extract as an adaptogenic remedy in stress, physical and psycho-emo-

tional strain, in extreme environmental conditions and as a remedy for prevention of various diseases.

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Table 1
The influence of the *F. uniflorum* extract on the evidence of the "Selye's triad" signs in rats exposed to 18-hour immobilization stress

Animal groups	Relative mass of organs (mg/100g)		
	thymus	spleen	adrenal glands
Intact (n=6)	47,0±2,88	491,6±37,84	16,8±1,77
Control (n=8) (stress+ H ₂ O)	34,6±3,89	282,6±20,56	25,0±2,24
Experimental 1 (n=8) (stress+ <i>F. uniflorum</i>)	51,5±5,79*	400,8±29,42*	17,5±1,72*
Experimental 2 (n=8) (stress+ <i>L. carthamoides</i>)	40,2±3,00	404,0±26,36*	17,6±0,75*

Note: * – hereinafter the difference is significant in comparison with the control when $p \leq 0.05$.

Table 2
The influence of the *F. uniflorum* extract on the evidence of the injuries in the stomach mucosa of rats exposed to 18-hour immobilization stress

Indices	Animal groups			
	Intact (n=8)	Control (stress+H ₂ O) (n=8)	Experimental 1 (stress + <i>F. uniflorum</i> extract) (n=8)	Experimental 2 (stress+ <i>L. carthamoides</i> extract) (n=8)
Hemorrhages, %	0	100	40	50
Mean hemorrhages per a rat	0	4,8	2,5	2,7
PI for hemorrhages	0	0,38	0,12	0,13
Erosions, %	0	60	0	30
Mean erosions per a rat	0	2,6	0	0,6
PI for erosions	0	0,13	0	0,02
Stripe-like ulcers, %	0	50	0	0
Mean ulcers per a rat	0	1,0	0	0
PI for ulcers	0	0,04	0	0

Note: PI – Pauls' index.

Table 3
The influence of the *F. uniflorum* extract on the intensity of the FRO processes and the state of the antioxidant system in rats exposed to 18-hour immobilization stress

Показатель	Groups			
	Intact (n=8)	Control (stress+H ₂ O) (n=8)	Experimental 1 (stress + <i>F. uniflorum</i> extract) (n=8)	Experimental 2 (stress+ <i>L. carthamoides</i> extract) (n=8)
MDA, μmol/l	4,8±0,21	10,3±0,55	7,5±0,28*	7,8±0,62*
Reduced glutathione, mmol/ml	0,73±0,041	0,56±0,024	0,69±0,07*	0,75±0,050*
Catalase, mkat/l	25,5±1,13	15,4±0,97	20,4±2,03*	25,8±1,54*
SOD, activity unit	11,2±0,78	4,3±0,31	7,3±0,65*	6,8±0,27*

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