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Pharmacological Properties of Stinky Ferula Gum and its Anti-Inflammatory Effects

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ABSTRACT: Preliminary pharmacological studies of the gum exatract of underground parts of Ferula tajikorum plant (EFT) were conducted. EFT witth LD50 5 g/kg in dose 10 mg/kg p.o. during prolonged administration decreased of spontane locomotors activity fall down to 25% and it was evaluated as sedation. In dose 30 mg/kg sedation was not stable. At a dose of 30 mg/kg sedation was unstable. Both doses enhanced amphetamine locomotor action, decreased haloperidole catalepsy and decreased arecoline M-cholinostimulating action, i.e. effects on neuroreceptors were noted. Antiinflammatory effect of a dose of 10 is more pronounced than from a dose of 30 mg/kg. Considering the literature data on a wide range of EFT pharmacological properties and the multidirectionality of the properties of EFT it is concluded that it is advisable to separate the extracts into components or fractions of structurally similar substances. This will reveal the specific activity and predictability of their practical application or use as a sample for synthesis in classdicine.

KEYWORD: Ferula tajikorum, Anti-inflammatory, amphetamine, locomotor activity.

Plants of the genus Ferulae, withem. Umbrella plants (Ferula, Umbelifera fam.) are widely distributed within the CIS countries, including Western Europe. Siberia, Kazakhstan and Central Asia [1,2,5]. In Uzbekistan, individual and total substances from fine-grained Ferula (F. tenuisecta) are studied and used as phytoestrogens in the form of Tefestrol, Tenestrol and Ferulen in medicine and agriculture (R. M. Khalilov and et al., 2009 [10]; M. A. Mamathanov and sovt., 2019) [9]. Another type of Ferula (Ferula tajikorum) has been studied to a lesser extent, and has not yet received practical application. Meanwhile, according to the literature, the plant of this species has a very wide spectrum of pharmacological activity and is widely used in folk medicine mainly in Asian countries and relatively rarely in scientific medicine. According to some sources, raw materials from Ferula in the form of tubers, mown aboveground parts and harvested resin are exported outside the country. Measures are being taken to cultivate the plant in Uzbekistan. Pharmacologists of Uzbekistan are tasked with finding ways to create effective therapeutic drugs from Ferula. It is obvious that the phytoestrogenic effect previously identified in Uzbekistan is not the only promising pharmacological property among many plant species. This report presents the results of preliminary studies of Ferula tadjiacorum resin extractcollected in the foothillsGissar ridge of Surkhandarya region of Uzbekistan. According to the literature, a very wide spectrum of pharmacological activity has been revealed in plants of this family. Of the many pharmacological properties of Ferula described, we were interested in sedation (P.Mahendra et.al., 2012 [2] bronchodilator (p.Mitchel et.al., 2019 [3,4,13,20], neurotropic and anti-inflammatory properties (S.Bagheri et.al., 2016 [4,20,28]. The effect of SFT on motor and research activity, feelings of anxiety, the effect on the sensitivity of the main

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neuroreceptors regulating mental activity, anti-inflammatory effect and acute toxicity when administered orally was studied. Objects and methods of research. The object of research is the extract of Tajik Ferula resin (FerulaFerula tajikorum), which is a condensed juice collected from a section of the trunk of a plant made near the earth's surface. According to the data of the co-authors of this article, the resin contains K. A.Eshbakova and B.J. Komilova coumarins of furan and clerodan structure, and sesquiterpenoids. The studied preparation has the form of a dark brown resin with a bitter taste, soluble in water. White male mice weighing 20-23 g and white male rats weighing 210-240 g were used in experiments. The effect of the substance on motor activity was studied according to Lapin etal., [5,15], research activity according to C. Hall [16,20,25], and the anti-inflammatory effect was tested by the method of Oivina and Monacocova [8], as well as the effect on anxiety according to T. Kilfoil et.al., 1989 [7,17,19]. The effect of SFT on the sensitivity of central alpha-adrenergic receptors was studied in experiments on mice by the effect of the substance on the severity of the locomotor effect of phenamine (5 mg / kg subcutaneous injection). Effect on M-cholinergic receptors by the severity of salivation and tremor stimulated by arecoline (5 mg / kg subcutaneously). The effect of SFT on central D-receptors was studied in a test on the effect on the duration of haloperidol (0.3 mg/kg subcutaneous injection) catalepsy. It was necessary to determine the value of effective doses of SFT affecting the nature of the experiments performed. The above set of tests was selected in accordance with the pharmacological properties of the Ferule known from the literature. Thus, the sedative and other psychotropic properties of Ferula asafetida are indicated by P.Mahendra e. a. 2012 [27,28,30], in bronchial asthma R. Mitchel e. a. 2019 [3], about anti-inflammatory properties writes (S.Bagheri e.a. 2016 [4]. Research results. Study of acute toxicity of SFT. Experiments were conducted on 6 white mice. SFT was administered at a dose of 5 g / kg. Observation of mice for 5 days did not reveal the death of mice, which confirms the low toxicity of total Ferula preparations. The study of the effect of SFT on DA in white mice with daily 33-day administration showed that at a dose of 10 mg/kg orally, an increasing depressive effect on DA was observed throughout all 33 days of administration. On the last day of the experiment, DA was 4 times more depressed than the control group. At a dose of 30 mg/kg orally, the effect on DA in severity was not the same without any regularity Influence SFT on the research activity of mice in the Hall test. In the experiment with chronic administration of SFT on the 14th day of administration, it was observed that the research activity, estimated by the number of minks examined, in experimental and control mice was almost the same. On the 1st day of administration, the number of examined minks in both groups of mice decreased: from a dose of 10 mg/kg by 60%, and from a dose of 30 mg / kg to 40%. (see Figure 2). This fact can be interpreted as a cumulative effect of SFT on research activity. Effect of SFT extract on the locomotor effect of phenamine. Experiments with phenamine were performed on mice with chronic administration of SFT at the indicated doses on the 14th day of administration. The aim of the experiment was to study the effect of SFT on the severity of the locomotor effect of phenamine. Experience has shown that DA increased in all groups, including the control group, but to the greatest extent with a dose of 30 mg / kg (see Figure 3).Effect of SFT on haloperidol catalepsy. In this experiment, the effect of SFT on the duration of catalepsy caused by the D-antagonist haloperidol was determined. Shortening of the duration of catalepsy was assessed as a central D-dopamine-positive effect of SFT and vice versa. The experiments revealed a shortening of the duration of catalepsy by 30-40% of both doses.SFT ,i.e. the effect of SFT on the pharmacological effects of arecoline was shown to be D-positive. In this experiment, the effect of SFT on the sensitivity of peripheral and central M-cholinergic receptors caused by arecoline (10 mg/kg subcutaneous injection) was tested. The study showed thatpre - administration of SFT at a dose of 10 mg/kg orally reduces salivation and tremor from arecoline by about 2 times .Effect of SFT on anxiety according to the Kilfoil method Kilfoil. The experiment was conducted in a 4-chamber maze with 2

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light and2 dark chambers located radially. As a rule, control animals prefer dark cameras and change cameras 4-6 times in 1 min during the experiment. Experimental mice under the influence of SPT at doses of 10 and 30 mg / kg changed the cameras from one and a half to two times, which is usually assessed as a manifestation of a sense of anxious behavior. It is noteworthy that a dose of 10 mg / kg had a more pronounced depressive effect than 30 mg/kg. Effect of SFT on ovalbumin inflammation in rats according to I. AOivin and K. N.Monacovastreet. In experiments on rats, SFT was administered 24 and 3-4 hours before the inflammatory process was triggered. It was found that against the background of SPT, the severity of inflammation is marked with the introduction of a 5% solution of native egg white (see Figure 6). It is noteworthy that a small dose (10 mg/kg) has a more pronounced effect. Discussion of materials. An introductory study of the total preparation from underground parts called resin extract from Ferula tadjiacorum(SFT) showed that in a small dose of 10 mg / kg inside, which is about 1/500 of LD50, it shows a pronounced sedative effect, and with the manifestation of accumulation. With a 3-fold increase in the dose, the sedative effect loses stability. It should be assumed that this is due to the heterogeneity of the resin composition and different directions and different thresholds of pharmacological activity, while the research activity remains stable for more than 2 weeks and it can be assumed that there is no parallelism between these 2 properties or it is relative. SFT in the used doses significantly increased the sensitivity of alpha-adreno, D-dopaminoreceptors and inhibited M-cholinergic receptors to the corresponding agonists. The credibility of this data is supported by other experiments. For example, the alpha-adrenopositive effect of SFT was indirectly confirmed in the Kilfoil experimentКилфоил, where an increase in the anxiogenic effect was noted in the form of an extension of stay in dark compartments characteristic of adrenopositive substances (I. P. Lapin etal., 1991 [25,27]. After analyzing the data on the ratio of dose values and pharmacological effects, it is necessary to state that the dose of 10 mg / kg was optimal for the manifestation of sedative and anti-inflammatory effects. On the impact on research activity by on all, both doses did not have a depressing effect for at least 2 weeks. To increase the sensitizing effect, the SFT dose of 30 mg / kg was more effective than 10 mg / kg in experiments on enhancing the locomotor effect of phenamine and the M-cholinopositive effect of arecoline, as well as antagonism to the cataleptogenic effect of haloperidol. The observed contradictions in the dependence of the dose size and the nature of pharmacological properties are related to the heterogeneity of the components of SFT, namely, coumarins of furan and clerodane structure and sesquiterpenoids, which leads to heterogeneity of their pharmacological effects. Based on the conducted studies that are always noticeable in the manifestation of sedative action. The conclusion suggests that for effective work with SPT, it is advisable to divide it into 3 components , or at least separate coumarins from ot sesquiterpenoids. The study of pharmacological properties separately will be more effective and will gain recognition in classical medicine. The division of SFT into its component parts will shed light on the existing inconsistencies in the pharmacological properties of the substance, including the discrepancy between the sedative effect of SFT and its adreno- and dopamine-positive properties. In addition, how to explain the greater severity of the anti-inflammatory effect of a lower dose of 10 mg / kg, compared with a higher dose of 30 mg/kg, what is the mechanism of the activating effect of a dose of 30 mg/kg revealed in their comparative studies on the effects on DA. After all, it is possible that this is due to the general toning of animals.

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