UDC 615.322

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STUDY OF CHEMICAL COMPOSITION OF THE SOLANACEAE FAMILY MEMBERS FOR NEW ANTIEPILEPTIC REMEDIES CREATION

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Introduction. The problem of epilepsy treatment has been described. The relevance of the search of new herbal anticonvulsants has been substantiated.
Aim. To find connections between different groups of lipophilic compounds content of Datura stramonium, Belladonna officinalis, and Hyoscyamus niger extracts and intensity of their anticonvulsant action.
Materials and methods. Above-ground parts of Datura stramonium, Belladonna officinalis, and Hyoscyamus niger, were gathered in Ukraine, cleaned, washed, dried and used for further research. The extracts were prepared using water as a solvent in a ratio 1 to 20 and then were dried under the vacuum. The Agilent Technologies gas chromatograph 6890 series with mass spectroscopy detector was used. Carrier gas was helium. Samples were starting to put into column when temperature of detector reached 250 °C. Compounds were identified by using the Nist 05 and Wiley 138 library databases of the GC-MS system.
Results. As a result of research, in dry aqueous extracts of Datura stramonium leaves, Hyoscyamus niger herb, and Belladonna officinalis herb 58, 50 and 59 lipophilic compounds, respectively, were determined. In mice subjected to Pentylenetetrazole-induced seizures, the dry aqueous extract of Hyoscyamus niger herb, has shown the most pronounced anticonvulsant activity.
Conclusion. The dry aqueous extract of Hyoscyamus niger herb can be a promising substance for original herbal remedy with anticonvulsant properties creation.
Key words: chemical composition, Solanaceae family, antiepileptic remedies.

Introduction. Epilepsy is a serious neurological disorder involving recurrent convulsions. It is well-known that this brain disorder may lead to serious neurobiological, cognitive, psychological, and social consequences. Besides, in adult patients some cognitive complaints, such as mental slowness, memory difficulties and attention deficits may happen. As a rule, in children patients, cognitive problems are more extensive and are in language troubles, learning difficulties, low achievements, behaviour problems and finally unfortunate socio-professional prognosis [5, 6]. Despite the availability of a wide range of antiepileptic medicines, one should not forget the significant risk of side effects when using all modern remedies for treatment epilepsy [3]. In the last few years, there has been an exponential growth in the herbal medicine research. Expansion and deepening of knowledge about chemical composition of herbs and research of pharmacological properties of the biologically active compounds recently have resulted in a significant increase of herbal medicines development and use [7]. This can be explained by the fact that herbal remedies are safer compared with synthetic therapies, even during long-term use. Probably, this property is usually due to multicomponent composition of herbs, because the synergism of biologically active compounds in herbal remedies precludes the efficiency of their individual substances or fractions [3, 4]. Therefore, the development of new

drugs derived from herbal remedies with anticonvulsant properties still remains problematic and is an important direction to solve this problem. During our previous research, anticonvulsant properties of the Solanaceae family members, such as Datura stramonium, Belladonna officinalis, and Hyoscyamus niger, were discovered. The anticonvulsant properties of extracts from the mentioned herbs were confirmed on experimental seizure models with different neurochemical mechanisms, and the strong antiepileptic potential these extracts was identified [8]. Obtained results demanded more depth study of anticonvulsant properties of herbs mentioned above, in particular, to analyze relations between chemical composition of Datura stramonium, Belladonna officinalis, and Hyoscyamus niger and their anticonvulsant properties. In the analysis of literature data devoted to this given scientific subject, our attention was drawn to the anticonvulsant activity of different lipophilic components of herbs. Therefore, the aim of our research was to find any connections between different groups of lipophilic compounds content of Datura stramonium, Belladonna officinalis, and Hyoscyamus niger extracts and intensity of their anticonvulsant action.

Materials and methods. Reagents from Sigma-Aldrich (USA) and Merck (Germany) were used and prepared according to the requirements of the State Pharmacopoeia of Ukraine. Above-ground parts of Datura stramonium, Belladonna officinalis, and Hyoscyamus niger, were gathered in Ukraine, cleaned, washed, and dried. After complete drying, the dry herbs were stored at room temperature. Then, herb samples were powdered and used for further research. The extracts were prepared as follows: 100 g of the air-dried and powdered herb (either Datura stramonium, or Belladonna officinalis, or Hyoscyamus niger) was placed into a percolator, and extraction was allowed to run using water as a solvent in a ratio 1 to 20 at 80°C for 2 hours. Then, the obtained extracts were filtered and concentrated in a vacuum-evaporation apparatus at 50-60°C and at 80-87 kPa to a thick consistency. Finally, the extracts were dried under the vacuum in the desiccators until a residual moisture content of 5% was attained. To determine lipophilic compounds, GC-MS analysis by previously developed method has been used [2]. The Agilent Technologies gas chromatograph 6890 series with mass spectroscopy detector was used; fitted with a column (30 m × 0.25 mm i. d.). The following oven temperature program was used: 50 °C for 1 min then 4 °C / min up to 320 °C: this final temperature was held for 9 min. Carrier gas was helium with a constant flow rate of 1.2 mL/min. Samples were starting to put into column when temperature of detector reached 250 °C. Compounds were approximately identified by using the Nist 05 and Wiley 138 library databases of the GC-MS system. The composition was computed from the GC peak areas according to the method without using any correction factors.

Results and discussion. As a result of research, in dry aqueous extract of Datura stramonium leaves 58 lipophilic compounds were determined. Among lipophilic compounds of dry aqueous extract of Datura stramonium leaves, fatty acids (caprylic, myristic, palmitic, stearic, linolenic, and docosanoic acids); carbohydrates (neophytadien, nonacosan, triacontan); alcohols, ketones, and carbon acids (phytol, farnesol, phtalat); terpenoids; alkaloids (anhydroatropine, hyoscine); and phytosterols characterized by the highest amount. Dry aqueous extract of Hyoscyamus niger herb characterized by the presence of 50 lipophilic compounds. Alkaloids (anhydroatropine, atropine, hyoscyamine); fatty acids

(isovaleric, caprylic, myristic, palmitic, stearic, linolenic, linoic, phenylacetic, lauric and eicosanoic acids); carbohydrates (neophytadien, heptacosan, nonacosan); alcohols, ketones, and carbon acids (phytol, farnesol, phtalat); terpenoids (loliolide, dihydroactinidiolide); phytosterols (squalene, sitosterol, tocopherol) were determined in the highest concentrations (Fig.).

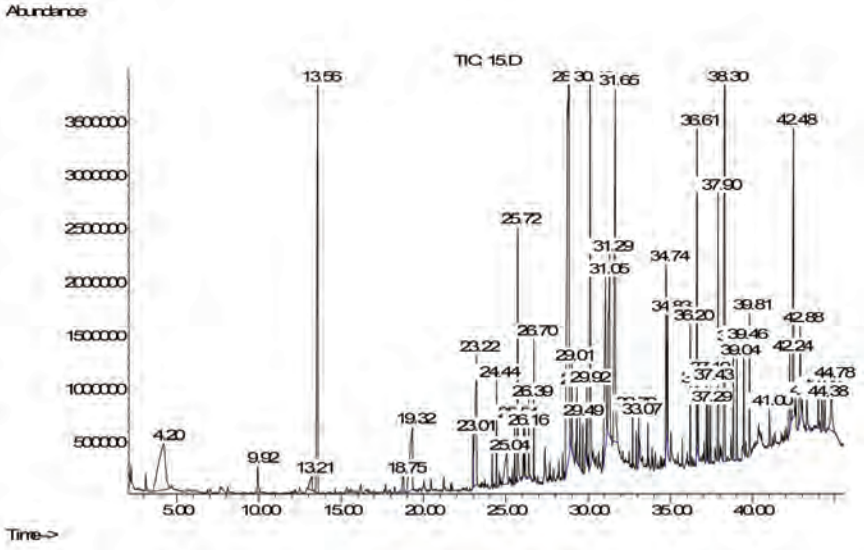

Figure. GC-MS chromatogram of lipophilic compounds of dry aqueous extract of Hyoscyamus niger herb

In dry aqueous extract of Belladonna officinalis herb 59 lipophilic compounds were determined, e.g.: fatty acids (isovaleric, caprylic, myristic, palmitic, lauric, oleic, linolenic, linoic); carbohydrates (neophytadien, nonacosan, triacontan); alcohols, ketones, and carbon acids (phytol, farnesol, phtalat); terpenoids (loliolide); alkaloids (anhydroatropine, hyoscine, hyoscyamine, scopoletin); and phytosterols (squalene, tocopherol). In mice subjected to Pentylenetetrazole-induced seizures [1], the dry aqueous extract of Hyoscyamus niger herb, as the reference drug Sodium valproate, has shown the most pronounced anticonvulsant activity, resulting in a significant increase in the latency period of the appearance of the first seizure, reducing lethality, severity of seizures and the duration of the convulsive period in the group. Both dry aqueous extracts from Datura stramonium leaves and Belladonna officinalis herb did not practically differ from each other in realization of the anticonvulsant activity, which is probably depend on differences in lipophilic compounds content. Considering the fact that the dry aqueous extract of Hyoscyamus niger herb has shown the highest anticonvulsant properties, it can be a promising substance for original herbal remedy with anticonvulsant properties creation.

Conclusion. Phytochemical analysis and research of anticonvulsant properties of dry aqueous extracts from Datura stramonium, Belladonna

officinalis, and Hyoscyamus niger has been carried out. Results have shown high amount of lipophilic compounds in the analyzed extracts with prevalence of fatty acids, carbohydrates, alcohols, ketones, carbon acids, alkaloids, and phytosterols. The dry aqueous extract of Hyoscyamus niger herb has shown the highest anticonvulsant properties, so it can be a promising substance for original herbal remedy with anticonvulsant properties creation.

Literature

1. Akdogan I. Experimental epilepsy models and morphologic alterations of experimental epilepsy models in brain and hippocampus / I. Akdogan, N. Yonguc. – In: Underlying Mechanisms of Epilepsy. -2011. – C. 269 – 282.

2. Analysis of lipophilic compounds from Corylus avellana leaves / Prokopenko Yu. S, Bliznyuk N. A., Georgiyants V. A. // Chemistry of Natural Compounds. - 2014. – № 50. – P. 120 – 121.

3. Brodtkorb E. Treatment non-adherence in pseudo-refractory epilepsy / E. Brodtkorb. – Epilepsy research, 2016. – № 122. – P. 1 – 6.

4. Devinsky O. Alternative therapies for epilepsy / O. Devinsky, C. Steven. – New York: Demosmedical. – 2012. – 225 p.

5. Dulaney A. W. Mortality in people with epilepsy: A statewide retrospective cohort study / A. W. Dulaney. // Epilepsy research.- 2016. – № 122. – P. 7 – 14.

6. Rijckevorsel K. Cognitive problems related to epilepsy syndromes, especially malignant epilepsies / K. Rijckevorsel. // European Journal of Epilepsy.- 2006. – № 4. – P. 227 – 234.

7. Schachter S. C. Botanicals and herbs: a traditional approach to treating epilepsy / S. C. Schachter // Neurotherapeutics. – 2009. – № 6. – P. 415 – 420.

8. Tsyvunin V. V. Experimental defining of anticonvulsant action of perspective phytogenic anticonvulsants / V. V. Tsyvunin, S. Yu. Shtrygol', Yu. S. Prokopenko [et al.]. // Ukr. Biopharm. J.- 2014. – № 3. – P. 45 – 49.

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Вивчення хімічного складу представників родини Solanaceae для створення нових протиепілептичних засобів

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Вступ. Охарактеризовано проблему лікування епілепсії та обґрунтовано необхідність пошуку нових рослинних антиконвульсантів.

Мета. Встановити взаємозв'язок між вмістом різних груп ліпофільних сполук екстрактів Datura stramonium, Belladonna officinalis та Hyoscyamus niger та їх протисудомною активністю.

Матеріали та методи. Надземні частини Datura stramonium, Belladonna officinalis та Hyoscyamus niger були зібрані в Україні, очищені, висушені та використані для дослідження. Для приготування екстрактів використовували воду як екстрагента у співвідношенні 1 до 20; потім екстракти висушували у вакуумі. Для дослідження використовували газовий хроматограф з мас-детектором Agilent Technologies gas chromatograph 6890. У якості газу-носія використовували гелій. Зразки починали вносити у колонку за температури детектора 250 °С. Сполуки ідентифікували за допомогою бібліотек мас-спектрів Nist 05 та Wiley 138.

Результати. В результаті дослідження у сухих водних екстрактах листя Datura stramonium, трави Hyoscyamus niger та трави Belladonna officinalis було

ідентифіковано 58, 50 та 59 ліпофільних сполук, відповідно. На коразоловій моделі судом у мишей сухий водний екстракт трави Hyoscyamus niger показав найбільш виражену протисудомну активність.
Висновки. Сухий водний екстракт трави Hyoscyamus niger виявився найбільш перпективною субстанцією для розробки оригінального протисудомного лікарського засобу рослинного походження.
Ключові слова: хімічний склад, родина Solanaceae, протиепілептичні засоби.

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Изучение химического состава представителей семейства Solanaceae для создания новых противоэпилептических средств

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Введение. Охарактеризована проблема лечения эпилепсии и обоснована необходимость поиска новых растительных антиконвульсантов.
Цель. Установить взаимосвязь между содержанием различных групп липофильных соединений экстрактов Datura stramonium, Belladonna officinalis та Hyoscyamus niger и их противосудорожной активностью.
Материалы и методы. Надземную часть Datura stramonium, Belladonna officinalis та Hyoscyamus niger собирали в Украине, затем очищали, высушивали и использовали для исследования. Для приготовления экстрактов использовали воду как экстрагент в соотношении 1:20, затем экстракты высушивали в вакууме. Для исследования использовали газовый хроматограф с масс-детектором Agilent Technologies 6890. В качестве газа-носителя использовали гелий. Образцы вводили в колонку при температуре детектора 250 °С. Соединения идентифицировали с помощью библиотек масс-спектров Nist 05 и Wiley 138.
Результаты. В результате исследования в сухих водных экстрактах из листьев Datura stramonium, травы Hyoscyamus niger и травы Belladonna officinalis были идентифицированы 58, 50 и 59 липофильных соединений, соответственно. На модели коразоловых судорог у мышей сухой водный экстракт травы Hyoscyamus niger показал наиболее выраженную противосудорожную активность.
Выводы. Сухой водный экстракт травы Hyoscyamus niger является наиболее перспективной субстанцией для разработки оригинального противосудорожного средства растительного происхождения.
Ключевые слова: химический состав, семейство Solanaceae, противоэпилептические средства.

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