RECENT ADVANCES AND FUTURE PROSPECTS OF THE USE OF HERBS IN EPILEPSY TREATMENT

Yuliya Prokopenko, Victoriya Georgiyants, Sergii Shtrygol', Vadim Tsyvunin, Liudas Ivanauskas
National University of Pharmacy, Kharkiv, Ukraine
Lithuanian University of Health sciences, Kaunas, Lithuania

Introduction. Herbs have a centuries-old tradition of use in many cultures around the world for treatment a number of diseases, and epilepsy is among them. As a rule, herbal therapies may be tried by patients in developing as well as developed countries for control of seizures or adverse effects from antiepileptic drugs (AEDs), or for general health maintenance, but usually without the knowledge of physicians who prescribe their AEDs. In Ukraine, as well as in other countries of the world, among the arsenal of AEDs, only drugs of synthetic origin are represented. However, the use of herbal medicines may be appropriate and rational, considering the complex effect on the mechanisms of convulsive attacks development and the mild psychotropic effect, which significantly reduces the development of epileptic personality changes symptoms. The high abundance of herbs, their safety profile, and various mechanisms of action make them favorable to be studied and developed as an alternative agents or adjuvant to modern therapeutic drugs in curbing the onset and progression of neurodegenerative diseases, in particular, epilepsy. To optimize the search for synthetic AEDs, *in silico* studies are used quite effectively. This was preceded by extensive systematic research on the qualitative and quantitative influence of the chemical structure on anticonvulsant activity based on the results of experimental studies, determination of primary and secondary pharmacophores. But for herbal anticonvulsants, such studies have not been systematically conducted. A comprehensive experimental study of the chemical composition and anticonvulsant activity of herbs and herbal extracts will make it possible to reveal the regularities of their combination and substantiate ways of optimizing the search for AEDs of herbal origin.

The aim of the study. The aim of the present study was to provide a concise overview of recent advances in research on the correlation between herbal compounds and anticonvulsant activity, and to discuss currently unmet needs as well as developments which are likely to occur in the foreseeable future.

Materials and methods. A comprehensive analysis of literary sources and the developed algorithm for experimental studies made it possible to select 27 types of herbs, members up to 10 botanical families: *Lamiaceae*, *Fumariaceae*, *Solanaceae*, *Betulaceae*,
Polemoniaceae, *Berberidaceae*, *Caprifoliaceae*, *Oleaceae*, *Hydrangeaceae*, and *Viscaceae*. Chemical composition of the studied herbs was analyzed using HPLC, UPLC, UPTLC, HILIC MS/MS, GC/MS methods, NIR and FTIR spectroscopy, UV spectroscopy, as well as wet chemistry methods. Pharmacological results were used for

correlation studies performed *in vitro* and *in vivo*. Scigress Explorer software was used to perform molecular docking. Visualizaton and analysis of the obtained results of the docking studies were carried out using Discovery Studio V17.2.0.16349. Construction of mathematical QSAR models was carried out using the BuildQSAR program using the GA-MLRA method.

Results. Quantitative content of compounds influencing the anticonvulsant potential was determined in the studied herbal samples. 4-hexanoic acid, a structural analogue of valproic acid, was found in *Betulaceae* and *Viscaceae* members. The presence of caprylic acid, which enhances anticonvulsant activity of valproic acid, was found in members of *Lamiaceae*, *Hydrangeaceae*, *Solanaceae* and *Polemoniaceae* families. Original technique using HPLC method and HILIC column with mass-detection was developed to determine neurotransmitter amino acids. Thus, quantitative content of GABA, glycine, histidine, tryptophan, alanine and valine was determined mainly in *Lamiaceae* and *Fumariaceae* families' members, as well as *Viscaceae* and *Solanaceae* ones. Regarding anticonvulsant potential of some phenolic compounds, flavonoids (rutin, hyperoside, lutheoline, and quercitrine), hydroxycinnamic acid (chlorogenic, neochlorogenic, rosmarinic, caffeic, fumaric), and polyphenols content was determined in the studied samples. Regarding high anticonvulsant potential of ursolic acid, its quantitative content was determined mainly in *Lamiaceae* family members.

Pharmacological screening results on the model of pentylenetetrazole-induced seizures have shown that 11 dry extracts have high anticonvulsant potential. To determine quantitative and qualitative influence of biologically active compounds on realization of anticonvulsant activity, chemical composition of the studied extracts was determined. It was found that high content of GABA was typical for the extracts having a pronounced anticonvulsant activity, unlike the proconvulsant ones. Besides, high content of flavonoids in the extracts having a pronounced anticonvulsant activity was determined – more than 7%, unlike proconvulsants having rutin content less than 0,6%. The summarized results of the dry extracts chemical composition study were compared with anticonvulsant activity parameters (latency period, duration of seizures). After that, quantitative correlation parameters "content of biologically active substances and anticonvulsant activity" using the program BuildQSAR were determined. A statistically significant correlation of the latency period with amino acid content ($r=0.580$) and rutin content ($r=0.614$) was found. Besides, correlation between anticonvulsant activity parameters and the sum of flavonoids content ($r=0.587$) was found. In general, correlation coefficients were up to 0.61, which is typical for herbal compounds. Obtained docking results pointed to the inability of individual herbal compounds to influence on GABA-ergic mechanism of seizures, probably, due to the other mechanism of their anticonvulsant action.

Conclusions. Results have shown that herbs of *Lamiaceae* and *Fumariaceae* families substances have high anticonvulsant activity level, mainly due to the complex

of flavonoids (rutin), polyphenol compounds and neurotransmitter amino acids. Due to hydrophilic nature of the most promising natural compounds of the selected herbs, it is recommended to use aqueous extracts for the further studies. QSAR studies showed no correlations when applied single-parameter models. Nevertheless, anticonvulsant activity in the best way correlated with the content of amino acids and flavonoids when using two and three parametric models.

ДОСЛІДЖЕННЯ НЕЙРОТРОПНОЇ АКТИВНОСТІ КУЛЬТИВОВАНИХ В УКРАЇНІ ВИДІВ ДЕКОРАТИВНИХ РОСЛИН

[1] Марчишин С. М., [2]Гарник М. С., [1]Демидяк О. Л., [1]Мілян І. І.
[1]Тернопільський національний медичний університет імені І. Я. Горбачевського МОЗ України, м. Тернопіль, Україна
[2]Вінницький національний медичний університет імені М. І. Пирогова, м. Вінниця, Україна

Вступ. Сьогодні близько 23 тис. видів рослин світової флори використовують як лікарські. Особливої уваги заслуговують рослини, які вирощують як декоративні, серед яких види родів Хризантема (*Chrysanthemum* L.) і Лілійник (*Hemerocallis* L.).

Рослини роду Лілійник у дикорослому вигляді поширені в Південно-Східній Азії, Європі, Північній Америці; широко культивуються як квітково-декоративні. Батьківщиною лілійників вважають територію Південно-Східної Азії, зокрема – сучасного Китаю. В Україні в дикорослому вигляді поширений один вид – лілійник буро-жовтий, інші види і сорти – лише в культурі. Лікувальні властивості лілійників згадуються у багатьох стародавніх китайських травниках. Соком молодих коренів у Китаї лікували жовтяницю та цироз печінки. Китайці вважали, що квітки лілійників позитивно впливають на нервову систему і психіку людини [1].

Рослини роду Хризантема зростають у помірних субтропічних областях Південно-Східної Азії. Багато видів і сортів *Chrysanthemum* – цінні декоративні рослини, які широко використовуються в озелененні. Хризантеми вирощують як декоративну рослину, але окремі види використовують як лікарські [2]. В культурі широко вирощують хризантему садову багаторічну. Квітки хризантеми здавна використовували у традиційній і доказовій медицині Індокитаю як засоби, які покращують коронарний кровобіг; усувають симптоми вегетосудинної дистонії; знижують артеріальний тиск; нормалізують обмін речовин; як загальнозміцнювальний та антиалергічний засіб. Ефірна олія квіток посилює гальмівні процеси в підкоркових вузлах при хворобі Паркінсона [3].