

ЛИТЕРАТУРА

1. Всемирная организация здравоохранения: официальный сайт. Информационный бюллетень. 164. 2013.URL: <http://www.who.int/mediacentre/factsheets/fs164/ru> (дата обращения: 24.09.2018).
2. Балукова, Е.В. Поражения печени различного генеза (токсического, лекарственного, дисметаболического): от этиологической гетерогенности к единой унифицированной терапии пациентов / Е.В. Балукова, Ю.П. Успенский, Ю.А. Фоминых. // РМЖ. – 2018. – № 1(1). – С. 35-40.
3. Машковский, М.Д. Лекарственные средства. – 16-е изд., перераб. и доп. / М.Д. Машковский. – М.: Новая волна, 2012. – 1216 с.
4. Соколов, С.Я. Фитотерапия и фитотерапевтика: руководство для врачей / С.Я. Соколов. – М.: МИА, 2000. – 976 с.
5. Венгеровский, А.И. Методические указания по изучению гепатозащитной активности фармакологических веществ: руководство по экспериментальному (доклиническому) изучению новых фармакологических веществ / А.И. Венгеровский, И.В. Маркова, А.С. Саратиков. – М.: Медицина, 2005. – С. 683-691.
6. Николаев, С.М. Растительные лекарственные препараты при повреждениях гепатобилиарной системы / С.М. Николаев. – Изд-во: Новосибирск, 1992. – 155 с.

REFERENCES

1. Vsemirnaya organizatsiya zdavookhraneniya: ofitsial'nyj sajt. Informatsionnyj byulleten'. 164. 2013.URL: <http://www.who.int/mediacentre/factsheets/fs164/ru> (data obrashheniya: 24.09.2018).
2. Balukova, E.V. Porazheniya pecheni razlichnogo geneza (toksicheskogo, lekarstvennogo, dismetabolicheskogo): ot ehtiologicheskoy geterogennosti k edinoj unifikirovannoj terapii patsientov / E.V. Balukova, YU.P. Uspenskij, YU.A. Fominykh. – RMZH. – 2018. – №1(1). S. 35-40.
3. Mashkovskij, M.D. Lekarstvennye sredstva. – 16-e izd., pererabotano, ispravleno i dopolneno / M.D. Mashkovskij. – M.: Novaya volna, 2012 – 1216 s.
4. Sokolov, S.YA. Fitoterapiya i fitofarmakologiya. Rukovodstvo dlya vrachej / S.YA. Sokolov. – M.: MIA, 2000. – 976 s.
5. Vengerovskij, A. I. Metodicheskie ukazaniya po izucheniyu gepatozashhitnoj aktivnosti farmakologicheskikh veshhestv // Rukovodstvo po ehksperimental'nomu (doklinicheskomu) izucheniyu novykh farmakologicheskikh veshhestv / A.I. Vengerovskij, I.V. Markova, A.S. Saratikov. – M.: Meditsina, 2005. – S. 683-691.
6. Nikolaev, S.M. Rastitel'nye lekarstvennye preparaty pri povrezhdeniyakh gepatobiliarnoj sistemy / S.M. Nikolaev. – Novosibirsk, 1992. – 155 s.

УДК 615.236:663.818:615.322
© Коллектив авторов, 2018

M.A. Mirsoatova, Ye.G. Makhova, S.K. Ordabayeva, Ye.K. Orynbassarov
**SUBSTANTIATION OF THE COMPOSITION OF THE SYRUP
BASED ON PHYTOPREPARATIONS OF ALTHEA AND LICORICE**
South Kazakhstan Medical Academy, Shymkent

The aim of the research is to develop the composition of syrup on the basis of complex phytopreparations of Althea and Lycorice.

Mukaltin substance (AND RK 42-5817-53, JCS «Chimpharm»), bioslastilin (RK M 3-№004554), fructose (SPh RK, v.2), tablets «Mukaltin» (AND RK 42-6855-14, JCS «Chimpharm»).

Taking into consideration the limitations of Mukaltin tablets in children practice, we offer the bicomponent syrup «Mukaltin+» for kids.

The following substances are recommended to include into the composition of Mukaltin+ syrup: Althea herbs (mukaltin), licorice roots (bioslastiline) and fructose (base). Combination of mukaltin and bioslastiline increases the pharmacological effect.

The composition of syrup on the basis of complex phytopreparations of Althea, Licorice and fructose has been justified.

Currently the technology of manufacturing is being experimentally developed.

Key words: althea, licorice, mukaltin, bioslastilin, syrup, phytopreparation.

«Mukaltin» is a medicinal phytopreparation having an expectorant effect and is used when the sputum is difficult to escape from the respiratory tract. The drug is based on the total extract of the tracheal althea drug, biologically active substances of which are polysaccharides, which have long been used to treat inflammatory processes of the respiratory tract. Slime of this plant, getting into the body, covers the walls of the mucous membranes and skin, protecting them from wrestling, keeps microbes and viruses on themselves, does not allow contact with the tissues of the body. The secretolytic effect of the drug «Mukaltin» ensures the dilution of sputum accumulated in the respiratory tract and accompanied by a moist cough, relieves respiratory tract irritation, and also has anti-inflammatory

and softening effect. It is used to relieve cough in diseases of the upper and lower respiratory tract for the treatment of acute and chronic bronchitis, laryngitis, pneumonia and many other respiratory diseases [1].

These days mukaltin is produced by various manufacturers (ICN Leksredstva (Russia), Wifitech (Russia), Galichpharm (Ukraine), Dalhimfarm (Russia), Irbit'sk Chemical-Pharmaceutical Plant (Russia), Mediisorb (Russia), Moscow Pharmaceutical Factory (Russia), Semashko Moshimfarmpreparaty (Russia), Experimental plant of the State Research and Production Center Ukrmedprom (Ukraine), Sti-Med-Sorb (Russia), Tatkhimfarmpreparat (Russia), Tyumen Chemical and Pharmaceutical Plant (Russia), Uralbiopharm (Russia), Pharmstandard-

Leksredstva (Russia), Kharkov State Medical Center (Ukraine), JSC «Chimpharm» (Kazakhstan) in the form of tablets, chewable tablets and syrups.

«Mukaltin» in the form of effervescent tablets, is intended for resorption or dissolution in a small amount of liquid. As a part of the preparation, the tartaric acid and sodium hydrogen carbonate are used as auxiliary substances. Upon contact with water as a result of chemical reaction between the acid of tartaric acid and sodium bicarbonate, a carbon-acid gas is formed, the bubbles of which give foaming and act as a super-baking powder. Dissolved in water effervescent tablets are characterized by rapid absorption and therapeutic effect, they cause less harm to the digestive system and improve the taste of the active substances. At the same time, the wine acid gives the sour taste to the tablets. Also, the interaction of the acid of tartaric and sodium bicarbonate leads to an increase in the acidity of the gastric juice and irritation of the gastric mucosa.

When using «Mukaltin» tablets in children practice, children of early age often refuse to take tablets because of their acidic aftertaste. In adults with high acidity of gastric juice and other gastrointestinal problems, the use of Mukaltin can cause undesirable side reactions. In this regard, «Mukaltin» tablets have contraindications: peptic ulcer of stomach and duodenum, chronic gastrointestinal diseases, diabetes mellitus [2].

Thus, the creation of a new pediatric dosage form that does not have shortcomings of «Mukaltin» tablets is an urgent task.

Purpose of the study is the development of the composition of syrup based on complex phytopreparations of althea and licorice.

Material and methods

The subjects of the study are: substance of Mukaltin (AND RK 42-5817-13, JSC «Chimpharm», RK), substance of bioslastilin (RK M-3-№004554), substance of fructose (SPh RK, v.2), «Mukaltin» tablets (AND RK 42-6855-14, JSC «Chimpharm», Shymkent, RK).

Results and discussion

Given the limitation of the use of the tablets «Mukaltin» in children practice, we offer the syrup «Mukaltin +» for children. Nowadays there are syrups of althea of various trade names and producers on the pharmaceutical market: Aleutia syrup (Jadran, Croatia), (JSC «Chimpharm», Kazakhstan), (CJSC «Wifitech», Russia), Alte (Gemi, Poland), Altemix (PhC «Zdorovie», Russia), etc.

In the known for this day, the althea root in the form of syrup, marshmallows are added to the formulation based on water infusion, sucrose is

used as the basis. To date, in the production of syrups due to the prevention of diabetes mellitus, there is a tendency to replace sucrose with fructose, which has advantages over sucrose:

- natural product contained in honey, fruits;
- carbohydrate with a low glycemic index;
- assimilated without the participation of insulin, which does not create a load on the pancreas and stabilizes the level of sugar in blood;
- the possibility of using in the diet of patients with diabetes mellitus;
- reducing the risk of dental caries by 35-40%, which is important for the treatment of children;
- high degree of sweetness;
- eliminates sharp hormonal changes and bouts of hunger; improves the absorption of active substances [3-4].

The use of fructose as the basis of the syrup has an advantage in the conduct of pharmacopoeial analysis. The quantitative content of polysaccharides regulatory documentation provides for conducting after hydrolysis in terms of glucose. Sucrose in acid hydrolysis splits into glucose and fructose, which will interfere with obtaining reliable results [5-6].

In the composition of the syrup, we recommend that, in addition to mucaltin, bioslastilin is added as an active ingredient.

Bioslastilin is a total malt root preparation containing up to 80% of glycyrrhizic acid, which is the main active ingredient of licorice root.

Bioslastilin was first obtained by MP Irismetov in 1997 [7]. As a medicine, bioslastilin was introduced into the State Register of Medicines of the Republic of Kazakhstan in 2000.

The advantage of bioslastilin over other phytopreparations of licorice is the content of glycyrrhizic acid, which varies over a wide range: up to 80% in bioslastilin, about 20% in dry extract, 14% in dense extract, 8% in licorice root [8].

The glycyrrhizic acid chemically is a triterpene saponin in which the aglycon is glycyrrhetic acid bound to two glucuronic acid residues.

High biological activity of HA is associated with its structure, similar to endogenous mineral- and glucocorticosteroids, due to the presence of the grouping of the α and β -unsaturated ketone, as well as the presence of a sugar residue that promotes the expansion of biological activity. HA is not toxic and does not cause unwanted side effects, characteristic of its structural analogs – corticosteroids.

In this regard, drugs based on glycyrrhizic, glycyrrhetic acid and their

derivatives, including bioslastilines, exhibit a wide range of pharmacological effects: anti-inflammatory, hepatoprotective, expectorant, immunomodulating, antioxidant, antitoxic, antiallergic, detoxification [9].

Numerous experimental and clinical studies in our country and abroad have shown a high anti-inflammatory activity of glycyrrhizin and glycyrrheic acids exceeding the known glucocorticosteroids, but lacking their specific side effects. The mechanism of pronounced anti-inflammatory activity of glycyrrhizin and glycyrrhetic acid is associated with inhibition of the enzyme of 11β -hydroxysteroid dehydrogenase, blocking the accumulation of a natural antiinflammatory steroid of hydrocortisone, as well as direct exposure to tissues and effects on arachidonic acid, the main inflammation-provoking compound. Glycyrrhizic acid is not toxic and does not cause unwanted side effects, characteristic of its structural counterparts - corticosteroids [10].

It was found that the presence of two residues of glucuronic acid in the molecule of glycyrrhizic acid provides antidote and hepatoprotective effect, which consists in the ability to influence the system of cytochrome P-450, inhibit lactate dehydrogenase of lipid peroxides in the liver. There is evidence of hepatoprotective action of glycyrrhizin in liver damage caused by chemicals, with relapse of hepatitis B, in cases of liver transplantation. The prospects of using glycyrrhizic acid for the treatment of toxic liver damage have been shown, it has been experimentally proven that bioslasticin has an antioxidant effect, which is expressed in a decrease in the level of products of lipid peroxidation. Glycyrrhizin inhibits the formation of free radicals, toxic products of lipid oxidation, acting as «traps» of free radicals. Licorice extracts affect the energy and plastic processes, the functional capabilities of central regulatory systems, form an increased nonspecific resistance of the organism [11].

Licorice root and its components have been used since antiquity for the treatment of tuberculosis as a tuberculostatic and immunocorrecting agent that enhances closed cavities in cavernous forms of tuberculosis (India, Vietnam, Tibet, China). Biologically active substances of licorice have antibacterial activity against gram-positive bacteria (staphylococcus, pathogens of viral infections, mycobacteria of tuberculosis) [12].

Acid glycyrrhizinic as the main component of the licorice root in bioslastilin potentiates the effect of drugs and reduces their toxicity, which is proved by experimental studies of foreign scientists in the United States, Japan, Russia, Korea, etc., domestic scientists [13-14].

Taking into account all the above-mentioned advantages of glycyrrizic acid, we assume that combining mucaltin with bioslastilin will lead to an increase in pharmacological activity. In this case, in an increased expectorant, anti-inflammatory and immunomodulating effect.

As a part of syrups, auxiliary substances are used in the form of sweeteners (flavors of taste), flavoring flavorants (flavors) to give the syrup acceptable organoleptic properties, which consist in a rapid and complete manifestation thereof; short aftertaste and absence of unwanted sensations. Bioslastilin in this respect has unique properties due to the sugary sweet taste and vegetable odor. The introduction of bioslastilin into the syrup eliminates the need for substances that correct the taste and color.

Thus, we offer a combined preparation in the form of a syrup containing mucaltin and bioslastilin based fructose.

Conclusion

The composition of the syrup «Mukaltin +», containing complex phytopreparations of althea and licorice based on fructose, is theoretically justified.

At present, experimental studies are underway to develop a technology for obtaining the recommended phytopreparation.

Authors:

Mirsoatova Mokhinur Abdikakhkharovna – master student of the Department of Pharmaceutical and Toxicological Chemistry of South Kazakhstan Medical Academy. Address: Kazakhstan, 160021, city Shymkent, Al-Farabi square, 1. E-mail: mirsoatova@mail.ru

Ordabaeva Saule Kutymovna – Doctor of Pharmaceutical Sciences, Professor, Head of the Department of Pharmaceutical and Toxicological Chemistry of South Kazakhstan Medical Academy. Address: Kazakhstan, 160021, city Shymkent, Al-Farabi square, 1. E-mail: ordabaeva@mail.ru

Makhova Elena Gennad'evna – Master of Pharmacy, Senior Lecturer of the Department of Pharmaceutical and Toxicological Chemistry of South Kazakhstan Medical Academy. Address: Kazakhstan, 160021, city Shymkent, Al-Farabi square, 1. E-mail: megarelena@mail.ru

Orynbasarov Erzhan Kasymkhanovich – Master of Pharmacy, Senior Lecturer of the Department of Pharmaceutical and Toxicological Chemistry of South Kazakhstan Medical Academy. Address: Kazakhstan, 160021, city Shymkent, Al-Farabi square, 1. E-mail: orynbasar_yerzh@mail.ru

REFERENCES

- 1 Sokolov, S.Ya. Fitoterapiya i fitofarmakologiya /S.Ya. Sokolov// Rukovodstvo dlya vrachei, M.:MIA.-2000.-976 s. (InRuss)

- 2 Mashkovskii M. D. Lekarstvennye sredstva /15-e izd. /M.D. Mashkovskii/ M.: RIA «Novaya volna»: izdatel' Umerenkov.-2008.-1206 s. (InRuss)
- 3 Bronnikova O.V. Lekarstvennye preparaty dlya detei: trebovaniya, oso-bennosti, informativnost' potrebitelei /O.V. Bronnikova// Provi-zor, 2005.- №4.- S. 27 -30. (InRuss)
- 4 Kim M.E. Siropy s fitopreparatami: nomenklatura, razrabotka, osobennosti sostava, tekhnologii (obzor) /M.E. Kim, T.A. Oleinikova, S.B. Evseeva// Aktual'nye problemy gumanitarnykh i estestvennykh nauk, 2015.- №2.-S.193-198 (InRuss)
- 5 Andreeva I.N. Siropy, soderzhashchie fitopreparaty - tekhnologiya, metodologicheskie printsipy issledovaniya /I.N. Andreeva, E.F. Stepanova, A.Yu. Albakov// Aktual'nye problemy sozdaniya novykh lekarstvennykh preparatov prirodnogo proiskhozhdeniya: tez. dokl. 5 Mezhd. s"ezda...5-7 iyulya 2001g. - SPb, 2001. – S.59-62. (InRuss)
- 6 Samylina I.A. Puti ispol'zovaniya lekarstvennogo rastitel'nogo sy-r'ya i ego standartizatsiya /I.A. Samylina, I.A. Balandina// Farmatsiya, 2004- № 3.-S.13-17. (InRuss)
- 7 Khimiya i primenenie prirodnoi glitsirrizinovoi kisloty i ee proizvodnykh /M.P. Irismetov [i dr.]// - Almaty.-2002.-287 s. (InRuss)
- 8 Arystanova A.A. Standartizatsiya lekarstvennykh preparatov kornya solodki /A.A. Arystanova// -Shymkent. -2001.-161S. (InRuss)
- 9 Sh. Nafisi Interaction of Glycyrrhizin and Glycyrrhetic acid with DNA//DNA and Cell Biology /Sh. Nafisi, M.Bonsai// i -2012.-31.- P.114-121 14
- 10 Glitsirrizinovaya kislota / G.A. Tolstikov [i dr.] //Bioorganicheskaya khimiya, 1997.- tom 23. M 9. - S. 691-709 (InRuss)
- 11 Glycyrrhizic acid in the treatment of liver diseases: literature revies. /J.Y.Li [et al.]// Biomed res Int. 2014; id 872139
- 12 Karimov M.M. Vliyanie preparatov Glycyrrhiza glabra na nekotorye pokazateli mestnoi zashchity legkikh u bol'nykh s zatyazhnymi pnevmoniyami /M.M.Karimov, A.S. Tadzhiev// Khimiya prirodn. soedin.-2000.-Spets.vyp.-S.133-134. (InRuss)
- 13 Tolstikov G.A. Solodka: bioraznoobrazie, khimiya, primenenie v medi-tsine. /G.A.Tolstikov, L.A. Baltina, V.P. Grankina// Novosibirsk: Akad. izd-vo «Geo».- 2007.- 311 s. (InRuss)
- 14 Arystanova T.A., Sposob polucheniya kompleksa glitsirrizinovoi kisloty s remantadinom /T.A. Arystanova, M.P. Irismetov, A.B. Shukirbekova// Mezhd. nauchn.-prakt. konf. «Nauka i innovatsii». – Dnepropetrovsk, 2005. –T.2.– S. 59-62. (InRuss)