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MATHEMATICAL SUPPORT FOR DOSING SYSTEMS OF DRY BULK MATERIALS OF MEDICINES USED IN CLINICAL AND HEMATOLOGICAL SYNDROMES

The quality of medicines required in modern conditions determines the high requirements for the composition of each component of bulk materials and the strict implementation of the recipe of the final product with the required accuracy. A prerequisite for the products is the operational reliability of the equipment with an increase in the level of automation and ensuring the safety of production and comfortable working conditions of personnel. The preparation of medicines poses the task of organizing the production process with fewer pieces of equipment, a shorter length of transport lines and, accordingly, a reduction in energy consumption. The article presents the relevance of the study and classification of medicines. The principle of operation of a screw weighing dispenser for the pharmaceutical industry as a control object is described. A mathematical model of a screw device for dosing bulk materials of the pharmaceutical industry has been developed.
Keywords*: pharmaceutical industry, medicines, tablets, screw feeder, dosing process, control object, supply bin, flow meter, strain gauge, clinical-hematological syndrome.*

Introduction. Pharmacology literally means "the doctrine of medicines" Pharmakon (Greek) – "medicine, poison"; logos (Latin) – "teaching". Currently, pharmacology is a complex science that studies the effect of drugs on healthy and diseased organisms, the science of purposeful search for new medicines and their rational use. From the point of view of legislation now, a drug is a drug listed in the state register of medicines. A medicine is a pharmacological agent in a certain dosage form, approved for use for the purpose of treatment, prevention, and diagnosis of diseases.[1]

The production of approved medicines must comply with the international requirements of the GMP standard, however, the introduction of this requirement on the territory of several CIS countries is carried out in stages, as the equipment of the main operating enterprises is updated. The sale of medicines (unlike biologically active additives) is carried out only by specialized stores (pharmacies, pharmacy kiosks) with the appropriate license.

The circulation of medicines is regulated by law and regulations, including regularly updating the list of vital and essential medicines (VED). Hematological studies are a complex of studies, because of which information is obtained on the quantitative and qualitative composition of the cellular elements of the blood system. Iron deficiency anemia (IDA)

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is a polyetiological disease, the development of which is associated with iron deficiency in the body due to impaired intake, assimilation or increased losses of this trace element, characterized by microcytosis and hypochromic anemia - a polyetiological disease, the development of which is associated with iron deficiency in the body due to impaired intake, assimilation or increased losses of this trace element, characterized by microcytosis and hypochromic anemia.

With iron deficiency anemia, lesions of the gastrointestinal tract are observed, manifested in the form of chronic gastritis and malabsorption syndromes in the intestine. At the same time, a decrease in secretion and acid formation in chronic gastritis is considered therefore, not a cause, of iron deficiency and is explained by dysregenerative processes in the gastric mucosa.

The goal of treatment for IDA is to administer iron in the amount necessary to normalize hemoglobin levels (women 120-140 g/l, men 130-160 g/l) and replenish tissue iron reserves (serum ferritin > 40-60 μg/l). For treatment and prevention, oral preparations of ferrous iron (code B03AA according to the ATC classification) or oral preparations of ferric iron (code B03AB according to the ATC classification) are used, most often iron sulfate. The quantitative and qualitative composition of iron medicinal preparations varies greatly: high- and low-dose, single-component and combined. According to WHO recommendations, the optimal dose of iron for the treatment of IDA is 120 mg per day, and for the prevention of iron deficiency - 60 g per day. In children, the dose of iron salt preparations depends on age and is 3 mg/kg per day in children under three years of age, in children over three years of age - 45-60 mg per day, in adolescents - up to 120 mg per day. Approximately 20% of patients develop diarrhea or constipation during treatment, which can be relieved with symptomatic therapy. Signs of gastric irritation, such as nausea and epigastric discomfort, can be minimized by taking iron supplements with meals or reducing their dose. The use of high-dose iron supplements is accompanied by an increase in the frequency of side effects from the gastrointestinal tract.

Currently, many automated complexes for the preparation of multicomponent mixtures have been developed. The requirements for such complexes are determined by such criteria as system autonomy, dosing accuracy, and energy efficiency. Based on these requirements, it is possible to analyze existing developments in this area.

The pharmaceutical industry is one of the largest industries of any state; it is designed to provide the population of countries with drugs for the treatment, prevention, and diagnosis of diseases. The pharmaceutical industry produces more than 620 types of tablets. About 3 billion packages annually. In tablets it is possible to dispense incompatible medicinal substances, masking, localization of action, compact form, ease of administration and transportation are possible. Therefore, it seems relevant to study the technology of preparing tablets [1].

There are several requirements for drugs:

– appearance and ratio of geometric dimensions.

– dosing accuracy.

– mechanical strength.

– disintegration.

As the production of tablets grows, their technology and quality control methods are improved. Much attention is paid to biopharmaceutical research - the influence of pharmaceutical factors (physicochemical properties of the drug, the degree of its grinding, the nature and number of excipients, granulation method, compression pressure, coatings used, etc.) on the effectiveness of tablets and the development of their rational production. To meet the requirements for tablets, knowledge of the physicochemical and technological properties of powdered medicinal substances and granules is necessary.

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Literature review. The technological scheme for preparing tablets consists of the following steps. Preparation of raw materials, dosing of raw materials. The technological scheme to produce tablets is presented in Figure 1 and consists of the following stages.

– powder preparation stage: grinding, sifting, mixing.

– stage of obtaining the mass for the dosage form: moistening, granulation, drying.

– stage of production of the finished dosage form: pressing, encapsulation, dust removal, coating.

– stage of packaging and packing: packing, packing.

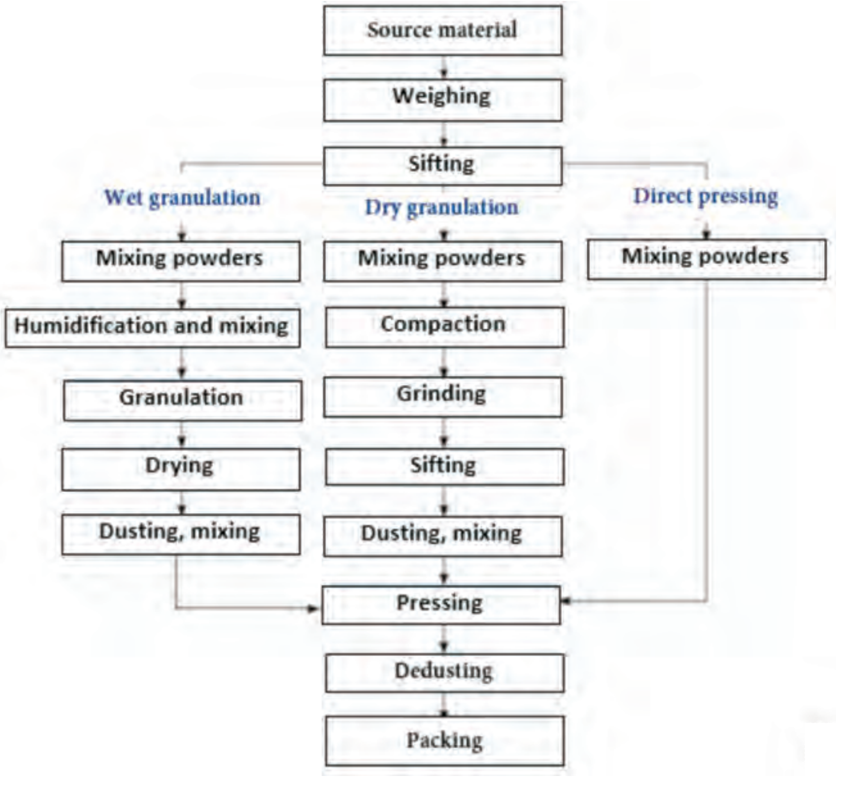

Figure 1 – Technological scheme of the drug production

The modern development of equipment in the pharmaceutical field poses the challenge of organizing the production process with fewer pieces of equipment, a shorter length of transport lines and, accordingly, reducing energy consumption. Also, a prerequisite is the high quality of products, the operational reliability of equipment with an increase in the level of automation and ensuring production safety and comfortable working conditions for personnel.

Let's consider automatic screw dispensers. Screw dispensers are designed for dispensing fine powders, granules, pastes, hard-flowing products, and dispensing a given quantity, mass, or volume of a substance in the form of a portion or a constant flow rate with a specified error.

Качество конечного продукта зависит от точности дозирования компонентов сыпучих материалов. Неточное дозирование может привести к снижению ценности выпускаемого продукта, перерасходу дефицитных и ценных компонентов и увеличению стоимости готовой продукции. Так как сыпучие материалы очень трудно точно дозировать вручную, на производствах применяются различные типы дозаторов [10]. To date, many designs of dosing devices have been developed. This is since the material flow has a wide range of physical, mechanical, and technological characteristics; In addition, equipment often has specific requirements depending on the characteristics of the process. Thus, dosing represents the main technological operation carried out at enterprises for processing pharmaceutical products [11].

Currently, there are no universal and at the same time effective methods for research and development of dosing systems for bulk materials. For each technological process, due to the specifics of the mathematical model and the technical means used, the problem arises of the correct choice of an effective method of research and synthesis, as well as the development of these methods in relation to new problems to be solved. Complex control algorithms make it possible to consider the dynamic properties of an object more accurately and can potentially provide higher control accuracy, material savings and product quality [12-18,20].

Of particular importance is the task of increasing the efficiency of control of an automated electrical complex for dispensing bulk materials, since its solution will significantly increase its productivity and reduce the incorrect dosage of especially critical, small volume, but expensive components [19].

Materials and research methods. Screw feeders (auger) dispensers are an excellent solution for transporting, unloading and dosing dry bulk materials of various types, from powdery to finely lumpy.

Screw feeders, dispensers for bulk and powdery materials, consist of the following main components: a transport mechanism with an electric motor, which allows you to change the speed of rotation of the screw, ensuring the movement of material through the working cavity, as well as a limiter, which allows you to change the flow of material. Screw dispensers for bulk and powdery substances are designed for dispensing bulk components such as flour, granulated sugar, powdered sugar, tea, coffee, cocoa powder, milk powder, polymer materials, building materials, granulated products, medicines, metals weighing up to 500 kg depending on the bulk weight of the component with a particle size of up to 5 mm, moisture content of up to 1.5% and bulk density of up to 1800 kg/m3 [2, 19,20].

The purpose of the research in this work is to develop a mathematical model of a screw dozer. The object of study is the feed hopper and the screw feeder.

To ensure high reliability, the hardware and software complex must consist of at least three levels. The lower level contains sensors and actuators. The middle level includes the control controller. The upper level is an automated operator workstation based on a personal computer. Raw materials are sequentially supplied from the supply bins through screw feeders into the dosing hopper in accordance with the recipe.

Screw dispensers are stationary horizontal pipes or trays, inside of which a horizontal mixer rotates, which has the shape of an auger (screw) and is the working element. The mixed bulk solid material takes on some liquid properties; even if the mixer doe s does not have helical surfaces, the material is transported along the axis of the horizontal device by leveling the height of the material layer over all zones of the device (like the spreading of liquid). The stirrer shaft is mounted using bearings at the ends of the pipe. If the pipe is long, the mixer is equipped with intermediate bearings inside the pipe to avoid sagging and jamming. Openings for supplying and discharging solid material, as well as for supplying and discharging gases, can be made in any part of the reactor, in the body itself and at the ends.

The productivity of screw feeders is on average 20 - 40 m3 / h. Due to such qualities as ease of design and maintenance, screw dispensers are used at enterprises in the chemical, construction, and food industries. Augers can be either with a flexible or rigid shaft. The presence of a flexible shaft allows you to transport material along the most optimal trajectory, obtaining high productivity and energy savings. Operating principle of a screw weigher (Fig. 2).

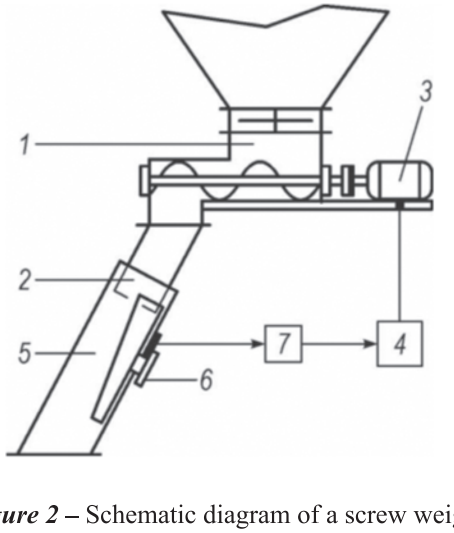

Figure 2 – Schematic diagram of a screw weigher

Four-screw feeder 1 takes bulk material from the supply hopper and directs it to the flow meter 2. The rotation speed of the screws can be smoothly changed using a controlled drive, which consists of an asynchronous gear motor 3 and a frequency converter 4. The material flow enters the flow meter and slides down the tray 5 attached to the strain gauge 6. The electrical signal from the strain gauge, proportional to the weight of the material on the tray, is sent to the microcontroller 7, which calculates the flow performance [2].

At the first stage, a block diagram of the linearized control object was drawn up, shown in Figure 3.

Figure 3 – Block diagram of the linearized contour of the control object

The open loop of the control object, tuned to the modular optimum, must have the following transfer function (1) [2]:

$$W_{ob} = W_{AM}(S) \cdot W_{FC}(S) \cdot W_{ST}(S) \quad (1)$$

where $W_{AM}(S)$ – transfer function of an asynchronous motor (*AM*), $W_{FC}(\mathbf{S})$ – transfer function of frequency converter (FC), $W_{SF}(S)$ – screw transmission transfer function.

Let us present the transfer function of the AM in the form of an aperiodic link of the 1st order (2), since the *AM* is an inertial link.

$$W_{AM}(S) = \frac{K_{AM}}{T_{AM}S+1} \quad (2)$$

where K_{AM} – asynchronous motor transmission ratio, T_{AM} – asynchronous motor time constant.

The numerical model has the following form:

$$\mathrm{W_{AM}(S)} = \frac{0{,}9}{0{,}07\mathrm{s} + 1}$$

where K_{AM}= 0,9, T_{AM} = 0,07sec

The transfer function of the FC is represented as an aperiodic link of the 1st order (3) since the FC is an inertial link.

$$W_{FC}(S) = \frac{K_{FC}}{T_{FC}S+1} \quad (3)$$

where K_{FC} – is the transmission coefficient of the frequency converter, T_{FC} – the time constant of the frequency converter,

Numerically, it can be represented as follows:

$$W_{FC}(S) = \frac{1}{0{,}5S + 1}$$

where K_{FC}= 1, T_{FC}= 0,5. The transfer function of the auger is equal to the transfer coefficient of the auger (4) since the auger is a non-inertia link.

$$W_{\mathrm{ST}}(S) = \mathrm{K}_{ST} \quad (4)$$

The productivity of the screw feeder is directly proportional to the speed of rotation of the screw, and the coefficient of the screw feeder is the coefficient of proportionality between the speed and the accumulation of mass in the hopper, which can be calculated by the formula (5):

$$К_{ST} = \frac{S}{D} \cdot R^3 \cdot \varphi_n \cdot \gamma_0 \qquad (5)$$

where S = 32 mm – screw pitch; d = 22 mm – shaft diameter; D = 38 mm – the outer diameter of the screw; R = 1,9 – screw radius; n = 149 r/min – rotational speed; φ_n – productivity factor; γ_0 – bulk volumetric mass of the material [2].

The direction of the screw is horizontal, as shown in Figure 4.

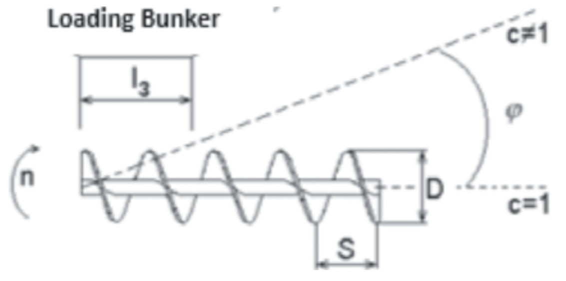

Figure 4 – Screw feeder parameters

The mathematical model has the form (6):

$$К_{ST} = \frac{3.2 \cdot 10^{-2} \cdot (1.9 \cdot 10^{-2})^3 \cdot 0.724 \cdot 550}{3.8 \cdot 10^{-2}} = 0.0023$$

Now we get the transfer function of the object in the form (6):

$$W_{ob} = \frac{K_{AM}}{T_{AM}S+1} \cdot \frac{K_{FC}}{T_{FC}S+1} = \frac{K_{AM} \cdot K_{FC}}{(T_{AM}S+1) \cdot (T_{AM}S+1)} = \frac{K_{AM} \cdot K_{FC}}{(T_{AM}T_{FC}S^2 + T_{AM}S + T_{FC}S + 1)} \qquad (6)$$

where $m_{зв}$ – component weight, m – actual measured mass of bulk material.

A simulation model of the linearized contour of the control object, developed in the Vissim 5.0 environment, is presented in Figure 5.

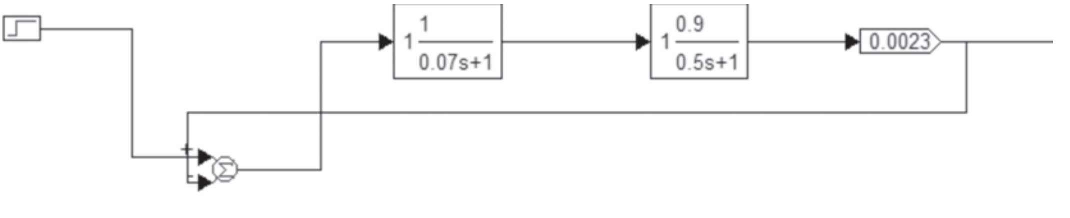

Figure 5 – Simulation model of the control object

By entering the obtained data into the program, we obtained the acceleration curve of the screw dozer as a control object (Figure 6).

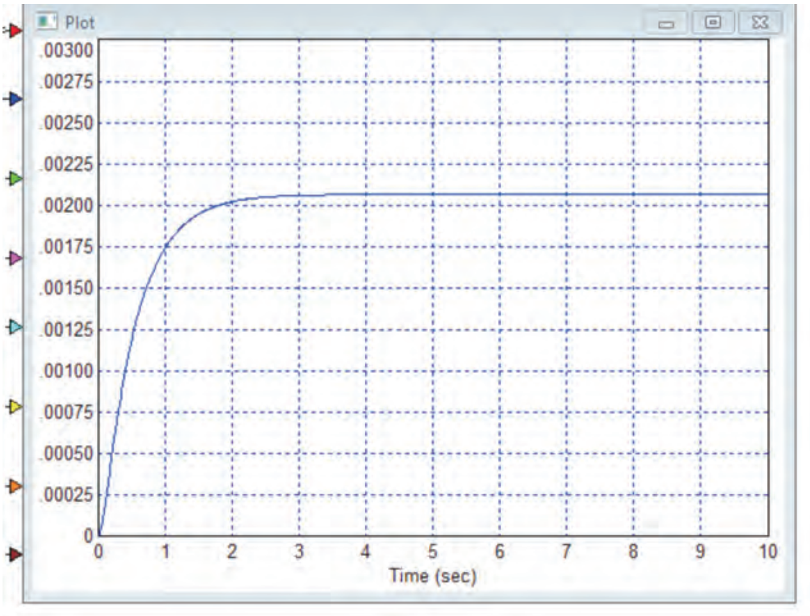

Figure 6 – Transient dosing process of the linearized contour of the control object

Results and discussions. An analysis of the quality of medicines for the treatment, prevention and diagnosis of diseases was carried out. An automatic screw device for dosing bulk materials, the principle of its operation is considered, and a mathematical model is developed. A block diagram of the dosing device as a control object has been drawn up. The control object is described by transfer functions in general and numerical form. A simulation model of the dosing device was developed in the Vissim 5.0 program. The acceleration curve of the object controlling the bulk materials dosing process was obtained.

Conclusion. As a result of the research, the following scientific and practical results were obtained. The main laws of the dosing process have been identified, which make it possible to draw up a physical and mathematical description of the object. The most progressive solutions aimed at increasing dosing efficiency are considered. The need for automatic flow control is substantiated.

The functional diagram of the automatic control system for the dosing process of bulk materials is formalized, a mathematical model of the screw dozer as a control object is obtained, and a structural diagram of the screw dozer is formed considering the real elements.

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КЛИНИКАЛЫҚ-ГЕМАТОЛОГИЯЛЫҚ СИНДРОМДАРДА ҚОЛДАНЫЛАТЫН ДӘРІЛІК ЗАТТАРДЫҢ ҚҰРҒАҚ СУСЫМАЛЫ МАТЕРИАЛДАРЫН МӨЛШЕРЛЕУ ЖҮЙЕСІНІҢ МАТЕМАТИКАЛЫҚ ҚАМТАМАСЫЗ ЕТУ

Қазіргі жағдайда қажетті дәрілік заттардың сапасы сусымалы материалдардың әр компонентінің құрамына және түпкілікті өнім рецептін қажетті дәлдікпен қатаң орындауға қойылатын жоғары талаптармен анықталады. Шығарылатын өнімнің сапасының міндетті шарты ретінде автоматтандыру деңгейін арттыру, өндіріс қауіпсіздігі мен персоналдың қолайлы еңбек жағдайларын қамтамасыз ету арқылы, жабдықтың пайдалану сенімділігін қамтамасыз етуді қарастырамыз. Дәрі-дәрмектерді дайындаудың өндірістік процесінде аз жабдықтарды қолдану және тасымалдау желілерін қысқарту арқылы энергияны тұтынуды азайту міндетін қояды. Мақалада дәрілік заттарды зерттеудің өзектілігі мен жіктелуі келтірілген. Фармацевтикалық өнеркәсіпке арналған шнекті салмақ диспенсерінің басқару объектісі ретінде жұмыс істеу принципі сипатталған. Фармацевтика өнеркәсібінің сусымалы материалдарын мөлшерлеу үшін бұрандалы құрылғының математикалық моделі жасалған.

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МАТЕМАТИЧЕСКОЕ ОБЕСПЕЧЕНИЕ СИСТЕМЫ ДОЗИРОВАНИЯ СУХИХ СЫПУЧИХ МАТЕРИАЛОВ ЛЕКАРСТВЕННЫХ СРЕДСТВ, ПРИМЕНЯЕМЫХ ПРИ КЛИНИКО-ГЕМАТОЛОГИЧЕСКИХ СИНДРОМАХ

Необходимое в современных условиях качество лекарственных средств определяет высокие требования к составу каждого компонента сыпучих материалов и неукоснительному выполнению рецепта конечного продукта с требуемой точностью. Обязательным условием качества выпускаемой продукции является эксплуатационная надежность оборудования с повышением уровня автоматизации и обеспечением безопасности производства и комфортных условий труда персонала. Приготовление лекарственных средств ставит задачу организовать процесс производства с меньшим количеством единиц оборудования, меньшей протяженностью транспортных линий и, соответственно, снижение энергопотребления. В статье приведена актуальность изучения и классификация лекарственных средств. Описан принцип действия шнекового весового дозатора для фармацевтической промышленности как объекта управления. Разработана математическая модель шнекового устройства для дозирования сыпучих материалов фармацевтической промышленности.

***Ключевые слова**: фармацевтическая промышленность, лекарственные средства, таблетки, шнековый питатель, процесс дозирования, объект управления, расходный бункер, расходомер, тензодатчик, клинико-гематологический синдром.*