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Technological Aspects of Development of A New Drug In Tablets Called «Lavaflam» And Its Pharmacoeconomic Evaluation.

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ABSTRACT

Hepatobiliary system diseases are actual medical and social problem in the world. Important issue is the development of a new complex of herbal medicine and its pharmacoeconomic study. Development of the technological scheme of the new drug in tablets called «Lavaflam»; analysis of the Ukraine pharmaceutical market of the analogues of «Lavaflam»; determination of socioeconomic accessibility of medicine called «Lavaflam» and its analogs, pharmacoeconomic advantages of «Lavaflam» compared with its analogs. The material of the study was dry concentrate of *Helichrysum arenarium* (Flamin) and *Lavender oil*; Ukraine pharmaceutical market of the drugs for the treatment of hepatobiliary system diseases; average retail price data of medicines published in the weekly journal «Pharmacy» in Ukraine in February, 2017; the average salary in Ukraine. Methods: average daily adult dose of the drugs included in the study was calculated as the average manufacturer recommended daily dose for adults (AMRDDA); calculation of socioeconomic coefficients of accessibility of included in the study drugs: solvency adequacy ratio (Ca.s.); cost minimization analysis, NNT-coefficient. The technological scheme of the drug in tablets «Lavaflam» was developed for treatment of hepatobiliary system diseases. 1 tablet of «Lavaflam» contains 50 mg of Flamin and 20 mg of Lavender oil. In the Ukraine pharmaceutical market an analog of «Lavaflam» was found. This medicine is called «Flamin-Zdorovia». The cost of AMRDDA of «Lavaflam» was 5.91 UAH, of «Flamin-Zdorovia» – 7.42 UAH. When studying the socioeconomic accessibility coefficients it was found: «Lavaflam» is more accessible for the population by 26% compared to «Flamin-Zdorovia». Using the drug «Lavaflam» can reduce cost of pharmacotherapy by 25%. A new complex herbal drug in tablets called «Lavaflam» which contains combination of dry concentrate of *Helichrysum arenarium* (Flamin) and *Lavender oil* was developed. It was established that «Lavaflam» had socioeconomic and pharmacoeconomic advantages compared to its analog called «Flamin-Zdorovia».

Keywords: technological scheme, a new complex herbal drug, hepatobiliary system diseases, pharmaceutical market, socioeconomic accessibility, pharmaco-economic advantages.

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INTRODUCTION

Hepatobiliary system diseases are considerable medical and social problem at the present time, the diseases affect people of all countries and apply to all social strata and to all age groups. The prevalence of these diseases is 45%, among young people is 43% [1]. An important role is played by medicinal herbs in the treatment of hepatobiliary system diseases. They have complex anti-inflammatory, choloretic, antiseptic, antispasmodic, antibacterial effects. They improve detoxification function of the liver, normalize of gallbladder tone. These effects are due to the presence of herbal composition of biologically active substances such as polyphenols, flavonoids, saponins, polysaccharides, essential oils and microelements [1-3]. These drugs are based on the following components: *Cynara scolymus*, *Silybum marianum*, *Helichrysum arenarium*. Also, previous studies [3] have shown that the addition of Lavender oil to the medicines will expand the spectrum of pharmacological action by increasing the peristalsis of the biliary tract, increased cholagogue activity, improve the function of liver detoxification, antimicrobial and anti-inflammatory actions. That is why we developed the drug as a combination of the following substances: dry concentrate of *Helichrysum arenarium* (Flamin) and *Lavender oil*. This drug allows extending the spectrum of action in the treatment of hepatobiliary system diseases, increasing the activity of the ingredients due to synergism and improved tolerability. In the limited financing of the Health Care System it is necessary to use pharmacoeconomic justified drugs to optimize drug provision [4,5].

The **purpose** of the research was development of the technological scheme of a new drug in tablets called «Lavaflam» and pharmacoeconomic justification of it.

OBJECTIVES

Development of the technological scheme of the new drug in tablets called «Lavaflam»; analysis of the Ukraine pharmaceutical market of the analogues of «Lavaflam»; determination of socioeconomic accessibility of «Lavaflam» and its analogs, pharmacoeconomic advantages of «Lavaflam» in comparison with its analogs.

MATERIALS AND METHODS

The material of the study was dry concentrate of *Helichrysum arenarium* (Flamin) and *Lavender oil*; pharmaceutical market of the drugs for the treatment of hepatobiliary system diseases; average retail price data of medicines published in the weekly journal «Pharmacy» in Ukraine in February, 2017; the average salary in Ukraine. Methods: average daily adult dose of the drugs included in the study was calculated as the average manufacturer recommended daily dose for adults; calculation of socioeconomic coefficients of accessibility of included in the study drugs: solvency adequacy ratio (Ca.s.); cost minimization analysis, NNT-coefficient.

Calculation of cost of the average daily dose for adults* in UAH by the formula [6]:

$$C = P / T \times D, \text{ where}$$

C – cost of average daily doses for adults, UAH;

P – cost of medicine packing of investigated drugs, UAH;

T – number of tablets in medicine packaging, units;

D – average daily dose for adults.

* – in this investigation the average daily doses for adults is the average manufacturer recommended daily dose for adults.

Research of socioeconomic coefficients of accessibility was carried out by solvency adequacy ratio (Ca.s.) for the population. This solvency adequacy ratio characterizes the relationship between the price of drug and solvency for the population, calculated by the formula [6, 7]:

$$Ca.s. = \frac{\bar{P}}{W_{a.w.}} \times 100\%,$$

Where,

P – weighted average price of average daily doses for adults* in the Ukraine pharmaceutical market for during the study period;

W_{a.w.} – average salary in the population for during the study period.

Between solvency adequacy ratio Ca.s. and price accessibility of drug there is feedback: the increasing Ca.s. reduces accessibility for consumers. To select the least costly drug the cost-minimization analysis was performed in the context of cost of AMRDDA of the drugs included to the study: «Lavaflam» and its analog «Flamin-Zdorovia» (in case of equal efficiency). The available savings in financial resources were calculated when using each test drug by the formula [6, 7, 8]:

$$CMA = DC_1 - DC_2, \text{ where}$$

CMA – the difference in the cost of compared drugs, UAH

DC₁ – direct costs when using cheaper drugs, UAH

DC₂ – direct costs when using expensive drugs, UAH

NNT-coefficient (number need to treat) shows the ratio of the number of patients receiving expensive drugs to the number of patients receiving cheaper drugs, and it was calculated by the formula [6, 7, 8]:

$$NNT = C_1 / C_2, \text{ where}$$

NNT-coefficient of the number of patients receiving expensive drugs to the number of patients receiving cheaper drugs

C₁ – direct costs when using expensive drugs, UAH

C₂ – direct costs when using cheaper drugs, UAH

RESULTS AND DISCUSSION

In the pharmaceutical market of Ukraine there are the groups of the drugs for treatment of hepatobiliary system diseases according ATC-classification:

1. A05A – drugs used for biliary pathology (Ursodesoxycholic acid, **Allocholum**, **Artihol**, Hepabene, Cholosasum, Chophytol, Species cholagogae, Helichrysum arenarium, Flamin);
2. A05B – drugs used for liver diseases, lipotropic substances (Arginine, Silymarin, Carsil);
3. A05C – drugs used for biliary pathology in combination with lipotropic substances (**Hepadif**, **Eslidine**).

The new original drug in tablets called «Lavaflam» which includes a combination of herbal substances Flamin and Lavender oil was developed (Table 1).

Table 1: Composition of the tablets «Lavaflam»

| Composition | g | % |
|--------------------------|---------------|------------|
| Lavender oil | 0.02 | 3.34 |
| Beta-cyclodextrin | 0.27 | 45.0 |
| Flamin | 0.05 | 8.33 |
| Mannitol | 0.20 | 3.33 |
| Potato starch | 0.022 | 3.67 |
| Sodium croscarmellose | 0.03 | 5.00 |
| Polyethylene glycol 6000 | 0.002 | 0.33 |
| Magnesium stearate | 0.006 | 1.00 |
| Total | 0.6000 | 100 |

The technological scheme of production of the drug in tablets «Lavaflam» shows the use of active substances and excipients at each stage of the technological process and graphically controlled parameters in

the manufacturing process (Figure 1)

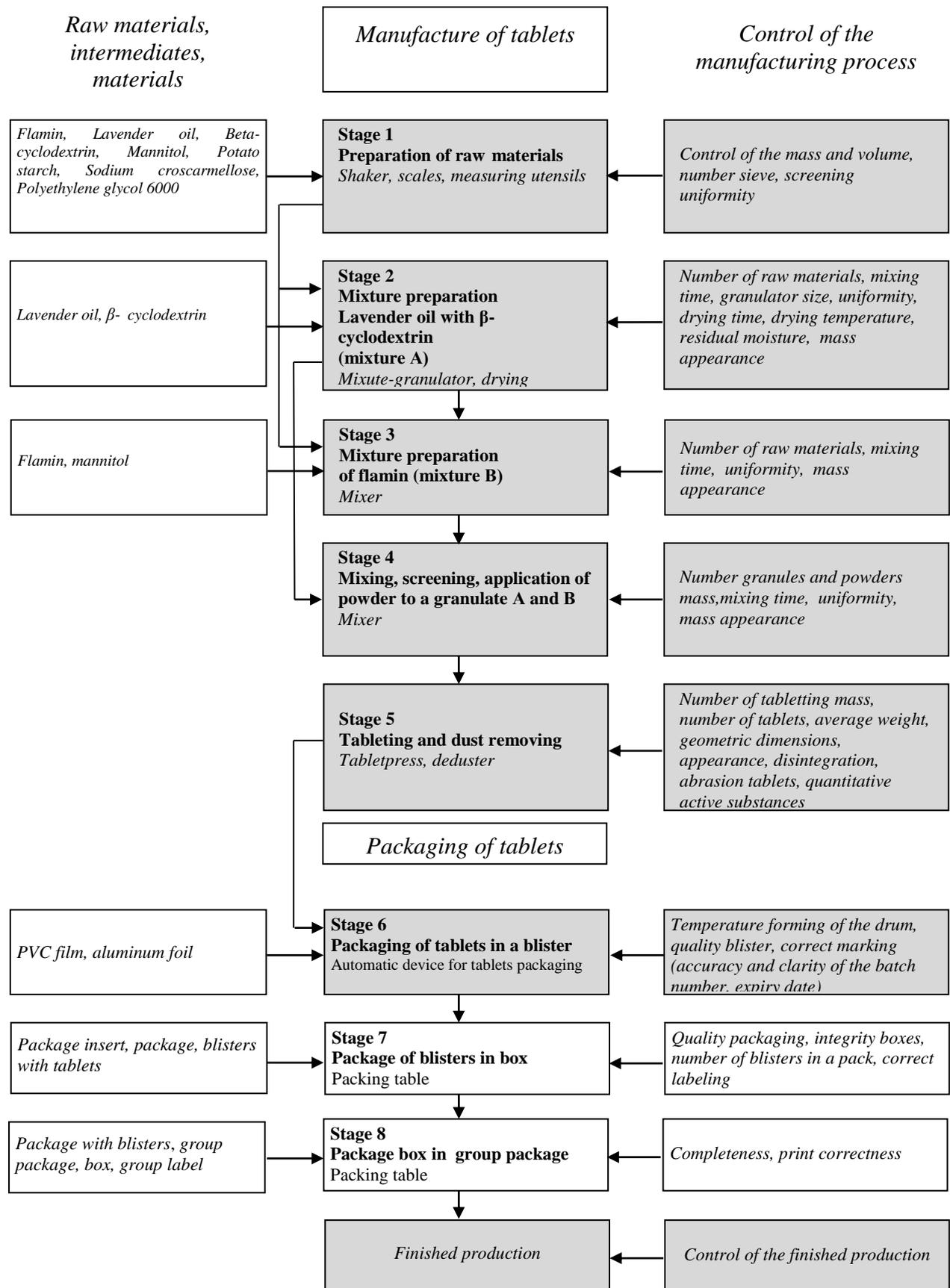


Figure 1: Technological scheme of production of the drug in tablets called «Lavaflam».

It was necessary to establish a standardized unit of average daily dose of the drugs for comparison of the cost of drugs for treatment of hepatobiliary system diseases. In the modern pharmaceutical market closest in composition to «Lavaflam» is the drug under the name «Flamin-Zdorovia» (Pharmaceutical company «Zdorovia», Kharkov, Ukraine), 1 tablet of which contains 50 mg of Flamin. That is why the drug called «Flamin-Zdorovia» was chosen as a reference medicine for carry out the pharmacoeconomic research. Average daily doses were calculated for both drugs as average manufacturer recommended daily dose for adults (AMRDDA). This is 1 tablet 3 times per day. Developed medical form of «Lavaflam» is tablets 0.6 grams №50 and retail cost of 50 tablets is 98.59 UAH (Table 2). No drugs with dry concentrate of *Helichrysum arenarium* (Flamin) and *Lavender oil* on the modern pharmaceutical market of Ukraine (Table 2).

Table 2: Average manufacturer recommended daily dose for adults (AMRDDA) of research drugs

| № | Drugs characteristic | Comparable drugs | |
|----|--|------------------|-----------------|
| | | Lavaflam | Flamin-Zdorovia |
| 1. | Retail cost of 1 medicinal packaging, UAH | 98.50 | 74.17 |
| 2. | Number of tablets in medicinal packing, tablets | 50 | 30 |
| 3. | Average manufacturer recommended daily dose for adults (AMRDDA), tablets | 3 | 3 |
| 4. | Cost of AMRDDA, UAH | 5.91 | 7.42 |

It has been found that the cost of AMRDDA of «Lavaflam» is 5.91 UAH, of «Flamin-Zdorovia» – 7.42 UAH.

According to the State Statistics Service of Ukraine the average salary in Ukraine in February, 2017 were 6108 UAH [9]. It has been found that the course of treatment of 1 patient for 1 month for «Lavaflam» is 177.30 UAH, for «Flamin-Zdorovia» – 222.60 UAH.

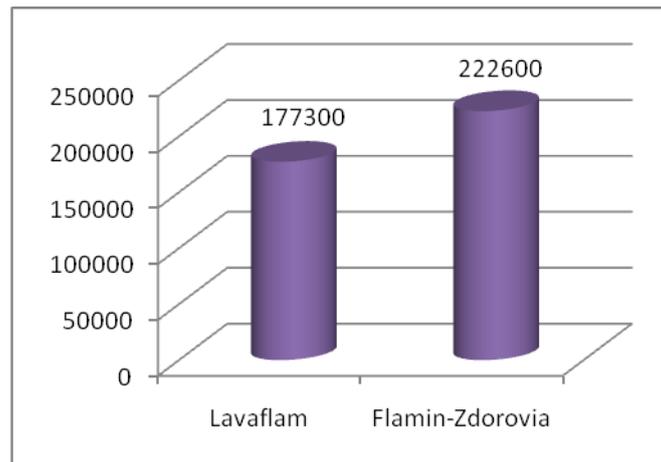
It was calculated that Ca.s. for «Lavaflam» was 2.9, for «Flamin-Zdorovia» – 3.64; therefore «Lavaflam» is more accessible for the population by 26% in comparison with «Flamin-Zdorovia».

The obtained results were the basis for further pharmacoeconomic research by cost minimization analysis and calculation of NNT-coefficient. Choice of pharmacoeconomic justified drugs is a part of the rational use of limited financial resources in Health Care System. Application of the obtained results of pharmacoeconomic researches in clinical practice promotes to optimization and efficiency of pharmaceutical care to the population [6-8].

According to the methodology of cost minimization analysis it has been found that the savings of financial resources were 1.51 UAH per 1 patient per day when using drug «Lavaflam» in comparison with drug «Flamin-Zdorovia»:

$$CMA = DC_1 - DC_2 = 7.42 - 5.91 = 1.51 \text{ UAH}$$

The use of the drug «Lavaflam» for treatment 1000 patients will require 5910 UAH daily, and 177300 UAH monthly. The use of the drug «Flamin-Zdorovia» – 7420 UAH daily and 222 600 UAH monthly (Picture 1).



Picture 1: The difference in value between «Lavaflam» and «Flamin-Zdorovia».

Savings of financial resources can be 1510 UAH per day and 45300 UAH per month for 1000 patients receiving «Lavaflam».

NNT-coefficient was calculated taking into account the cost of average manufacturer recommended daily dose for adults for 1 patient using the formula:

$$\text{NNT} = C_1 / C_2 = 7.42 / 5.91 = 1.25$$

So, it has been found that the cost of treatment for 1000 patients with cheaper drug called «Lavaflam» can provide treatment for only 750 patients receiving expensive drug called «Flamin-Zdorovia» per day.

Thus, the use of «Lavaflam» in clinical practice allows reducing the cost of pharmacotherapy by 25%, what is very important for the family or state budget.

CONCLUSIONS

1. It was developed the technological scheme of production of the drug in tablets called «Lavaflam» that contains in 1 tablet 50 mg of *Helichrysum arenarium* (Flamin) and 20 mg of *Lavender oil* for treatment of hepatobiliary system diseases.
2. The analog of «Lavaflam» was found in the pharmaceutical market of Ukraine: it is a drug called «Flamin-Zdorovia»; the cost of average manufacturer recommended daily dose for adults of «Lavaflam» was 5.91 UAH, of «Flamin-Zdorovia» – 7.42 UAH.
3. The research showed that the drug called «Lavaflam» is more accessible for the population by 26% in comparison with the drug called «Flamin-Zdorovia».
4. Using drug «Lavaflam» can reduce cost of pharmacotherapy by 25%.

PROSPECTS FOR FURTHER RESEARCH: Based on the obtained data it will be possible to identify cost-effectiveness and cost-utility advantages of investigated drugs.

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