WITH REDUCED EMISSIONS OF HARMFUL PRODUCTS AND REDUCED COSTS IN THE PRODUCTION OF CLAVULANIC ACID (SODIUM CLAVULANATE)

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Introduction. Clavulanic acid has a β -lactam structure similar to penicillins, and is capable of inactivating β -lactamase enzymes inherent in microorganisms resistant to penicillins and cephalosporins.

In particular, it has a pronounced activity in regard to clinically important plasmid β -lactamases, which are often responsible for the emergence of cross-resistance to antibiotics.

Peak plasma concentration is reached 1 hour after oral administration of the antibacterial agent. This is one of the benefits of antibacterial agents with clavulanic acid. Today, clavulanic acid is used with amoxicillin (Augmentin, Amoxiclav, Amosil, Baktoclav).

In the future, it is possible to create combinations with cephalosporins, which will significantly increase the activity of the latter and reduce their therapeutic doses. so antibacterial drugs with clavulanic acid may be used for pregnant women.

Synthesis of clavulanic acid occurs in two stages:

1. Creation of a bacterial broth:

The primary substrate based on high-density triglycerides of glycerin and glucose from Streptomyces clavuligerus is kept in an incubator at a temperature of 20-40 ° C, followed by microfiltration. When fermentation is monitored the level of phosphates.

2. Extraction from a bacterial broth:

There are 5 main ways to get clavulanic acid. purification of broth by microfiltration, chromatographic membrane, vulgarisation, separation and deposition. The pharmaceutically acceptable salts are obtained by chromatographic separation, vulgarisation, microfiltration and isolation. Industrial synthesis of Clavulanic acid is carried out in two ways: selectivity with tertbutylamine (EP-A-0026044, EP-A-0562583, EP-A-0594099, WO-94/22873) and vinification using Lithium aluminate in the range of pH 6.3 - 6.7 (GB 1543563). Both methods of extraction from the bacterial broth give toxic by-products.

Aim. Reducing the environmental impact of recycling tert-butylamine in the cyclic phase in the production of clavulanic acid.

Materials and methods. Cyclic application production, re-purification and rectification of tertbutylamine, the restoration of aluminum salts to industrial production, the creation of closed pharmaceutical and chemical combines.

Results and discussion. The possibility of solving such problems may be the creation of closed cycles of purification and re-use tret-butylamine in the pharmaceutical industry, which will reduce the costs and risks associated with the recycling and transportation of caustic substances.

Tret-butylamine itself is a substance (CAS-No 75-64-9) of category 2 for REACH-volatile poisons, explosive substances. 1 kg of finished substance consumes an average of 8 liters of tert-butyamine.

This substance is not soluble in water and alcohols and has a low toxicity: 2000 mg in rat units.

Regarding lithium and aluminum salts – cause a sharp change in pH soil, causing constipation, digestive disorders, aluminum, disturbances of the functioning of the central nervous system, suppression of hematopoiesis. Lithium aluminate is used to create galvanic elements as well as electronic sensors. Also in the alloyed state with graphite is a powerful piezoelectric element that allows it to be widely used in industry. The recovery of Lithium aluminate acid occurs in 3 stages. For such a conversion, there is a need for NaOH, BaCO₃ purified and a muffle furnace.

- 1) $Al_2(SO_4)_3 + 6NaOH \rightarrow 3Na_2SO_4 + 2Al(OH)_3$ with the subsequent "Bayer" process.
- 2) $\text{Li}_2\text{SO}_4 + \text{BaCO}_3 \rightarrow \text{BaSO}_4 \downarrow + \text{Li}_2\text{CO}_3$ followed by crystallization of the solution
- 3) $\text{Li}_2\text{CO}_3 + 2\text{Al} (\text{OH})_3 \rightarrow 2\text{LiAlO}_2 + \text{CO}_2^{\dagger} + \text{H}_2\text{O} \text{ sintering.}$

Conclusion. By introducing a system of cycling and correct use of environmental management systems, it is possible to achieve:

1. Reduction in the costs of transport and disposal of chemicals.

2. Reduce the risks of storing, transporting and packaging toxins.

3. To reduce the life time of hazardous elements of production to save on the synthesis of clavulanic acid.

4. Increased spectrum of potential antibacterial drugs use.

5. Subsequently, the process of regeneration of lithium aluminum mattes can be improved both economically and environmentally (replacement of carbonate barium with calcium carbonate followed by precipitation of oxalate).

PROSPECTS FOR THE DEVELOPMENT OF PROLONGED ACTION SOLID DOSAGE FORMS BASED ON BORAGE OIL AND DRY EXTRACT OF BLACK POPLAR BUDS FOR THE TREATMENT OF CYSTITIS

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Introduction. Cystitis is one of the quite frequent nosological forms of infectious and inflammatory diseases of the urinary tract, the main morphological substrate of which is inflammation in the epithelium and stroma of the bladder wall. In general, urinary tract infections (UTI), including cystitis, are most commonly diagnosed in women. According to statistics, about 50% of women had a history of at least one episode of UTI during their lifetime, and almost one third of all women had at least one case before the age of 24.

Bacterial infection is the most common cause of chronic cystitis. According to the analysis of literature data, in 20-30% of women there is a relapse within 3-4 months after a primary urinary tract infection. About 10–20% of them suffer from recurrent cystitis throughout their lives, which significantly affects the quality of life and has a great social importance in general.

According to the results of marketing research, it has been found that in the treatment of cystitis in 80% of cases antibacterial drugs are used: fluoroquinolones, nitrofurans, cephalosporins, which have a number of side effects. The use of herbal remedies can help reduce them while maintaining the necessary therapeutic efficacy.

Aim. To work out new medicinal preparation on basis of borage grass – Borago officinalis and black poplar buds –Populus nigra.

Materials and methods. Borage grass – Borago officinalis and black poplar buds –Populus nigra; physical and chemical, physical, technological methods.

Results and discussion. A promising direction in the treatment of cystitis is the use of borage grass – Borago officinalis and black poplar buds –Populus nigra. According to the literature, both plants contain flavonoids, essential oils, phenolic compounds, tannins. Borage herb is a pharmacopoeial plant of many European countries, provides anti-inflammatory and diuretic action.Black poplar buds are used in folk medicine as a diuretic, anti-toxic, analgesic, antiseptic, bactericidal agent. They promote granulation, epithelialization and regeneration of the inflamed epithelium of the urethra.Preparations of black poplar buds are widely used in the treatment of urinary diseases (nephritis, urethritis, cystitis, prostatitis). The use of a combination of these plant components will enhance their therapeutic effect.

According to the literature, solid dosage forms that provide accurate dosing, modified release of active pharmaceutical ingredients, have optimum consumer properties are widely popular among the population. To reduce the frequency of taking the drug and to improve its compliance, it is rational to create a solid dosage form in the form of prolonged-action tablets.

Conclusions. Thus, the development of drugs for the treatment of inflammatory processes of the bladder in the form of solid dosage forms of prolonged action based on plant materials will reduce the risk of side effects and improve patient compliance. Also, the use of drugs based on borage grass and black poplar buds will provide effective therapy with minimal side effects.