

DEVELOPMENT OF TECHNOLOGY OF QUANTITATIVE ESTIMATION OF PARACETAMOL IN FORMULA OF SUPPOSITORIES WITH ANTIPYRETIC AND IMMUNOMODULATORY EFFECTS

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Temperature rise and febricity development in acute respiratory diseases (ARD) is one of protective reactions of organism, however when temperature rises up to above 38,5°C, the World's Health Organization recommends to apply antipyretic medicines. This group of medicines is the most requested in pediatric practice that caused by a danger of complications development. The rectal application of drugs is the most perspective due to a high drugs bioavailability which is close to injections bioavailability.

The researches of pharmaceutical markets of Kazakhstan and Ukraine have shown that there are not enough medicines with antipyretic and immunomodulatory effects which are intended for use in pediatric practice.

At the Department of Industrial Technology of Drugs, the medicine is being created in form of rectal suppository with antipyretic and immunomodulatory effects for practical use in pediatric. It is supposed to create suppositories on the lipophilic basis (hard fat) with paracetamol (antipyretic component) and herbal extract «Mix-factor» which is glycoprotein oligopeptide composite and has an immunomodulatory effect.

An important stage in drug design is creation of analytical regulative documentation (ARD) for its quality control within manufacturing. One of the most spread methods of ready-made drugs' analysis is an adsorption spectrophotometry.

The aim of our research was development of technology of paracetamol quantitation in lipophilic-based suppositories which contain paracetamol and «Mix-factor». In order to reach the goal stated, it was needed to study spectra of paracetamol absorption in different dissolvents and to find the optimal conditions for quantitative estimation, to define frontiers of subjection to the Beer-Lambert-Bouguer law, to develop technology of sample processing and to characterize the quantitation statistically.

In the ultraviolet spectrum of absorption of water solution of paracetamol standard sample (SS) (Fig.1) a wide intensive line with the maximum in 244 nm is

evident. In the range of 270 nm is a bend of absorption line, which is correspond with the third maximum of absorption of the line of benzene type. The dissolvent substitution to the 0,1 M solution of HCl does not lead to any changes in spectrum parameters, that testifies lack of phenylic hydroxyl dissociation in water solution. Regarding the 0,1 M NaOH solution, the hyperchromic effect and bathochromic shift of the absorption band to 258 nm can be observed. This is connected with the positive inductive effect of phenolate-ion. The calibrating diagram (Fig.2); (Table 1) is ruled in a rage from 0,4 to 2,0*10⁻³%. Specific indicator of absorption $A_{1sm}^{1\%}$ equals 717±4.

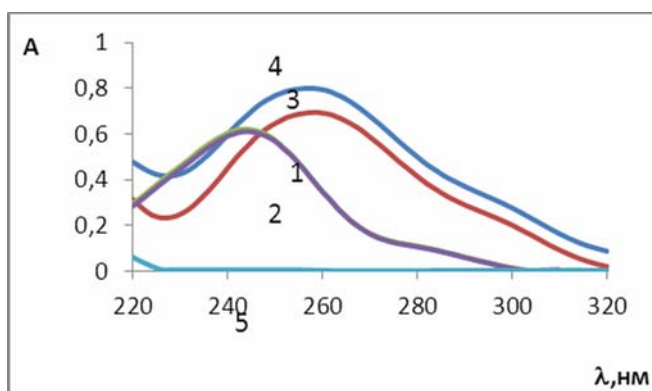


Fig.1

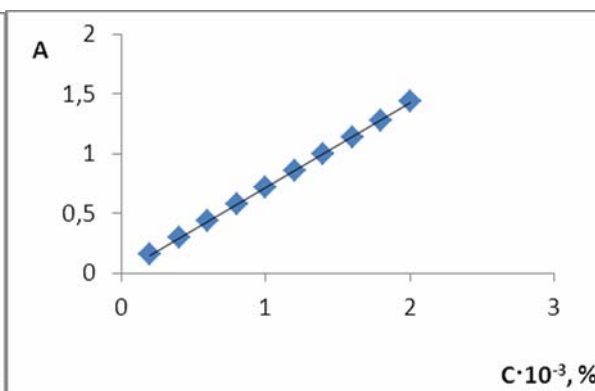


Fig.2

Table 1.

$C \cdot 10^{-3}, \%$	0,2	0,4	0,6	0,8	1,0	1,2	1,4	1,6	1,8	2,0
A	0,155	0,293	0,433	0,573	0,712	0,852	0,997	1,138	1,280	1,438
$A_{1sm}^{1\%}$	775	732	721	716	712	711	711	711	711	719

In case of research, the methodic of sample processing was developed which is consists of paracetamol extraction from suppository by 50% water solution. The absorption spectrum of the preparation's solution does not differ from SS spectrum. The placebo spectrum created analogically reveals the lack of influence of auxiliaries and «Mix-factor» to the medicine spectrum. Statistical characteristic of technology of paracetamol quantitation in suppositories, created by model samples, has shown ability of quantitative measurement of reactant according to this technology. The relative indefiniteness of a certain definition is not higher than 1,6%. The technology created is to be used for creation of Superior pharmacopoeial article based on suppository with paracetamol and «Mix-factor».