International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 04, 2020
ISSN: 1475-7192

PRE-CLINICAL STUDY OF EXPECTORANT PROPERTIES OF "AMBROL" TABLETS

Z.Kh. Abdijalilova[1*], Kh.M. Yunusova[2], N.B. Ilkhamova[3]

Abstract---*Ambrol is used in conditions where there is a lot of viscous secretion or mucus in the airways. Ambrol is intended for the treatment of acute and chronic infectious respiratory diseases associated with impaired secretion. It stimulates the formation of low viscosity tracheobronchial secretion due to a change in the structure of sputum mucopolysaccharides and increases the secretion of glycoproteins (mucokinetic effect). It stimulates the motor activity of cilia of the ciliated epithelium and improves mucociliary transport, increases the synthesis, secretion of surfactant and blocks its decay. We aimed to study the bioequivalence of the drug "Ambrol", to study acute toxicity and specific activity.*

Key words---*biopharmaceutical properties, pharmacological properties, acute toxicity, specificity, bioequivalence, in vivo.*

I. INTRODUCTION

The development of new drugs is complex, expensive and quite time-consuming in the process, including preclinical trials, the use of new drugs, clinical trials and the approval of generic dosage forms.

The question of whether a new drug improves treatment of upper respiratory tract inflammation in patients can ultimately be resolved only in clinical trials. However, due to ethical, medical, and economic limitations and the number of patients eligible for clinical trials, most studies should be conducted in experimental systems. For many decades, experimental therapy researchers have developed proven, reliable in vitro and in vivo methods to evaluate the response to disease treatment.

Ambroxol has a secretomotor, secretolytic and expectorant effect: it stimulates serous cells of the glands of the bronchial mucosa, increases the content of the mucous secretion and the release of surface-active substance (surfactant) in the alveoli and bronchi; normalizes the disturbed ratio of serous and mucous components of sputum [8, 9].

This report presents the results of an in vivo study of the pharmacological properties of the recommended expectorant properties of Ambrol tablets.

Objective: to study the bioequivalence of the drug "Ambrol - tablets." The study of acute toxicity, specific activity.

Object of research: the drug "Ambrol", manufactured by LLC "SAMO" Uzbekistan, and the comparison drug "Ambronol", manufactured by Marion Biotech Pvt. Ltd. India.

[1]***PhD at the Department of Industrial Technology of Medicines, Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan (zilola.pharm@mail.ru)*
[2]Doctor of pharmaceutical sciences, professor, Department of Industrial Technology of Medicines, Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan
[3]Teaching assistant, doctor of pharmaceutical sciences, chief technologist at the "SAMO" LLC, Tashkent, Uzbekistan

DOI: 10.37200/IJPR/V24I4/PR201345
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

II. METHODS

The study of specific activity. Acute toxicity was studied by the generally accepted method described in the literature by a single administration of drugs with the determination of LD50 and toxicity class [1, 7].

Species and number of animals: the experiment was carried out on white mice in the amount of 36 animals, weighing 19 - 21 g, quarantined for 14 days. Preparation of aqueous solutions: in order to study acute toxicity and determine LD50, a 3% aqueous suspension (1 tab+1 ml of H_2O) was prepared from the compared preparations.

The study of mucolytic activity was carried out on guinea pigs, weighing 270 - 320 g in the amount of 18 goals. Animals were anesthetized under urethane [5]. A cannula was inserted into the trachea of the animal, after which the animal was placed upside down at an angle of 45 °. Sputum from the cannula was collected by suction using a syringe for 2 hours after drug administration.

The experiment

an experiment to study the acute toxicity of the compared drugs was carried out in two series. In the first series of the experiment, white mice were divided into 3 groups of 6 animals each. The mice of each group were once intragastrically injected with a 3% aqueous suspension of the drug "Ambrol" - tablets, manufactured by LLC "SAMO" as follows:

Group 1 (6 mice) - per os in a dose of bOOmg / kg (0.4 ml);

Group 2 (6 mice) - per os in a dose of 900 mg / kg (0.6 ml);

Group 3 (6 mice) - per os at a dose of 1200 mg / kg (0.8 ml);

In the second series of the experiment, similarly to white mice, they were divided into 3 groups of 6 animals each. Mice of each group were once intragastrically injected with a 3% aqueous suspension of the drug "Ambronol", manufactured by Marion Biotech Pvt. Ltd. India as follows:

Group 1 (6 mice) - per os in a dose of 600 mg/kg (0.4 ml);

Group 2 (6 mice) - per os in a dose of 900 mg/kg (0.6 ml);

Group 3 (6 mice) - per os at a dose of 1200 mg/kg (0.8 ml);

III. OBSERVATION

On the first day of the experiment, animals were monitored hourly in the laboratory, while indicators of appearance were recorded (condition of the coat, mucous membranes, etc.); functional state (survival during the experiment, general condition, possible convulsions and death) and behavior. Then, every day, for 2 weeks under vivarium conditions, animals of all groups were monitored for the general condition and activity, behavioral characteristics, response to tactile, pain, sound and light stimuli, the frequency and depth of respiratory movements, the rhythm of heart contractions, and the condition of the hair and skin, the position of the tail, the number and consistency of fecal masses, the frequency of urination, changes in body weight and other indicators. All experimental animals were kept in the same conditions and on a common diet with free access to water and food [3, 4].

IV. Results of the study of acute toxicity

1. In the study of acute toxicity of the drug “Ambrol” - tablets, production of “SAMO” LLC received the following data:

Group 1 (dose 600 mg/kg): after administration of the drug during the day, the mice remained active, changes in behavior and functional state of visible changes were not observed. The condition of the coat and skin was normal without

DOI: 10.37200/IJPR/V24I4/PR201345
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

changes, they did not refuse food and water, and the death of mice was not observed. On the second day and in the subsequent period of observation of pathological changes in the behavior and physiological parameters of mice there were no changes. The use of water and feed was normal, and there was no lag in growth and development. The death of mice within 14 days was not.

Group 2 (dose 900 mg/kg): after administration of the drug during the day, the mice were active, no changes in behavior and functional state of visible changes were observed. The condition of the coat and skin was normal without changes, they did not refuse food and water, and the death of mice was not observed. On the second day and in the subsequent period of observation of pathological changes in the behavior and physiological parameters of mice there were no changes.

The use of water and feed was normal, and there was no lag in growth and development. The death of mice within 14 days was not.

Group 3 (dose 1200 mg/kg) after administration in mice observed short-term lethargy and inactivity, which passed through 30-40 minutes. After 1 hour, the mice returned to their previous state, active behavior, physical indicators did not deviate from the norm.

On the second day and during the entire observation period for 14 days, no changes were observed in the behavior and other physical indicators of mice, the mice eagerly consumed food and water, the reactions to light and sound stimuli remained normal, the coat and skin were clean, urination and feces normal, weight and growth of mice did not lag behind in development. The death of mice was not observed (Table 1).

Table 1. Determination of acute toxicity of Ambrol, LLC SAMO and production of Ambronol, Marion Biotech Pvt. Ltd. India

	Weight, g	**“Ambrol”, “SAMO” LLC**				**“Ambronol”, Marion Biotech Pvt.Ltd India**			
		Dose		**route of administration**	**number of dead mice**	**Dose**		**route of administration**	**number of dead mice**
		mg/kg	**ml**			**mg/kg**	**ml**		
	19-21	600	0,4	Per os	0/6	600	0,4	Per os	0/6
	19-21	900	0,6	Per os	0/6	900	0,6	Per os	0/6
	19-21	1200	0,8	Per os	0/6	1200	0,8	Per os	0/6
I-D50		>1200 mg / kg							

Similar data were obtained in the study of the acute toxicity of the drug AMBRONOL tablets manufactured by Marion Biotech Pvt. Ltd. India Since, according to the literature, the volume of fluid administered with a single intragastric administration is not more than 0.8 ml, the introduction of a larger dose of drugs was not possible. LD50 of Ambrol

DOI: 10.37200/IJPR/V24I4/PR201345
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

preparations manufactured by SAMO LLC, Uzbekistan and AMBRONOL tablets, produced by Marion Biotech Pvt. Ltd India, is> 1200 mg / kg.

According to the classification of toxicity of substances, drugs are low toxic [7].

Study of the specific activity

The study of mucolytic activity was carried out on guinea pigs, weighing 270 - 320 g in the amount of 18 goals. Animals were anesthetized under urethane [5]. A cannula was inserted into the trachea of the animal, after which the animal was placed upside down at an angle of 45°. Sputum from the cannula was collected by suction using a syringe for 2 hours after drug administration. .

Compared drugs were administered intragastrically as follows:

1. Group - control - purified water 1 ml per os;

2. The group - experimental - per os 30 mg/kg preparation “Ambrol” - tablets, manufactured by LLC "SAMO" Uzbekistan

3. The group - experimental - per os 30 mg/kg preparation “Ambronol” - tablets manufactured by Marion Biotech Pvt. Ltd. India

The data obtained were processed using the STATISTICA program [6].

The results of the study of specific activity

The results of studies on the mucolytic activity showed that after administration of drugs, sputum volume was expressed as a percentage of untreated control. The data obtained are presented in table 2.

Table 2. The study of mucolytic activity of Ambrol, LLC “SAMO”

Uzbekistan and AMBRONOL, Marion Biol			
Weight, g	**dose, mg/kg**	**Sputum volume**	**Sputum volume per 1 ml / 100 g**
Control group + purified water			
283,2 ± 14	0,12 ±0,01		0,04 ± 0,08
Ambrol manufactured by “SAMO” LLC, Uzbekistan			
290 ±7,1	30	0,22 ± 0,02 P<0,05	0,07 ± 0,07 P>0,5
AMBRONOL, manufactured by Marion Biotech Pvt. Ltd. India			

DOI: 10.37200/IJPR/V24I4/PR201345
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

288 ±8	30	0.23 ± 0.01 P<0,05	0.07 ± 0,08 P>0,5

As can be seen from the table, the volume of sputum in guinea pigs received

Ambrol, manufactured by SAMO LLC, Uzbekistan was increased by 75% compared with the control group, and in guinea pigs receiving

"AMBRONOL", manufactured by Marion Biotech Pvt. Ltd. India, the sputum volume was increased by 75%. That is, the compared preparations had an equivalent reliable mucolytic effect, which indicates their biological equivalence.

V. CONCLUSION

1. Thus, the data obtained show that the compared drug "Ambrol – tablets" (p. 011018, SG 10/2020), manufactured by LLC "SAMO", Uzbekistan in comparison with a drug analogous to "Ambronol" (p. ABT1605 of this year 07/2020 No. and date of registration DV / X 03934/01/20; 03934/01/21), manufactured by Marion Biotech Pvt. Ltd. India, in terms of acute toxicity were biologically equivalent.

2. As shown by the data, the compared drugs "Ambrol - tablets" (p. 011018, SG 10/2020), manufactured by LLC "SAMO", Uzbekistan in comparison with the drug analogue "Ambronol" (s. ABT1605 SG 07/2020 No. and date of registration DV/X 03934/01/20; 03934/01/21), manufactured by Marion Biotech Pvt. Ltd. India, have an equivalent mucolytic effect.

Competing Interests

The authors state that the study was conducted in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

REFERENCES

[1] Belenky M.L. Elements of a quantitative assessment of the pharmacological effect. L., 1963, -C.81-90.
[2] Burbello A.T., Shabrov A.V. Modern medicines. Moscow, 2007.-S. 283.
[3] Guskova T.A. Toxicology of drugs. Moscow, 2008. - p. 27-30.
[4] Guidelines for the study of the general toxic effects of pharmacological substances. In the Guide to the experimental (preclinical) study of new pharmacological substances. Under the general editorship of a corresponding member of RAMS, professor R. U. Khabriev. Second edition, revised and enlarged. M.: - 2005. - M.: OJSC "Publishing house Medicine", 2005. p. 41-54.
[5] Guidelines for the study of antitussive and mucolytic drugs / In the Guidelines for conducting preclinical studies of drugs. Edited by Doctor of Medical Sciences A.N. Mironova. // M.: Grif and K, 2012. - S. 502 - 508.
[6] The main methods of statistical processing of the results of pharmacological experiments. // In the Manual on the experimental (preclinical) study of new pharmacological substances under the general editorship of the corresponding member of RAMS, Professor R. U. Khabriev. Second edition, revised and enlarged. M.: - 2005. - M: OJSC "Publishing house" Medicine", 2005. p. 763-774.
[7] Stefanov A.V. Preclinical studies of drugs, Kiev 2002. p. 91.
[8] Abdijalilova Z. Kh. and YunusovaKh. M. "The substantion of the tablet mass" Ambrol composition choice for tabletizing" // World Journal of Pharmacy and Pharmaceutical Sciences. 2019. Vol.8, Issue 1, p. 260-266. (SJIF Impact Factor 7.421)

DOI: 10.37200/IJPR/V24I4/PR201345
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

[9] Abdijalilova Z. Kh. and YunusovaKh. M. “Study of influence of technological factors on indicators of quality of tablets of secrolitic action” // World Journal of Pharmacy and Pharmaceutical Sciences.-2019.-Vol.9, Issue 1, -p. 373-380. (SJIF Impact Factor 7.632)

[10] Farhan, F.K.Evaluation diffusion coefficient and thermal conductivity for epoxy –nTiO 2(2018) International Journal of Pharmaceutical Research, 10 (1), pp. 277-282.https://www.scopus.com/inward/record.uri?eid=2-s2.0-85059615739&partnerID=40&md5=377aab3970394ed2cf19aaaa8b0013b9

[11] Gowtham,S., &Karuppusamy,S. (2019). Review of Data Mining Classification Techniques. Bonfring International Journal of Software Engineering and Soft Computing, 9(2), 8-11. doi:10.9756/BIJSESC.9013

[12] Dev,P.,Syiemiong,J.V.,Iawphniaw,O., &Bhutia,R.D., (2019). IOT Based Accident Preventing and Reporting System. Bonfring International Journal of Software Engineering and Soft Computing, 9(2), 12-15. Almurshedi, A., Ismail, A.K. Neural correlation of maturity and perceptual decision making: An event related potential evidence, time-frequency and measure projection analysis (2018) NeuroQuantology, 16 (12), pp. 10-26.

[13] Sonkaya, A.R., Bayazıt, Z.Z. A neurolinguistic investigation of emotional prosody and verbal components of speech (2018) NeuroQuantology, 16 (12), pp. 50-56.

DOI: 10.37200/IJPR/V24I4/PR201345
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020