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

BIOPHARMACEUTICAL ASPECTS OF CAPSULIRINE DRUG BASED ON NSAIDs

Yunusova Kh.M.,[1]Jaloliddinova M.Sh.[*2]

Abstract--*This report presents the results of a study of the theoretical and experimental justifications for creating compositions based on diclofenac sodium and omeprazole, the main criteria of the approach to developing the composition and technology of capsules with analgesic effects are considered and briefly formulated.*

Keywords*: rotating baskets, technological properties, dissolution, and capsule, in vitro.*

INTRODUCTION

Among the main problems of pharmacy, the leading ones are expanding the range of drugs and improving the biopharmaceutical properties of existing ones. One of the biopharmaceutical criteria that determine the therapeutic efficacy of a drug is its bioavailability. The latter is provided by the dosage form, which should be reasonable pharmacokinetically and rationally in the qualitative and quantitative selection of auxiliary components. Bioavailability is an objective characteristic of therapeutic efficacy, since the value of a drug ultimately lies in the manifestation of a therapeutic effect [1,5].

One of the main biopharmaceutical characteristics, which largely determines the bioequivalence of the drug, is the solubility of the drug, which determines the possibility of creating a dosage form with an effective dose of the drug, the kinetics of its release from the dosage form, speed and completeness of absorption [2].

The first step in the study of bioavailability is to determine the solubility or time of release of the drug from the dosage form. It was found that the solubility test, to a first approximation, characterizes the bioavailability of the drug, since in practice there is a very frequent correlation between the rate of dissolution and absorption. The main criterion for the quality indicator of the newly developed dosage forms is the conduct of biopharmaceutical studies in the in vitro and in vivo experiments. The study of the bioavailability of drugs, drugs or their dosage forms usually begins with in vitro experiments, and ends with in vivo experiments with further investigation in a clinical setting [5,6,7].

General requirements for determining the dissolution rate were introduced in the United States Pharmacopeia (USP XIX) back in 1970 and are retained in subsequent editions (USP XX-XXIII). In the last XXIII edition of the US Pharmacopoeia, the quality of more than 600 oral dosage forms of solid dosage forms is evaluated by individual dissolution tests. In 1983, the dissolution article was introduced in the UK Pharmacopoeia (BP XIX), as well as in addition to the German Pharmacopoeia (DAV X 1992), in the French, Japanese and European pharmacopeias. This indicator is also widely used in regulatory documents of pharmaceutical companies. In 1985, the indicator “dissolution” was introduced in the second volume of the Global Fund of the 11th edition (section of the general article “Tablets”), which made it possible to more objectively evaluate the quality of solid dosage forms [2, 7].

[1]Doctor of pharmaceutical sciences, professor, the Department of Industrial Medicine Technology, Tashkent Pharmaceutical Institute, 100015, Tashkent, Street Oybek, 45, Republic of Uzbekistan, [2]Teaching assistant, PhD, the Department of Industrial Medicine Technology, Tashkent Pharmaceuticals Institute, Tashkent, Uzbekistan (– corresponding author, email: samina1809@mail.ru)*

DOI: 10.37200/IJPR/V24I4/PR201333
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

Dissolution in in vitro experiments is an important instrumental method for studying the biopharmaceutical quality of drugs [1,2,3].

Given this circumstance, in the next series of experiments, we studied the rate of release of active substances from "Dikomz" capsules. In this case, the generally accepted "Rotating Basket" method was used, which was included in the Global Fund XI [4].

The aim of our research is to study the time of release of the active substance from Dikomz capsules in in vitro experiments.

EXPERIMENTAL PART

Experimental studies of the bioavailability of the recommended drugs were carried out using the in vitro method. To study the dissolution rate of drugs from tablets, powders, dragees, capsules and other solid dosage forms, such devices as a "rotating basket" and a "rotating blade", less commonly a "rotating flask" device, are used. The main method for assessing the biopharmaceutical properties of drugs in in vitro experiments is the "Rotating Basket" method included in the Global Fund XI. Therefore, to determine the rate of release of the active substance from the recommended capsules, the experiments were carried out by this method [4, 7, 8].

It is known that when using the above method, various factors influence the release of active substances: the rotation speed of the basket, the volume and pH of the solvent medium, etc.

This method (in vitro method), as mentioned above, is relatively simple to use. It should be noted that various factors, such as: the auxiliary substances used, the volume and pH of the solvent, and the rotation speed of the basket, have an effect on the release rate of the active substance.

To select the optimal pH value of the solvent, we used solvent media with different pH values.

As neutral, purified water, acidic - 0.1 N hydrochloric acid and alkaline - 0.1 N sodium hydroxide. Figure 1, 2 shows the results of a study of the effect of pH of the solvent on the dissolution rate of Dikomz capsules.

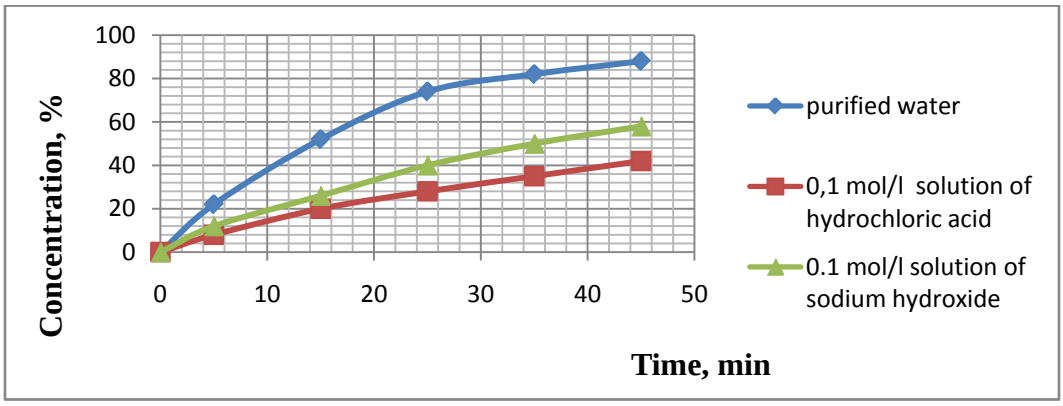


Fig. 1. The results of a study of the effect of pH of a solvent on dissolution rate of capsules "Dikomz" (diclofenac sodium)

1-neutral medium (purified water)
2-acid medium (0.1 N HCI solution)
3-alkaline medium (0.1 N NaOH solution)

DOI: 10.37200/IJPR/V24I4/PR201333
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

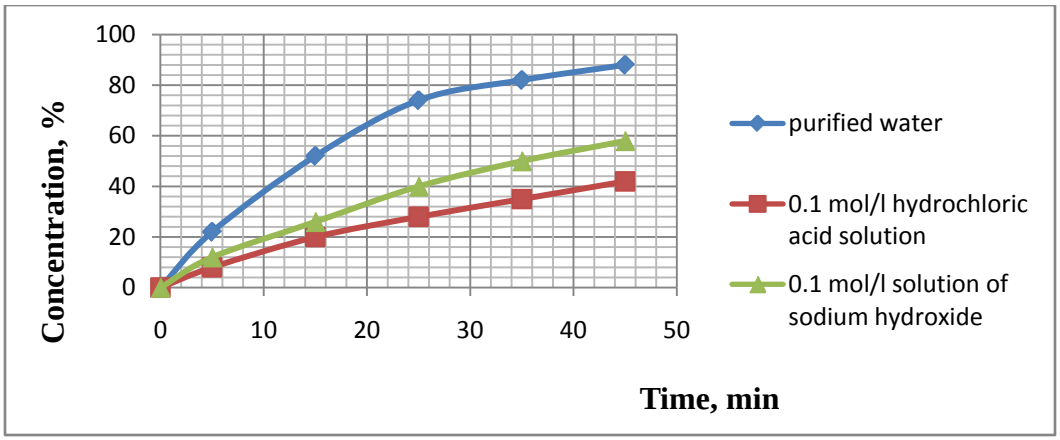


Fig. 2. The results of a study of the effect of pH of a solvent on dissolution rate of capsules "Dikomz" (omeprazole)

1-neutral medium (purified water)

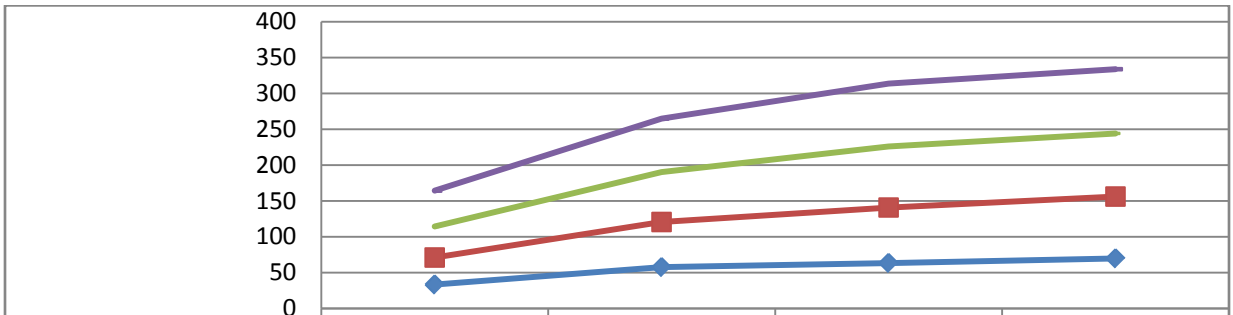
2-acid medium (0.1 N HCI solution)

3-alkaline medium (0.1 N NaOH solution)

In experimental studies, the volume of the solvent medium was standard - 1000 ml. Based on the results of experiments to study the effect of pH on the dissolution rate of Dikomz capsules, we recommended the use of a neutral medium, purified water, for further research.

Next, studies were conducted to determine the dependence of the process of transition of active substances from tablets on the rotation speed of the basket. The tablets were dissolved at the following basket rotation speeds: 50, 100, 150, 200 rpm. Every 15 minutes from the start of the experiment, samples were taken to quantify the active substances that transferred to the solvent medium.

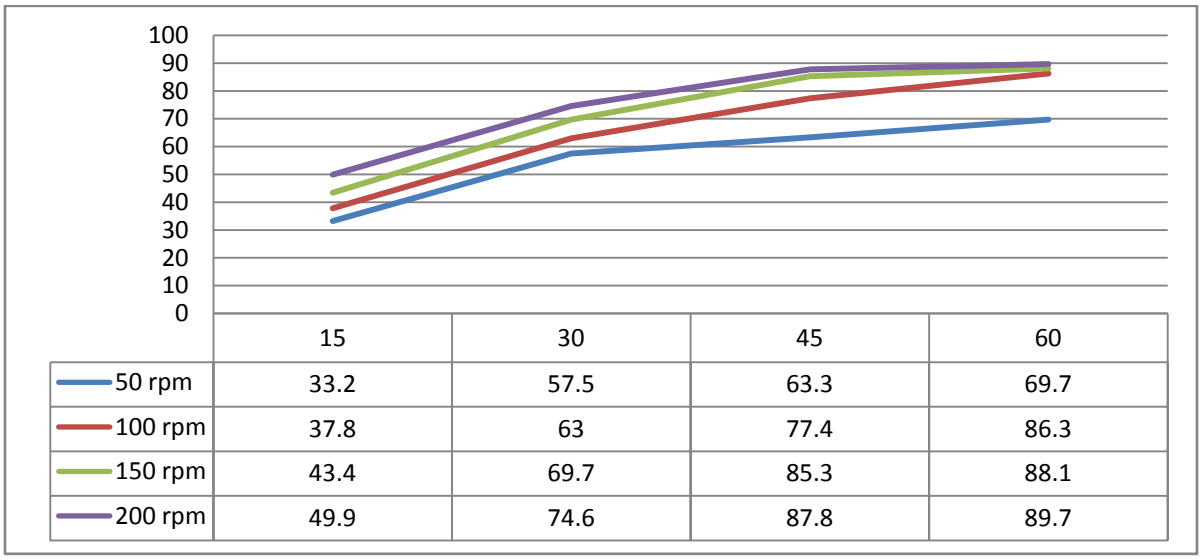
Figure 3.4 shows the experimental results. From the obtained results it is seen that the release of the active substance from the Dikomz capsules at various speeds of rotation of the basket occurs intensively.



	15	30	45	60
200 rpm	49.9	74.6	87.8	89.7
150 rpm	43.4	69.7	85.3	88.1
100 rpm	37.8	63	77.4	86.3
50 rpm	33.2	57.5	63.3	69.7

DOI: 10.37200/IJPR/V24I4/PR201333
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

Fig. 3. Results of studying the influence of basket rotation speedon the intensity of the release of diclofenac sodium from Dikomz capsules



	15	30	45	60
50 rpm	33.2	57.5	63.3	69.7
100 rpm	37.8	63	77.4	86.3
150 rpm	43.4	69.7	85.3	88.1
200 rpm	49.9	74.6	87.8	89.7

Fig. 4. Results of studying the influence of basket rotation speedthe intensity of the release of omeprazole from capsules "Dikomz"

According to the data obtained, at a basket rotation speed of 50 rpm, the release of active substances from the encapsulated dosage forms analyzed was less than 75%. Therefore, in diclofenac sodium capsules, this indicator turned out to be equal to 69.7%, in omeprazole capsules - 68.9%.

The analysis results show that at a basket rotation speed of 100 rpm, the concentration of active substances that have passed into the solution in 45 minutes is more than 75%, which meets the requirements of the Global Fund XI, which proves that under such conditions, the kinetics of the release of the active substance according to the first-order equation is observed.

Also, the results show that the dissolution rate of "Dikomz" capsules has a directly proportional relationship with the speed of rotation of the basket.

Based on the foregoing, for further research on the quality of finished products from a biopharmaceutical point of view, it is recommended that the basket rotate at 100 rpm, the volume of which is dissolved among 1000 ml.

In all cases of research it is necessary to maintain the temperature regime of 37±10°C.

The next stage of the study was devoted to experiments with recommended capsules stored for 6, 12 and 36 months. The final stage of research on the development of dosage forms is the study of shelf life, the time during which this drug must meet all the requirements of the FS or VFS. The following methods were used to establish the shelf life of the developed capsules: the in vivo storage method (long-term studies) and the "accelerated aging" method [9, 10].

Studies by natural storage were carried out in laboratory rooms at a temperature of 22±20°C. The above qualitative and quantitative indicators were determined every 6 months.

Research by the method of "accelerated aging" was carried out in accordance with the Interim Instructions for the work to determine the shelf life of drugs based on the method of "Accelerated aging" at elevated temperature. The following temperature conditions were used in this series of experiments: 600C. A study on the compliance of the recommended dosage forms with the required standards was carried out every 11.5 (6 months) days.

DOI: 10.37200/IJPR/V24I4/PR201333
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

Determination of the constancy of qualitative and quantitative characteristics was carried out according to the methods given in the scientific and technical documentation.

The stability of the developed drugs directly depends on the nature of the packaging material, so this issue is paid so much attention.

Recommended research capsules were packaged in the following packaging materials:

1. blister packaging according to OST 64-074-91 from a polyvinyl chloride film in accordance with GOST 25250-88;

2. blister packaging according to OST 64-074-91 from aluminum foil printed varnished according to TU 48-21-270-78;

3. cans of colorless glass melt type according to TU 13-7308001-477-85;

4. cans of sun-shielded glass melt type BDS-25 according to TU 64-228-84;

After the study time has elapsed, we determined all the qualitative and quantitative indicators and their compliance with the requirements for GF XI, including bioavailability.

Studies were conducted above established conditions i.e. for further research on the quality of finished products from a biopharmaceutical point of view, the basket rotation speed of 100 rpm was recommended according to the results of the study, the volume of which was dissolved among 1000 ml

The quantitative content of diclofenac sodium and omeprazole was determined by spectrophotometric methods. Before determining the quantitative content of diclofenac sodium and omeprazole, which passed into the dissolution medium, the selected samples were filtered through a paper filter “blue tape". According to the data obtained, at a basket rotation speed of 100 rpm, the release of active substances from the analyzed capsules in the studied periods was more than 75% (89%, 96%, 90%, respectively), which meets the requirements of the Global Fund XI.

The results of the study after the expiration of six months are shown in figures 5, 6 and 7.

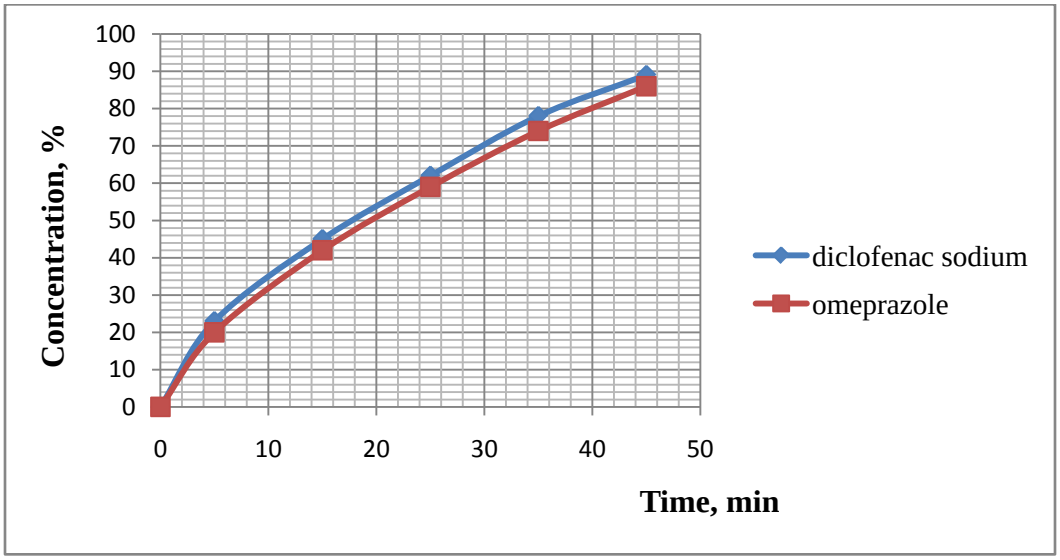


Fig. 5. The solubility results of the active substances (after 6 months)

DOI: 10.37200/IJPR/V24I4/PR201333
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

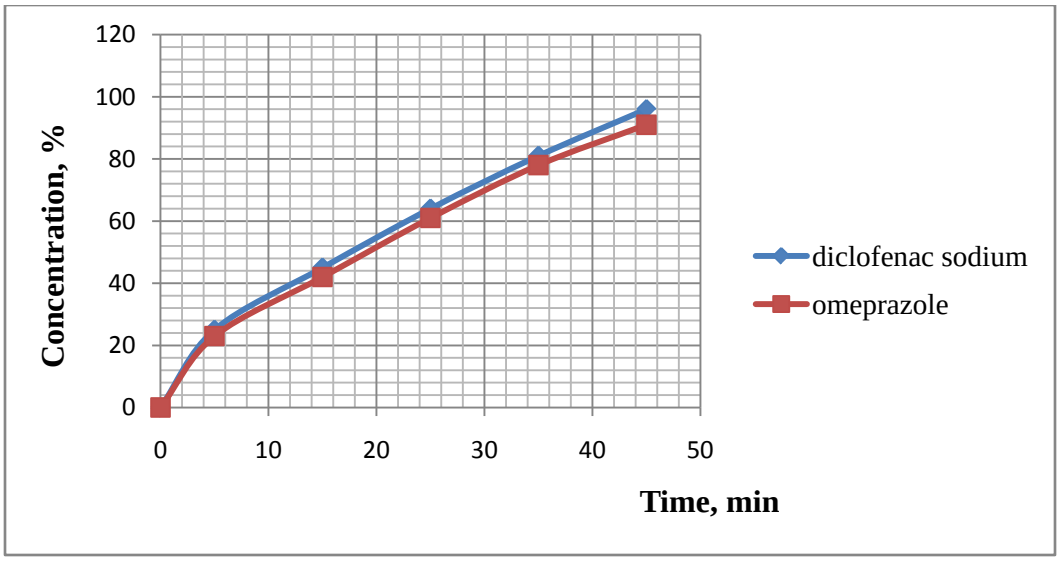


Fig. 6. The solubility results of the active substances (after 12 months)

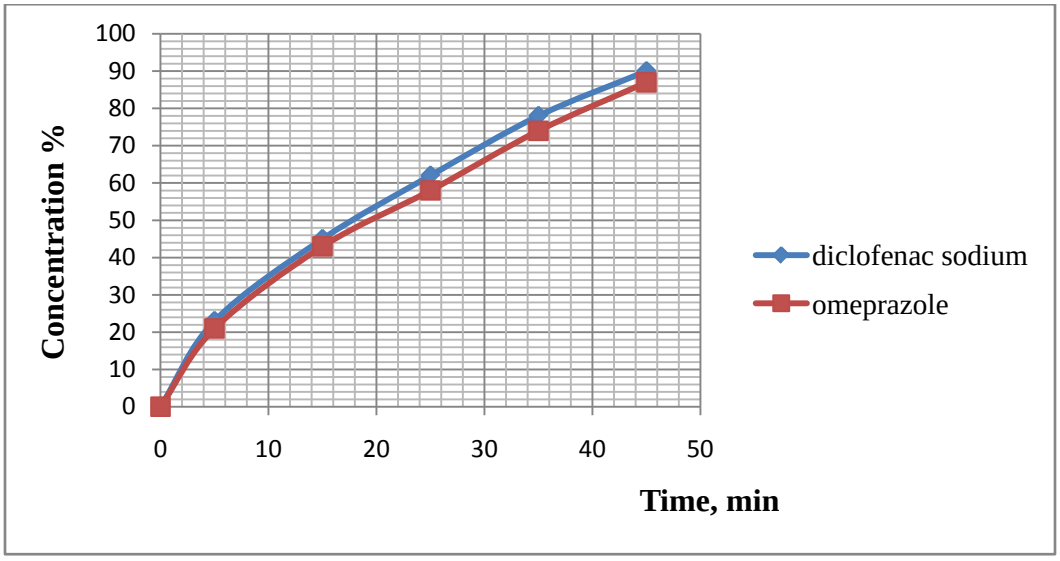


Fig. 7. The solubility results of active substances (after 36 months)

From the data in Figs. 5,6 and 7 it can be seen that the study of shelf life with both natural and "accelerated" aging methods, the above types of packaging ensure the stability of the quality characteristics of tablets, such as appearance, authenticity, strength, disintegration, quantitative including and solubility is the content of the active substance.

Thus, the selected composition and recommended technology of Dikomz capsules, as well as the packaging used, ensure the stability of the capsules for 3 years both in studies using the "accelerated aging" method and during storage under ordinary conditions.

CONCLUSIONS

1. Based on the results of studying the effect of pH on the dissolution rate of Dikomz capsules, it is recommended that a neutral medium, purified water, be used for further studies.

DOI: 10.37200/IJPR/V24I4/PR201333
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

2. In the experiments, the volume of the solvent medium was set in an amount of 1000 ml, which was chosen taking into account the sensitivity of the method for the quantitative determination of active substances developed by us.

3. Based on the data obtained, for further research on the quality of finished products from a biopharmaceutical point of view, a basket rotation speed of 100 rpm is recommended.

4. As a result of the study, the selected composition and the recommended technology of Dikomz capsules, as well as the packaging used, ensure the stability of the tablets for 3 years both in studies using the “accelerated aging” method and during storage under ordinary conditions.

CONFLICTS OF INTEREST

The authors declare that they do not have any personal conflicts of interest.

FUNDING

No external funding/support was used.

ETHICAL APPROVAL

Being this present study a paper review, it is exempt from prior evaluation by the ethics committee.

CONSENT

Written informed consent was obtained from the experiment for publication of this study and accompanying data. (A copy of the written consent is available for review by the Editor-in-Chief of this journal on request).

References

Azimova I.D., Teplyakova N.G., Dorofeev V.L. The test "dissolution" in the evaluation of drugs, genericomeprazole // Pharmacy.-2009.-No 1.-S.-9-11.

YunusovaKh.M., JaloliddinovaM.Sh. Studying Pharmacotechnological Aspects and Stability of “Ortof-S” Tablets // World Journal of Pharmacy and Pharmaceutical Sciences.-2019.- Vol.8, Issue1.-P.-277-288.

KarievaYo.S., YunusovaKh.M. Comparative study of meloxicam drugs bioequi-valence // Medical and Health Science Journal (Prague) .- 2011.-Vol.5.-P.-112-114.

State Pharmacopoeia XI, no. 1.2 ..- M .: Medicine, 1990.- 398 p.

Shodieva N.B., YunusovaKh.M. Stability study and storage conditions for Piracetam-SM tablets // Proceedings of the scientific-practical conference "Integration of education, science and production in pharmacy".- Tashkent.-2012.-P.-178.

Yarushok T.A., I.E. Shokhin, G.V. Ramenskaya, A.Yu. Savchenko. Assessment of biopharmaceutical solubility (under conditions simulating physiological) of drugs from the list of Vital and Essential Drugs (review) // Biopharmaceutical journal. 2012.V. 4. No. 2. P. 25-31.

S. Nainar, K. Rajiah, S. Angamuthu et al. Biopharmaceutical Classification System in vitro / in-vivo Correlation: Concept and Development Strategies in Drug Delivery // Trop J Pharm Res. 2012.V. 11 (2). R. 319-329.

F.Kh. Maқsudova // Biopharmaceutical studies of combined capsules of non-steroidal anti-inflammatory action // Pharmaceutical journal.-2016.-No. 1.-P.88-90.

DOI: 10.37200/IJPR/V24I4/PR201333
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020

YunusovaKh.M., AbdizhalilovaZ.Kh. The study of storage conditions and shelf life of tablets "Ambrol" // International scientific and practical remote conference "Modern achievements of pharmaceutical technology." -Harkov.-2018.-S.447-448.

Sh.Z. Ziyaev, Kh.M. Yunusova, Z.Kh. Zufarova. Biopharmaceutical studies of tablets “Tribulipil” in vitro // Collected materials. IV interdisciplinary scientific-practical conference “Scientific discussion: innovation in the modern world.” P-II-Moscow, 2012.-S.94-98.

Mohite p.b, khanage s.g., harishchandre v.s, shirsath yogita (2016) recent advances in microsponges drug delivery system. Journal of Critical Reviews, 3 (1), 9-16.

Sabarirajan,K.M.,Sudarsanan,P.,Srinithi,V.,Thirumalsundar,V., &Senthil,T. (2017). Household Computerization with Internet of Things (IOT). Excel International Journal of Technology, Engineering and Management,4(1), 20-22.

Parameshwaran,R. (2017). Design of Low Power Based Efficient Multiplier for Signal Processing Applications. Excel International Journal of Technology, Engineering and Management,4(1), 30-33.

Caponigro, M. No only god play dice: Philosophy of quantum nonlocality (2018) NeuroQuantology, 16 (9), pp. 20-27.

Mondal, S., Majumdar, S. Gates for conversation in microbes (2018) NeuroQuantology, 16 (8), pp. 1-8.

DOI: 10.37200/IJPR/V24I4/PR201333
Received: 22 Sep 2019 | Revised: 13 Oct 2019 | Accepted: 15 Jan 2020