https://doi.org/10.30857/2786-5371.2021.5.2

**УДК 615.074. 615.221:54.03**

**[1,2]WANG HONGJUAN, [1,2]HU WEI, [3]SALIY O. O.**
[1]School of Chemistry and Chemical Engineering, Qilu University of Technology (Shandong Academy of Sciences), Jinan, China
[2]Kyiv College, Qilu University of Technology (Shandong Academy of Sciences), Jinan, China
[3]Kyiv National University of Technology and Design, Ukraine

# PORE SIZE EFFECT AND MORPHOLOGY OF MESOPOROUS SILICA ON METOPROLOL TARTRATE RELEASE

***Purpose.*** *Study pore size effect and morphology of mesoporous silica on metoprolol tartrate release.*

***Methodology.*** *A sample of hollow mesoporous silicon dioxide with amino-functional groups containing 12.7 wt. % metoprolol tartrate has been investigated as potential carriers for the controlled release of active substance. Studies of the release profiles of metoprolol tartrate were performed under the following conditions: dissolution medium was buffer solution with a pH of 7.4 (phosphate buffer); sampling time: from 0.5 h before 18 h. The metoprolol concentration in the liquid phase was evaluated by a UV-Vis spectrophotometer (Persee TU-190, Beijing, China) by use of quartz cuvettes with an optical path length of 1 cm at a maximum wavelength of 274 nm.*

***Findings.*** *In this work we have studied mesoporous silica as possible carrier to controlled release of metoprolol tartrate, a drug used in the treatment of some diseases of the cardiovascular system. The material for research was a sample of hollow mesoporous silicon dioxide with amino-functional groups 200–400 nm in size and 20–30 nm in shell thickness. A calibrated curve to determine the amount of metoprolol was constructed by determining the absorption dependence of the concentration of metoprolol in the range from 10 to 300 ppm. The same drug concentration was obtained as calculated from the drug release test formula, which concludes that the release of metoprolol is controlled.*

***Originality.*** *The controlled release of a sample of hollow spheres of mesoporous silicon dioxide filled with metoprolol tartrate was studied, which was synthesized by the School of Chemistry and Chemical Engineering, Qilu University of Technology, using a new technology, where hollow spheres of mesoporous silicon dioxide with amino groups were synthesized using $CO_2$ gas bubbles as templates.*

***Practical value.*** *The metoprolol release amount could achieve a 50% release amounts within 1 hour and 90% within 5 hours, indicating that the synthesized mesoporous hollow sphere could achieve controlled drug release, and shows the potential of carriers with stimulus response and targeted therapy.*

***Keywords:*** *hollow mesoporous silica; metoprolol tartrate; drug controlled release; dissolution.*

**Introduction.** Hypertension is a leading cause of cardiovascular disease, stroke, and death. It affects a substantial proportion of the population worldwide, and remains underdiagnosed and undertreated [1]. The attack of hypertension usually begins in the morning when the patient wakes up from a situation of relative hypotension. Therefore, the development of controlled drug delivery is of great importance in chronopharmacology, for example, to minimize the risk of morning hypertension attack [2].

Beta-adrenoblocker metoprolol is wide used in arterial hypertension and ischemic heart disease. Metoprolol has salt such as tartrate (MPT) which is used for production of immediate release (IR) and may need to be taken multiple times per day [3].

In the last years many efforts have been devoted to the development of new formulations that can control both rate and period of drug delivery. Mesoporous silica carriers have a number of attractive features for enhancing drug dissolution, such as high surface area, large pore volume and ordered pore networks and they can also provide an adjustable drug release profile [4]. Silica matrices show high biocompatibility and these materials are biodegradable to monosilicic acid (in the long run, in the intestine) and resistance to microbial attack. Moreover, physico-chemical and textural properties of silica can be modulated ad hoc by the choice of a tailored synthetic approach [5, 6]. Mesoporous silica nanoparticles (MSNs) have been widely studied as drug carriers to get controlled

release behaviors, however, their application in sustained release of MPT is limited. The possible reason is due to MPT molecule being bulky, while normal type MSNs like MCM-41 and SBA-15 have pore sizes of only 3–6 nm [7]. Studies for the controlled release of MPT are described, which are aimed at both new approaches to synthesis and characterization of silica carriers: a one-time sol-gel approach and wetness impregnation method, where MPT is adsorbed on a silica support by wet impregnation after synthesis [5]. MSNs with MTP were synthesized through the reaction of tetraethyl orthosilicate (TEOS) in the water medium at 353 K, with introducing some cetyltrimethylammonium bromide (CTAB) as porogens [8]. A novel technique ultra-fine particle process system (UPPS) was employed to develop sustained-release MPT microspheres for oral administration [9]. Scientific interest is hollow structured amino-functionalized mesoporous silica, which was usually prepared by hard templates or selective etching of solid spherical silica in a basic solution [10]. The obtained hollow mesoporous silica showed good $CO_2$ capture amounts and high performance in Knoevenagel reaction due to the presence of abundant amine groups. In addition, mesoporous silica hollow spheres displayed excellent performance in drug-controlled release characteristics for a number of drugs and are promising for molecular modeling of the bulky MPT molecule delivery system [7, 11].

Despite significant progress in the characterization and development of mesoporous drug delivery systems to improve drug dissolution, more research is needed such as Dissolution test to establish the kinetic profile of drug release from mesoporous silica materials, the rate of release of the active ingredient (API) from the carrier, and the possibility of re-adsorption API on the surface of mesoporous silica [12]. The interaction of dispersion medium with the drug-silica matrix and the release rate of the API are dependent on factors such as porosity, the initial drug load, the drug's solubility in the release medium and the diffusion coefficient of the drug molecules in the medium and importance of utilizing relevant and effective in vitro dissolution methods with discriminating dissolution media [13].

**Statement of the problem.** Aim of our work has been the investigation pore size effect and morphology of mesoporous silica on metoprolol tartrate release. The solubility of metoprolol (tartrate form) in water is >1000 (mg/ml) at 25°C (freely soluble in water). Metoprolol can quickly disperse into phosphate buffer solution system once it diffuse from nanopores of mesoporous silica. Samples of MPT drug-loaded mesoporous silica hollow spheres were previously synthesized by the School of Chemistry and Chemical Engineering, Qilu University of Technology, using the novel technology, where amino-functionalized mesoporous silica hollow spheres were synthesized by using $CO_2$ gaseous bubbles as templates.

**Research results.** The material for research was a sample of hollow mesoporous silicon dioxide with amino-functional groups 200–400 nm in size and 20–30 nm in shell thickness, containing 12.7 wt. % MPT. In addition, the robust hollow mesoporous silica could well-dispersed in aqueous systems, showing excellent drug-controlled release. The morphology of the amino-functionalized mesoporous silica with loaded MPT used in the present study is shown in Fig. 1.

Studies of the release profiles of the active substance MPT were performed under the following conditions:

- device with stirrer;
- volume of dissolution medium: 100 mL;
- dissolution temperature: 25.0 ± 0.5ºC;
- dissolution medium: buffer solution with a pH of 7.4 (phosphate buffer);
- speed of rotation of the stirrer: 100 rpm;
- sampling time: 0.5 h, 1 h, 1.5 h, 2 h, 2.5 h, 3 h,3.5 h, 4 h, 5 h, 6 h, 8 h, 10 h, 18 h.

Drug release experiments: First, 10.0 mg of MPT-loaded mesoporous silica as powder was added in 100 mL of phosphate buffer with a stirring speed at 100 rpm at certain temperature. Extraction solution of 2.0 mL was taken out at different time to monitor the concentration of metoprolol in the solution by a UV-Vis spectrophotometer (Persee TU-190, Beijing, China) by use

of quartz cuvettes with an optical path length of 1 cm at a maximum wavelength of 274 nm. After every extraction 2.0 mL fresh phosphate buffer was replenished. The reference solution was prepared by dissolving a standard sample of metoprolol tartrate in a phosphate buffer as dissolution medium.

Calibration curve of metoprolol was determined by taking absorbance vs. metoprolol concentration between 10 and 300 ppm. Figure 2 showed calibration curve of the strongest absorption peak at 274 nm to quantify the concentration of drug molecules in the solution.

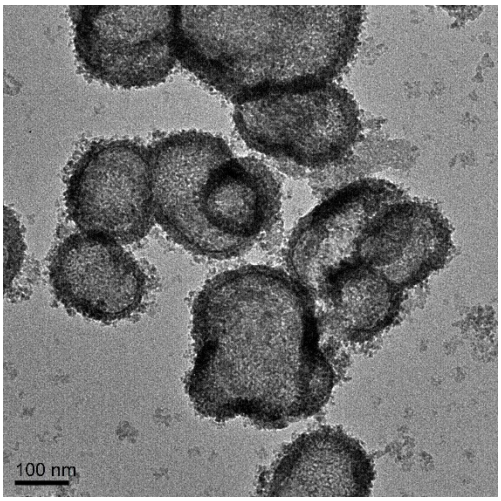


*Fig. 1.* **TEM images of the amino-functionalized mesoporous silica with loaded MPT**

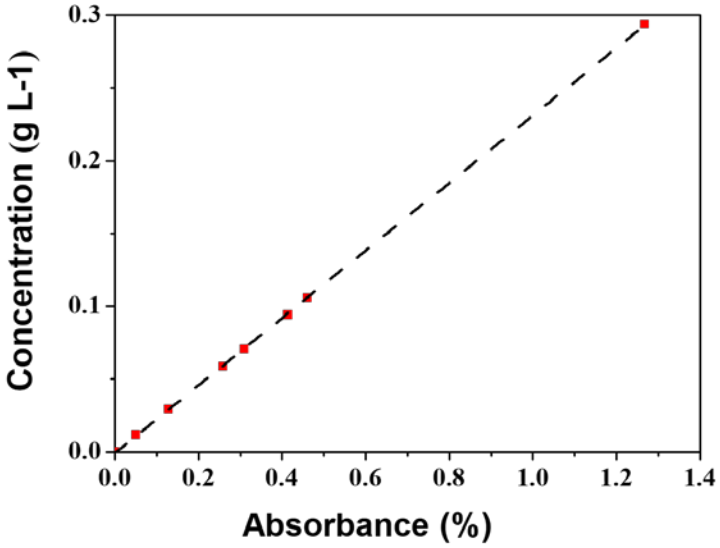


*Fig. 2.* **Calibration curve of the absorption peak to quantify the concentration of drug MPT in the solution**

The effective concentration in solution was calculated on the basis of the following equation (1) [5, 14]:

$$C_{eff} = C_{app} + \frac{v}{V}\sum_{1}^{t-1} C_{app} \qquad (1)$$

where $C_{eff}$ – is the corrected concentration at time, t;
$C_{app}$ – is the apparent concentration at time, t;

*v* – is the volume of sample taken;
V – is the total volume of the dissolution medium.

In relation to our conditions, the formula has the form: $C_{eff} = C_{app} + 0.02 \times \sum_1^n C_{app}$.

The test was performed thrice. We have obtained the same drug concentration value of that calculated on the basis of the formula for a drug release test, studied and concludes that the release of metoprolol is controlled.

Figure 3 showed the MPB drug release curve.

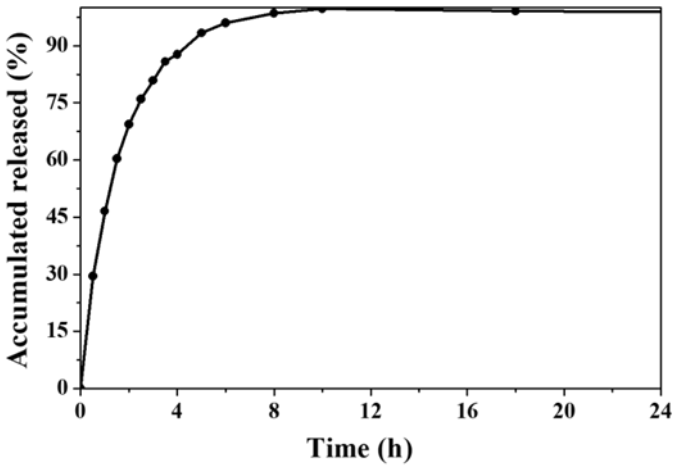


*Fig. 3.* **Metoprolol tartrate (%) release from amino-functionalized mesoporous silica hollow spheres (n = 3)**

The drug release amount could achieve a 50% release amounts within 1 hour and 90% within 5 hours, indicating that the synthesized mesoporous hollow sphere could achieve controlled drug release, which showed potential in carriers with stimulus response and targeted therapy.

**Conclusions.** In this work we have studied hollow mesoporous silica as possible carrier to the controlled release of metoprolol tartrate (MPT), a drug used in the treatment of several diseases of the cardiovascular system. MPT drug is a kind of bulky in molecular volume therefore porous structure and relatively large pore size was proper carrier for MPT to achieve desirable controlled release behaviors. Amino-functionalized hollow mesoporous silica with 200–400 nm in size and 20–30 nm in shell thickness was showed excellent metoprolol tartrate drug-controlled release. It is obtained the same drug metoprolol concentration value of that calculated on the basis of the formula for a drug release test, and concludes that the release of metoprolol is controlled.

## References

1. Oh, G. C., Cho, H. J. (2020). Blood pressure and heart failure. *Clin Hypertens*, 26(1). https://doi.org/10.1186/s40885-019-0132-x.
2. Meng, Y., Liu, X. L., Liu, J., Cheng, X. L. (2017). A prospective study on the impact of heart rate control achieved with metoprolol on cardiac performance, motor function and quality of life in Chinese chronic heart failure patients. *International Journal of Cardiology*, 227: 267–271. https://doi.org/10.1016/j.ijcard.2016.11.115.

## Література

1. Oh G. C., Cho H. J. Blood pressure and heart failure. *Clin Hypertens.* 2020. 26(1). https://doi.org/10.1186/s40885-019-0132-x.
2. Meng Y., Liu X. L., Liu J., Cheng X. L. A prospective study on the impact of heart rate control achieved with metoprolol on cardiac performance, motor function and quality of life in Chinese chronic heart failure patients. *International Journal of Cardiology*. 2017. 227: 267–271. https://doi.org/10.1016/j.ijcard.2016.11.115.

3. Leonova, M. V., Maneshina, O. A., Belousov, Iu. B. (2010). Evolution of oral drug forms of metoprolol: advantages of long acting modified release forms with modified release. *Kardiologiia*, 50(12): 79–83. PMID: 21591398.

4. Samira Jafari, Hossein Derakhshankhah, Loghman Alaei, Ali Fattahi, Behrang Shiri Varnamkhasti, Ali Akbar Saboury (2019). Mesoporous silica nanoparticles for therapeutic/diagnostic applications. *Biomedicine & Pharmacotherapy*, Vol. 109, P. 1100–1111. https://doi.org/10.1016/j.biopha.2018.10.167.

5. Ghedini E., Signoretto M., Pinna F., Crocellà V., Bertinetti L., Cerrato G. (2010). Controlled release of metoprolol tartrate from nanoporous silica matrices. *Microporous Mesoporous Mater*, 132: 258–267. https://doi: 10.1016/j.micromeso.2010.03.005.

6. Wu, J., Williams, G. R., Niu, S., Gao, F., Tang, R., Zhu, L. M. (2019). A Multifunctional Biodegradable Nanocomposite for Cancer Theranostics. *Advanced science* (Weinheim, Baden-Wurttemberg, Germany), 6(14): 1802001. https: //doi.org/10.1002/advs.201802001.

7. Luo, S., Hao, J., Gao, Y., Liu, D., Cai, Q., Yang, X. (2019). Pore size effect on adsorption and release of metoprolol tartrate in mesoporous silica: Experimental and molecular simulation studies. *Materials science & engineering. C, Materials for biological applications*, 100: 789–797. https://doi.org/10.1016/j.msec.2019.03.050.

8. Jia, X. Y., Wu, Y. Z., Cai, Q., Yang, X. P., Liu, D. P., Lin, Y. H. (2014). Modulating Release of Metoprolol Tartrate with Nanostructured Silica Particles. *In Key Engineering Materials*, Vols. 602–603, P. 55–58. Trans Tech Publications, Ltd. https://doi.org/10.4028/www.scientific.net/kem.602-603.55.

9. Ying Huang, Yueyun Zhou, Jiayuan Huang, Chune Zhu, Meiwan Chen, Xin Pan, Chuanbin Wu (2015). Metoprolol tartrate sustained-release binary matrix microspheres for oral administration produced by novel ultra-fine particle processing system. *Powder Technology*, Vol. 285, P. 44–50. https://doi.org/10.1016/j.powtec.2015.05.008.

10. Wei Chen, Chi-An Cheng, Cosco, E. D., Shyam Ramakrishnan, Lingg, J. G. P., Bruns, O. T., Zink, J. I., Sletten, E. M. (2019). Shortwave infrared imaging with J-aggregates stabilized in hollow mesoporous silica nanoparticles. *Journal of the American Chemical Society*, 141: 12475–12480. https://doi.org/10.1021/jacs.9b05195.

3. Leonova M. V., Maneshina O. A., Belousov Iu. B. Evolution of oral drug forms of metoprolol: advantages of long acting modified release forms with modified release. *Kardiologiia*. 2010. 50(12): 79–83. PMID: 21591398.

4. Samira Jafari, Hossein Derakhshankhah, Loghman Alaei, Ali Fattahi, Behrang Shiri Varnamkhasti, Ali Akbar Saboury. Mesoporous silica nanoparticles for therapeutic/diagnostic applications. *Biomedicine & Pharmacotherapy*. 2019. Vol. 109. P. 1100–1111. https://doi.org/10.1016/j.biopha.2018.10.167.

5. Ghedini E., Signoretto M., Pinna F., Crocellà V., Bertinetti L., Cerrato G. (2010). Controlled release of metoprolol tartrate from nanoporous silica matrices. *Microporous Mesoporous Mater*. 2010. 132: 258–267. https://doi: 10.1016/j.micromeso.2010.03.005.

6. Wu J., Williams G. R., Niu S., Gao F., Tang R., Zhu L. M. A Multifunctional Biodegradable Nanocomposite for Cancer Theranostics. *Advanced science* (Weinheim, Baden-Wurttemberg, Germany). 2019. 6(14). 1802001. https: //doi.org/10.1002/advs.201802001.

7. Luo S., Hao J., Gao Y., Liu D., Cai Q., Yang X. Pore size effect on adsorption and release of metoprolol tartrate in mesoporous silica: Experimental and molecular simulation studies. *Materials science & engineering. C, Materials for biological applications*. 2019**.** 100: 789–797. https://doi.org/10.1016/j.msec.2019.03.050.

8. Jia X. Y., Wu Y. Z., Cai Q., Yang X. P., Liu D. P., Lin Y. H. Modulating Release of Metoprolol Tartrate with Nanostructured Silica Particles. *In Key Engineering Materials*. 2014. Vols. 602–603, P. 55–58. Trans Tech Publications, Ltd. https://doi.org/10.4028/www.scientific.net/kem.602-603.55.

9. Ying Huang, Yueyun Zhou, Jiayuan Huang, Chune Zhu, Meiwan Chen, Xin Pan, Chuanbin Wu. Metoprolol tartrate sustained-release binary matrix microspheres for oral administration produced by novel ultra-fine particle processing system. *Powder Technology*. 2015. Vol. 285. P. 44–50. https://doi.org/10.1016/j.powtec.2015.05.008.

10. Wei Chen, Chi-An Cheng, Cosco E. D., Shyam Ramakrishnan, Lingg J. G. P., Bruns O. T., Zink J. I., Sletten E. M. Shortwave infrared imaging with J-aggregates stabilized in hollow mesoporous silica nanoparticles. *Journal of the American Chemical Society*. 2019. 141: 12475–12480. https://doi.org/10.1021/jacs.9b05195.

11. Zhaogang Teng, Wei Li, Yuxia Tang, Ahmed Elzatahry, Guangming Lu, Dongyuan Zhao (2019). Mesoporous Organosilica Hollow Nanoparticles: Synthesis and Applications. *Advanced Materials*, 31: 1707612. https://doi.org/10.1002/adma.201707612.

12. McCarthy, C. A., Ahern, R. J., Dontireddy, R., Ryan, K. B., Crean, A. M. (2016). Mesoporous silica formulation strategies for drug dissolution enhancement: a review. *Expert opinion on drug delivery*, 13(1): 93–108. https://doi.org/10.1517/17425247.2016.1100165.

13. Bremmell, K. E., Prestidge, C. A. (2019). Enhancing oral bioavailability of poorly soluble drugs with mesoporous silica based systems: opportunities and challenges. *Drug Development and Industrial Pharmacy*, 3(45): 349–358. https://doi.org/10.1080/03639045.2018.1542709.

14. Siepmann, J., Siepmann, F. (2013). Mathematical modeling of drug dissolution. *International journal of pharmaceutics*, 1(453): 12–24. https://doi.org/10.1016/j.ijpharm.2013.04.044.

11. Zhaogang Teng, Wei Li, Yuxia Tang, Ahmed Elzatahry, Guangming Lu, Dongyuan Zhao. Mesoporous Organosilica Hollow Nanoparticles: Synthesis and Applications. *Advanced Materials*. 2019. 31: 1707612. https://doi.org/10.1002/adma.201707612.

12. McCarthy C. A., Ahern R. J., Dontireddy R., Ryan K. B., Crean A. M. Mesoporous silica formulation strategies for drug dissolution enhancement: a review. *Expert opinion on drug delivery*. 2016. 13(1): 93–108. https://doi.org/10.1517/17425247.2016.1100165.

13. Bremmell K. E., Prestidge C. A. Enhancing oral bioavailability of poorly soluble drugs with mesoporous silica based systems: opportunities and challenges. *Drug Development and Industrial Pharmacy*. 2019. 3(45): 349–358. https://doi.org/10.1080/03639045.2018.1542709.

14. Siepmann J., Siepmann F. Mathematical modeling of drug dissolution. *International journal of pharmaceutics*. 2013. 1(453): 12–24. https://doi.org/10.1016/j.ijpharm.2013.04.044.

***WANG HONGJUAN***
*Master, School of Chemistry and Chemical Engineering, Qilu University of Technology (Shandong Academy of Sciences), Jinan, China*
*https://orcid.org/0000-0002-1257-3186*
*E-mail: hongjuanwang2015@163.com*

***HU WEI***
*PhD (Physical Chemistry), Professor, School of Chemistry and Chemical Engineering, Qilu University of Technology (Shandong Academy of Sciences), Jinan, China*
*https://orcid.org/0000-0002-7467-4783*
*E-mail: weihu@qlu.edu.cn*

***SALIY OLENA***
*PhD, Associate Professor*
*Department of Pharmaceutical Industry,*
*Kyiv National University of Technologies and Design, Ukraine*
*https://orcid.org/0000-0001-7103-2083*
*Researcher ID: AAC-5721-2019*
*E-mail: saliy.oo@knutd.edu.ua*

**[1,2]ВАН ХУНЦЗЮАНЬ, [1,2]ХУ ВЕЙ, [3]САЛІЙ О. О.**
[1]Школа хімії та хімічної інженерії, Технологічний університет Цілу (Академія наук Шаньдун), Цзінань, Китайська Народна Республіка
[2]Київський коледж, Технологічний університет Цілу (Академія наук Шаньдун), Цзінань, Китайська Народна Республіка
[3]Київський національний університет технологій та дизайну, Україна

## ВПЛИВ РОЗМІРУ ПОР ТА МОРФОЛОГІЇ МЕЗОПОРИСТОГО КРЕМНІЮ НА ВИВІЛЬНЕННЯ МЕТОПРОЛОЛУ ТАРТРАТУ

***Мета.*** *Вивчити вплив розміру пор та морфології мезопористого кремнезему на вивільнення метопрололу тартрату.*

***Методика.*** *Зразок порожнього мезопористого діоксиду кремнію з амінофункціональними групами, що містить 12,7 мас. % метопрололу тартрату досліджено як потенційний носій для*

*контрольованого вивільнення активної речовини. Дослідження профілів вивільнення тартрату метопрололу проводили за таких умов: середовище розчинення - буферний розчин з pH 7,4 (фосфатний буфер); час відбору: від 0,5 год до 18 год. Концентрацію метопрололу в рідкій фазі визначали на спектрофотометрі UV-Vis (Persee TU-190, Пекін, Китай) з використанням кварцових кювет з товщиною шару 1 см при максимумі довжини хвилі 274 нм.*

***Результати.*** *У цій роботі ми вивчили мезопористий діоксид кремнію як можливий носій для контрольованого вивільнення метопрололу тартрату, препарату, який використовується при лікуванні деяких захворювань серцево-судинної системи. Матеріалом для дослідження був зразок порожнього мезопористого діоксиду кремнію з розміром аміно-функціональних груп 200–400 нм і товщиною оболонки 20–30 нм. Калібровану криву для визначення кількості метопрололу будували шляхом визначення залежності абсорбції від концентрації метопрололу в діапазоні від 10 до 300 ppm. Отримано таке саме значення концентрації лікарського засобу, яке було розраховано на основі формули для тесту на вивільнення лікарського засобу, що дозволяє зробити висновок про те, що вивільнення метопрололу знаходиться є контрольованим.*

***Наукова новизна.*** *Досліджено контрольоване вивільнення зразку порожніх сфер мезопористого діоксиду кремнію, заповненого метопрололу тартратом, що синтезований Школою хімії та хімічної інженерії Технологічного університету Цілу, з використанням найновітньої технології, де порожні сфери мезопористого діоксиду кремнію з аміногрупами були синтезовані з використанням бульбашок газу $CO_2$ у якості темплатів.*

***Практична значимість.*** *Кількість вивільнення метопрололу може досягати 50% вивільнення протягом 1 години та 90% протягом 5 годин, що вказує на те, що синтезована порожниста мезопориста сфера може досягати контрольованого вивільнення лікарського засобу, і показує потенціал носіїв зі стимул-реакцією та таргетною терапією.*

***Ключові слова:*** *порожній мезопористий діоксид кремнію; метопрололу тартрат; контрольоване вивільнення препарату; розчинення.*

**[1,2]ВАН ХУНЦЗЮАНЬ, [1,2]ХУ ВЕЙ, [3]САЛИЙ Е. А.**

[1]Школа химии и химической инженерии, Технологический университет Цилу (Академия наук Шаньдун), Цзинань, Китáйская Нарóдная Респýблика

[2] Киевский колледж, Технологический университет Цилу (Академия наук Шаньдун), Цзинань, Китáйская Нарóдная Респýблика

[3]Киевский национальный университет технологий и дизайна, Украина

## ВЛИЯНИЕ РАЗМЕРА ПОР И МОРФОЛОГИИ МЕЗОПОРИСТОГО КРЕМНИЯ НА ВЫСВОБОЖДЕНИЕ МЕТОПРОЛОЛА ТАРТРАТА

***Цель.*** *Изучить влияние размера пор и морфологии мезопористого кремнезема на высвобождение метопролола тартрата.*

***Методики.*** *Образец полого мезопористого диоксида кремния с амино-функциональными группами, содержащий 12,7 мас. % метопролола тартрата, был исследован как потенциальный носитель для контролируемого высвобождения активного вещества. Исследования профилей высвобождения тартрата метопролола проводили при следующих условиях: среда растворения – буферный раствор с pH 7,4 (фосфатный буфер); время отбора: на протяжении от 0,5 ч до 18 ч. Концентрацию метопролола в жидкой фазе опрееделяли на спектрофотометре UV-Vis (Persee TU-190, Пекин, Китай) с использованием кварцевых кювет с толщиной слоя 1 см при максимуме длине волны 274 нм.*

***Результаты.*** *В этой работе мы изучили мезопористый диоксид кремния как возможный носитель для контролируемого высвобождения метопролола тартрата, препарата, используемого при лечении некоторых заболеваний сердечно-сосудистой системы. Материалом для исследования служил образец полого мезопористого диоксида кремния с размером амино-функциональных групп 200–400 нм и толщиной оболочки 20–30 нм. Калиброванную кривую для определения количества метопролола строили путем определения зависимости абсорбции от концентрации метопролола в диапазоне от 10 до 300 ppm. Получено такое же значение концентрации лекарственного средства,*

*какое было рассчитано на основе формулы для теста на высвобождение лекарственного средства, что позволяет сделать вывод о том, что высвобождение метопролола контролируемое.*

***Научная новизна.*** *Исследовано контролируемое высвобождение образца полых сфер из мезопористого диоксида кремния, заполненного метопролола тартратом, который синтезирован Школой химии и химической инженерии Технологического университета Цилу с использованием новейшей технологии, где полые сферы из мезопористого диоксида кремния с аминогруппами были синтезированы с использованием пузырьков газа $CO_2$ в качестве темплатов.*

***Практическая значимость.*** *Количество высвобождения метопролола может достигать 50% высвобождения в течение 1 часа и 90% в течение 5 часов, что указывает на то, что синтезированная полая мезопористая сфера может достигать контролируемого высвобождения лекарственного средства, и показывает потенциал носителей со стимул-реакцией и таргетной терапией.*

***Ключевые слова:*** *полый мезопористый диоксид кремния; метопролола тартрат; контролируемое высвобождение препарата; растворение.*