UOT: 544.23.02/.03

RESEARCH INTO SORPTION PROCESS OF LEVOTHYROXINE WITH ALKYL-SUBSTITUTED CHITOSAN SCHIFF-BASED HYDROGEL

Samira Safaraliyeva[a], Dilgam Tagiyev[a], Nizami Zeynalov[a], Shamo Tapdiqov[b], Sevda Fatullayeva[a], Maria Raucci[c]

[a]Acad M. Nagiyev Institute of Catalysis and Inorganic Chemistry of the National Academy of Sciences of Azerbaijan (NASA)
H. Javid ave.113, AZ 1143, Baku, E-mail: safaraliyeva2017@mail.ru
[b]SOCAR Oil and Gas Research Project Institute
[c]Institute of Polymers, Composites and Biomaterials, National Research Council of Italy

Received 07.11.2021
Accepted 22.02.2022

Abstract: *In order to reduce the side effects of thyroid hormone substitute levothyroxine sodium pentahydrate, its sorption with a quaternized salt of a new alkyl derivative of chitosan was studied. The drug amount in the salt (gel) is in micrograms, and the gel-levothyroxine is in the form of a complex that can show biological activity. With that end in view, a sorption process of levothyroxine sodium from an aqueous solution to the inside and surface of the hydrogel was carried out under static conditions. The capacity of the hydrogel depending upon the pH medium, the ionic strength, the hydrogel dose, the concentration of the drug and the temperature was studied. It was shown that the effective sorption of levothyroxine by chitosan-based hydrogel was optimal at pH of 6-8.5, at 50 mg/L concentration of levothyroxine in the presence of 10-50 mg of hydrogel dose but the sorption degree begins to decrease after T=40 °C. The isotherm results of sorption processes have been found to be subordinate mainly to Langmuir and to some extent Freundlich equations. It revealed that gel degradation in the oxidizing medium is about 70% within 2 weeks, and in the elastase and PBS medium is about 17-20%.*

Keywords: *chitosan; quaternization; gel; thyroid hormone; levothyroxine sodium pentahydrate; sorption capacity; isotherm.*
DOI: 10.32737/2221-8688-2022-1-18-27

Introduction

Polymer-based hydrogels are indispensable materials in modern medicine and biotechnology, as well as in various industries [1,2]. Hydrogels are macromolecular networks that have the property of swelling in water obtained from modifications of natural and synthetic polymers. They are widely used as a matrix for effective sorption of organic compounds as well as for the delivery of drugs [3,4].

Among natural polymers, the application of chitosan and its derivatives as both drug immobilization and super absorbent is of great interest. Chitosan is a water-insoluble polyaminosaccharide with a cellulose structure but characterized by the presence of amine and acetoamide groups in content (Fig. 1) [5].

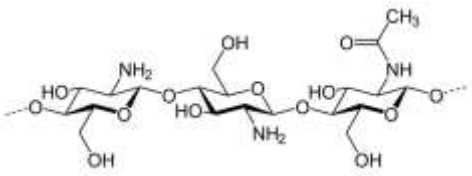

Fig. 1. Chitosan sturcture

The high density of hydrogen bonds between amine and hydroxyl groups in the chitosan chain limits its solubility in water. In this regard, by modifying the macromolecule, its various substitutes were obtained, and polymer-drug delivery systems were synthesized by immobilizing small-molecule organic compounds by sorption.

It is known that levothyroxine-Na pentahydrate, a substitute for L-thyroxine, a thyroid hormone should be taken by the body long time after thyroid surgery. This drug is used not free but in combination with various polymers and inorganic substances. For example, the drug currently used as L-thyroxine name contains a mixture of microcrystalline cellulose, povidone, Mg-stearate and lactose excipients along with the active ingredient [6]. These substances are involved in the delivery of the active drug to the required absorption site and circulazation in the bloodstream.

Given the sufficient side effects, the development of new dosage forms with effective sorption of levothyroxine-Na into chitosan-based polymer hydrogels is a topical issue. The analysis of the reference is indicative that there is a need to form new chitosan-levothyroxine complexes, which can regulate the amount of active ingredient by loading levothyroxine into chitosan-based matrixes. Thus, the amount of drug release from the chitosan-based gel structure can be directly regulated by the chemical composition of the matrix and the rate of sorption [7]. Besides, the bioavailability and gastroprotective properties of chitosan make it possible to be used as a matrix for the delivery of drugs.

The aim of the study was to investigate the sorption of levothyroxine-Na from aqueous solutions with hydrogel synthesized by low-temperature treatment of ion exchange salt with NaCl of quaternized product of N,N-diethyl alkyl derivative chitosan (*DEMX*) with methyl iodide. Thus, for the preparation of complexes with different content of levothyroxine with hydrogel, the sorption process was conducted dependent on the pH of the medium, the ionic strength of the solution and the concentration of the drug, the amount of gel and temperature. In addition, the degree of swelling and the kinetics of degradation of the synthesized hydrogel in different media were studied. Each of the levothyroxine-DEMX forms obtained is suitable for medical use by preserve the active drug in the required dose. Each sample differs in the amount of levothyroxine in micrograms, which determines its required dose.

Experimental part

Reagents

Chitosan average molecular weight 35 kDa (deacetylation degree 85-87%), acetaldehyde (≥99.0%), $NaBH_4$ (chemically pure ≥96%), acetic acid (Glacial), ethanol (95%), acetone (≥99.9%), diethyl ether (1 ppm inhibitor, anhydrous, ≥99.7%), NaCl (BioXtra, ≥99.5%), acetonitrile (99.8% anhydrous), and NaOH from Sigma-Aldrich. To recall, methyl iodide stabilized with metallic copper (99% c.p.) is from Acros Organics.

Thyroxine-Na pentahydrate (CAS 6106-07-6) was also obtained from Sigma Aldrich. The molar mass is 816.67 $g \cdot mol^{-1}$ and adsorption maximum is observed at a wavelength of 227 nm. The pK values of ionizing chemical functional groups are as follows (Fig. 2):

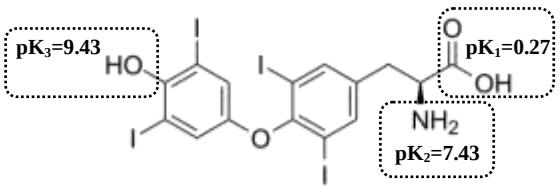

Fig. 2. Chemical structure of levothyroxine

pK_{a1}=0.27; pK_{a2}=7.43 and pK_{a3}=9.43 where K_1, K_2 and K_3 belong to –COOH, phenol and -OH groups, respectively.

Preparation of hydrogel sorbent

The synthesis of DEMX was carried out in line with the appropriate method [8] and improved by us. Thus, 5 g of DEMX is dispersed in 20 ml of 1% acetic acid solution and mixed continuously until it is completely dissolved. The solution is poured into a Petri dish and stored at -20 °C for 15 hours, then added to a 3 M solution of alkali in cold ethanol and stored again at -20 °C for one day. Finally, the hydrogel is washed with 50% ethanol solution, then with distilled water until a neutral medium is obtained, dried at 35-40 °C for 2 days to a stable weight, crushed and passed through a 0.02 mm sieve.

Absorption study

The effect of pH medium,initial concentration of the drug, dose of hydrogel and temperature on the sorption of levothyroxine with a DEMX-based hydrogel structurally absorbent was carried out systematically. Thus, sorption processes were performed in the amount of 5-200 mg of DEMX, in the range of pH 1-10 medium, and in the concentration range of 10-50 mg/L of drug for 24 hours at 20; 30; 40 and 50 °C temperatures. The sorption volume was 20 ml in all cases and sorption degree ($R_{\%}$) and equilibrium sorption capacity of gel (Q_{eq}, mg·gr^{-1}) were calculated according to equations 1-2.

$$R_{\%} = \frac{C_0 - C_{eq}}{C_0} \times 100 \quad (1) \qquad Q_{eq} = \frac{C_0 - C_{eq}}{m} \times V \quad (2)$$

Where, C_0 and C_{eq} were initial and equilibrium concentrations of levothyroxine, mg·L^{-1},

V- sorption volume, mL, *m* was *DEMX* dose, g.

Based on the sorption values, the dependence of the sorption capacity and the C_{eq}/Q_{eq} ratio on the equilibrium concentration of levothyroxine and the function $logQ_t=f(lgC_t)$ were established. Based on the equilibrium state, linear dependence plots were formed according to the Langmuir and Freundlich isotherm models of sorption.

The degree of swelling of the gel was calculated by equation equation (3) according to the increase in the mass of the dry sample at certain time intervals. The degradation tests of *DEMX*-based hydrogel were performed using equation (4) according to the weight loss by incubation for 1-30 days in a phosphate buffer saline solution (PBS), 3 mol/L H_2O_2, and 1 mg/ml elastase solution.

$$Swelling\ ratio_{\%} = \frac{W_w - W_{dry}}{W_{dry}} \times 100 \quad (3) \qquad Weight\ loss_{\%} = \frac{W_2}{W_1} \times 100 \quad (4)$$

Results and discussion

The structure and content of the DEMX derivative of chitosan synthesized by us in order to increase the hydrophilicity have been studied in detail [8].

The gel structure and schematic description of the process obtained gel at freeze temperature are shown in Fig.3. It found that the processing of quaternized alkyl derivatives of chitosan at freeze temperature forms crystalline and hydrogen bonds between functional groups in macromolecules which is characterized by its cross-linking structure. As a result, the polymer forms a gel in aqueous and pH solutions. The formation of a gel structure and the ability ionization of functional groups by absorbing water molecules to volume allow the immobilization of drugs with DEMX by sorption [7].

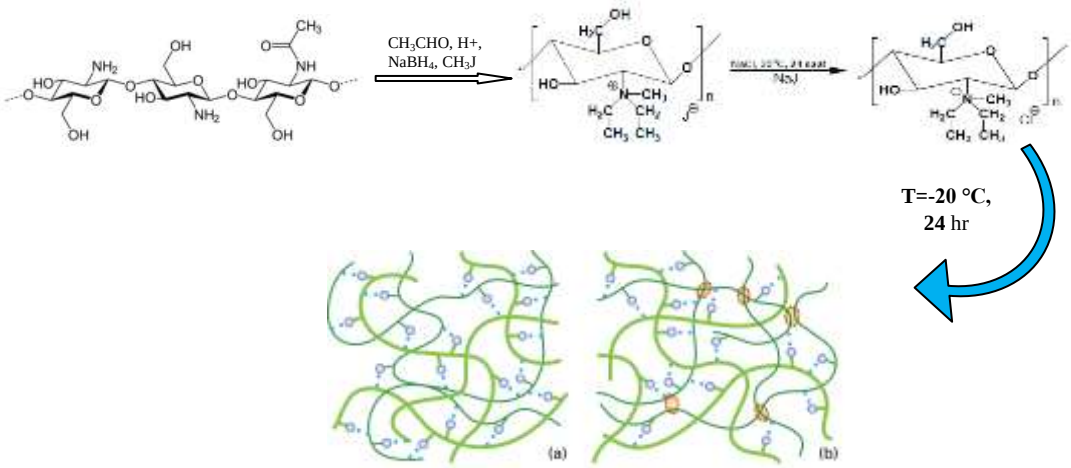

Fig. 3. Synthesis reactions of *DEMX* from chitosan and hydrogel, a - hydrogen bond, (b) - crystalline bond

As is known, chitosan is a macromolecule with pK_a=6.3-6.5 with 80-85% - NH_2 groups [9,10]. Substitution of amine groups with ethyl groups to certain extent after quaternation reduces its pKa value to 3.8-4.3 which affects its solubility. Besides, the DEMX hydrogel has more positively charged chains. This allows it to easily sorb small-molecule drugs with relatively high pKa.

Initially, levothyroxine with an initial concentration of 50 mg/L was sorbed with 2.50 $g \cdot L^{-1}$ DEMX at 20 °C for 24 hours at pH=1-10, equilibrium concentrations were determined, gel drug capacity and sorption degree were calculated (Fig. 4).

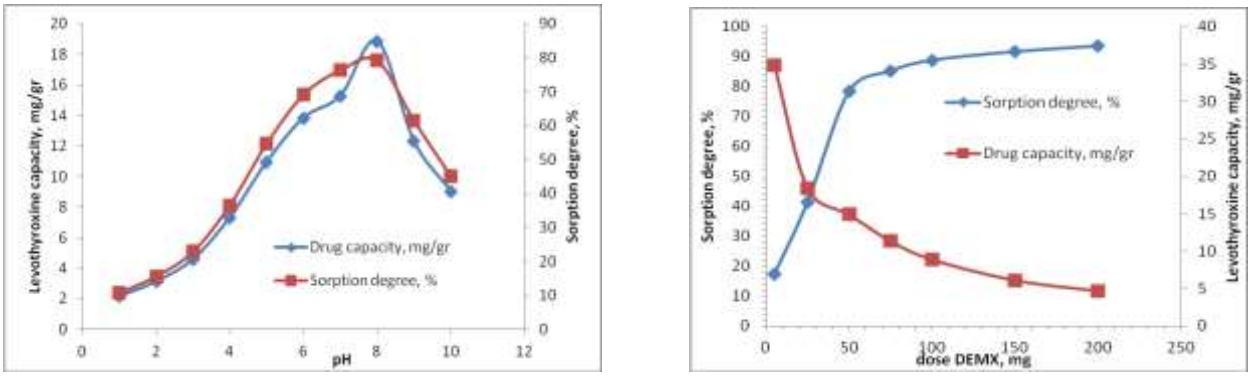

Fig. 4. Dependence of levothyroxine sorption with *DEMX*-based hydrogel from the pH medium and gel dose, T=20 °C, t=24 hr, V=20 mL, C_0=50 mg/L.

As can be seen from Figure 4, the DEMX gel has a levothyroxine sorption rate of 10-18% and a drug capacity of 2-2.4 mg/g at low pH. This is due to the positive charge of both phases in the same medium due to the protonation of the functional groups of the gel and levothyroxine. In this case, sorption occurs with a small part of charge interaction between the -COO- groups in levothyroxine and the protonated amine groups. Effective and higher sorption with DEMX was found to occur in the pH range of 6-9. This is explained as being due to the fact that levothyroxine is easily attracted to DEMX by hydrogen bonding, electrostatic and orientation forces due to its neutral and more negatively charged in this medium [11]. In next studies, pH=8 of the medium were taken as the optimal sorption conditions.

Fig.4 also shows the results of the dependence of levothyroxine sorption on the dose of DEMX at pH=8. As can be seen, the sorption degree of the gel decreases as the dose of gel increases, and after 50 mg of the dose it reaches equilibrium with a sorption rate of 80-83%. This is due to the increase in the concentration of active centers in a unit volume with an increase in the dose of gel. The decrease in drug capacity is due to the increase in the value of the dose of gel in the denominator in (2) equation. The optimal dose of 50 mg of gel for next sorption processes was selected.

The initial concentration of sorbate in sorption processes is the main factor affecting its distribution in the solid and liquid phases. Conducting such studies at different temperatures helps to obtain detailed information about the mechanism of sorption. For this purpose,, the presence of 50 mg DEMX dose, at pH=8, in drug solutions with an initial concentration of 10-50 mg/L range the sorption process was carried out at steady state at 20; 30; 40 and 50 °C for 24 hours.

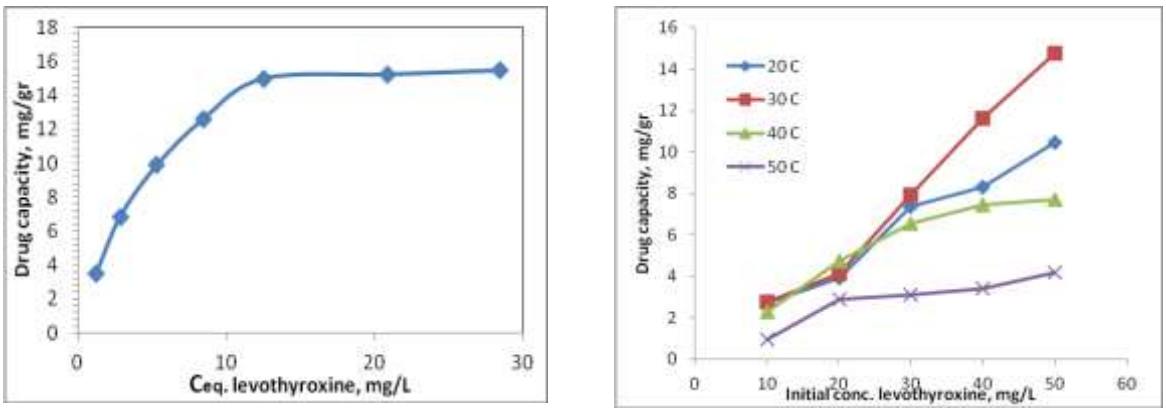

Fig. 5. Dependence of *DEMX* drug capacity from equilibrium and initial concentration of levothyroxine at different temperatures

As can be seen from Fig. 5, after the 10-12 mg/L equilibrium concentration of levothyroxine, the gel drug capacity begins to remain stable, and at a temperature of 30-40 °C the sorption was more effective and characterized by a high drug capacity. An increase in the concentration of levothyroxine in the solution results in rapid saturation of the sorbent due to the constant gel mass. The stable proportion of active centers in the hydrogel content does not allow the more absorption of drugs. [12]. After 40 °C, the gel capacity decreases which is due to the dual nature of the sorption process. The observed sorption by a different mechanism depending on the temperature was explained in the next study.

It is known that according to the experimental results of sorption isotherms [13], the most optimal models for the isotherm in Fig.5 are Langmuir and Freundlich models. The Langmuir model is suitable for ideal homogeneity of the sorption surface, while the Freundlich model is suitable for extremely heterogeneous surfaces. The functions $C_e/Q_e=f(C_e)$ (Langmuir model) and log $logQ_e=f(logC_e)$ (Freundlich model) of the sorption isotherm results were established and the dependence was determined to be linear (Fig. 6).

It is possible to determine the empirical constants of levothyroxine sorption by *DEMX* by applying regression coefficients and the formulas of the two-parameter Langmuir and Freundlich models from Fig. 6. As can be seen, the sorption of levothyroxine at 1.5-13 mg/L equilibrium concentration by *DMEX*-based gel is compatible with both Freundlich and Langmuir models of isotherm.

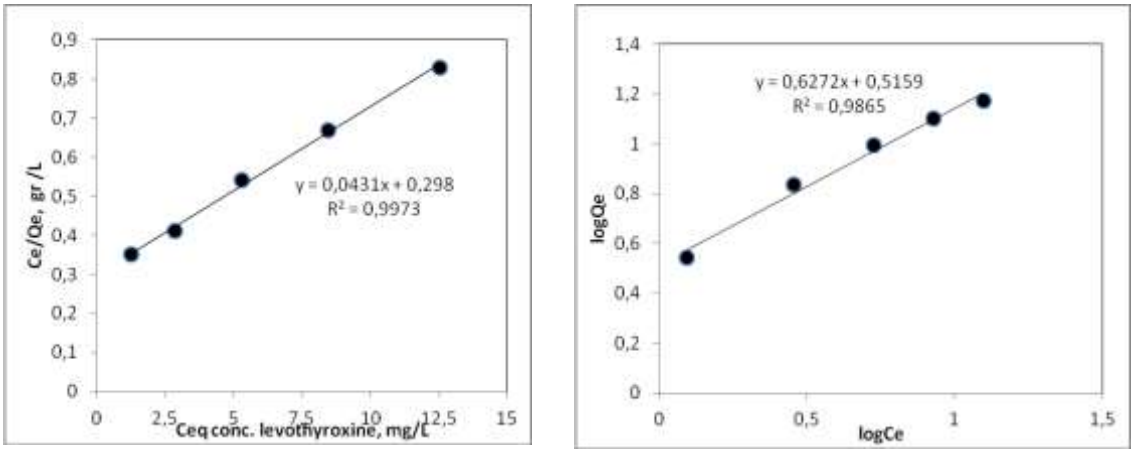

Fig. 6. Linear form of levothyroxine sorption isotherm according to Langmuir and Freundlich models

Thus, the sorption of levothyroxine up to the 12-15 mg/L equilibrium concentration takes place in energetic equivalent centers, and the sorbate is localized in separate sorption centers. In this case, a monomolecular layer is formed because each center interacts with only one sorbate, and levothyroxine molecules do not interact with each other because the sorption takes place in separate sorption centers. At subsequent values of equilibrium concentration, the sorption takes place mainly in non-equivalent centers, ie on heterogeneous surfaces, and the monomolecularity of the drug is maintained. The study made it possible to show that the sorption isotherms fitted to the Langmuir model at all temperature values (Fig.7).

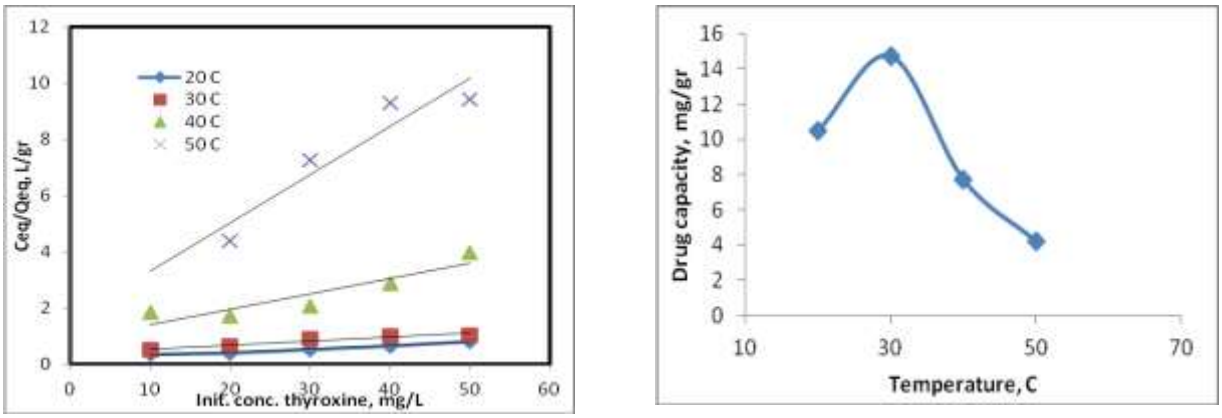

Fig. 7. Fitt of levothyroxine sorption isotherm to Langmuir model at different temperatures. Temperature dependence of drug capacity

It revealed that an increase in temperature of 30-37 °C leads to an increase in the capacity of the levothyroxine which proves that the process is endothermic in nature. Also, an increase in the mobility of the macromolecule up to 37 °C leads to the opening of active sites, and this process is accelerated by increasing the mobility of the levothyroxine molecule [14]. This proves that levothyroxine is immobilized to *DEMX*-based gel by chemical sorption between 30 and 40 °C. In the next increase of temperature, the decrease of gel capacity is due to the desorption process. This suggests that levothyroxine was immobilized to the active centers of the gel not by covalent bonding but by coordination or weak forces.

The swelling and degradation characteristics of the matrix are important

factors in determining the delivery ability of levothyroxine after immobilization by sorption to *DEMX*-based hydrogel. For this purpose, both swelling degree and degradation of 50 mg gel samples were studied in different medium (Fig. 8).

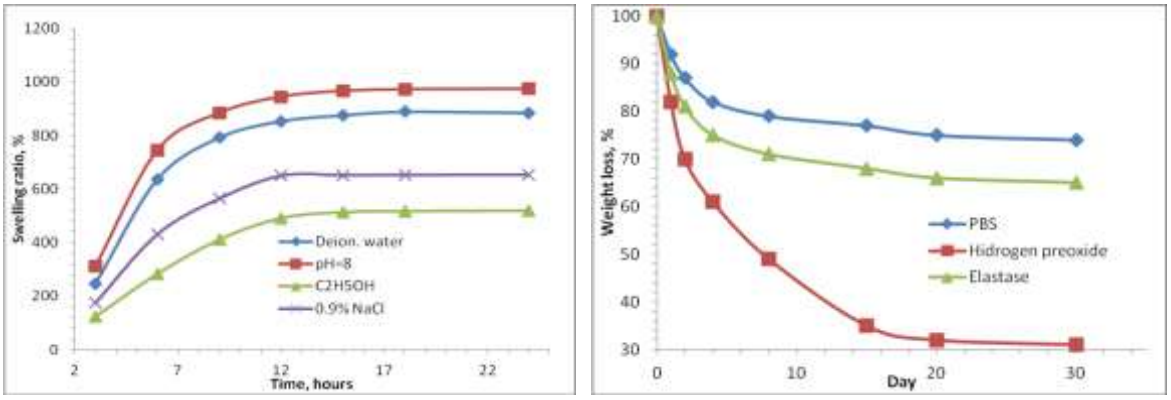

Fig. 8. The swelling kinetics and degradation tests of *DEMX*-based gel in different mediums, T=24 °C, V=20 mL.

As can be seen, the good ionization of the functional groups of the gel at pH=8 makes its swelling degree higher than in other mediums. The swelling in a 50% alcohol solution is mainly caused by the absorption of water molecules and the formation of hydrogen bonds [15,16]. It was also found that in a relatively aggressive H_2O_2 environment, oxidation of the functional groups of the gel and the start of destruction lead to more mass loss. In the elastase and PBS mediums, the degradation was 28% and 17%, respectively, within 10 days.

The results obtained suggest that *DEMX*-based hydrogel can be used in biotechnology and medicine by sorption of levothyroxine under existing conditions and preparation of complexes containing 5-50 mcg of the active drug [17-20].

Acknowlegements

The research was carried out in collaboration with the National Academy of Sciences of Azerbaijan and the Italian National Research Council in keeping with the project *"In vivo biological study of the encapsulation of L-thyroxine in chitosan N-trimethyl iodine derivative and its long-term controlled release*" according to the order of the Presidium of ANAS No.7/5 March 14, 2018.

References

1. Feksa L.R., Troian E.A., Muller C.D., Viegas F., Machado A.B., Rech V.C. Hydrogels for biomedical applications. *Nanostructures Eng.Cells.Tissues Organs*. 2018, vol. 54, pp. 403–438.
2. Sevda F., Dilgam T., Nizami Z. A review on enterosorbents and their application in clinical practice: Removal of toxic metals. *Colloid and Interface Science Communication*s**,** 2021, vol. 45, pp.1-11.
3. Zhao W., Jin X., Cong Y., Liu Y., Fu J. Degradable natural polymer hydrogels for articular cartilage tissue engineering. *J. Chem Technol Biotechnol*, 2013, vol. 88 (3), pp. 327-339.
4. Tapdiqov Sh.Z., Zeynalov N.A., Taghiyev D.B., Humbatova S.F., Mammedova S.M., Nasiyyati E.F., Babayeva D.T. Hydrogels for Immobilization of Trypsine Based on Poly-N-vinypyrrolidone and Arabinogalactan Graft Copolymers. *Journal Chemical Society of Pakistan*, 2015, vol. 37 (12), pp. 1112-1118.

5. Domalik-Pyzik P., Chłopek J., Pielichowska K. Chitosan-Based Hydrogels: Preparation, Properties, and Applications, in: Mondal, M.I.H. (Ed.), Cellulose-Based Superabsorbent Hydrogels. Springer International Publishing, Cham, 2019, pp.1665–1693.
6. Jayeon S., Hansol K., Chang Y.L., Junhyeok Y., Won S.Y., Hyun G.P. Identification of thyroid hormone/thyroid hormone receptor interaction based on aptamer-assisted protein-induced fluorescence enhancement. *Biosensors and Bioelectronics,* 2021, vol. 191, p.113444.
7. Aleem A.R., Shahzadi L., Alvi F., Khan A.F., Chaudhry A.A., Rehman I.Ur., Yar M. Thyroxin releasing chitosan/collagen based smart hydrogels to stimulate neovascularization. *Materials and Design*, 2017, vol. 133, pp. 416-425.
8. Tapdigov Sh.Z., Safaraliyeva S.F., Theato P., Zeynalov N.A., Tagiyev D.B., Raucci M.G., Hasanova M.X. Synthesis of N,N-Diethyl, N-Methyl Chitosan Chloride with Certain Quaternization Degree and Molecular Spectroscopic and Thermo-Morphological Study of the Alkylation. *J. Biomimetics, Biomaterials and Biomedical Engineering*, 2018, vol. 39, pp. 77-88.
9. Tapdigov Sh.Z. A Drug-Loaded Gel Based on Graft Radical co-Polymerization of N-Vinylpyrrolidone and 4-Vinylpyridine with Chitosan. *Cellulose Chemistry and Technology*, 2020, vol. 54 (5-6), pp. 429-438.
10. Tapdiqov Sh.Z., Zeynalov N.A., Tagiyev D.B., Safaraliyeva S.F., Gasimov E.M., Hasanova M.Kh., etc al. Optimal Conditions for graft radical copolymerization of N-vinylpirrolidon and 4-vinylpiridine into chitosan. *Chemical Problems*, 2018, vol. 16(4), pp. 505-513.
11. Islam K.N., Ihara M., Dong J.H., Kasagi N., Mori T., Ueda H. Direct Construction of an Open-Sandwich Enzyme Immunoassay for One-Step Noncompetitive Detection of Thyroid Hormone T4. *Analitical Chemistry*, 2011, vol. 83, pp.1008–1014.
12. Mammadova S.M., Tapdigov Sh.Z., Humbatova S.F., Zeynalov N.A., Guliyeva A.R., Gasimov E.M., Research into Sorbtion Properties and Structures of Polymer Hydrogel Immobilized by Doxorubicin. *Chemical Problems,* 2018, vol.16 (3), pp. 316-322.
13. Muhammad H.M., Lubna Sh., Razia B., Sher Z.S., Abdul S.K., Ather F.K., Aqif A.C., Ihtesham Ur.R., Muhammad Y. Thyroxine-loaded chitosan/carboxymethyl cellulose/hydroxyapatite hydrogels enhance angiogenesis in in-ovo experiments. *International Journal of Biological Macromolecules,* 2020, vol. 145, pp.1162-1170.
14. Wang X., Chen H., Lin J.M., Ying X.T. Development of a highly sensitive and selective microplate chemiluminescence enzyme immunoassay for the determination of free thyroxine in human serum. *International Journal of Biological Sciences*, 2007, vol. 3, pp. 274–280.
15. Tapdigov Sh.Z. The bonding nature of the chemical interaction between trypsin and chitosan based carriers in immobilization process depend on entrapped method: A Review. *International Journal of Biological Macromolecules,* 2021, vol. 183, pp.1676-1696.
16. Tapdiqov Sh.Z., Zeynalov N.A., Taghiyev D.B., Akhmedova U.M., Mammadova A.I., Hasanova M.Kh., Amirov M.A. Research into properties and structure of basic polysaccharide in *prunus domestica* (cherry). *Chemical Problems*, 2018, vol.16, no. 1, pp. 35-43.
17. Mammedova S.M., Tapdiqov Sh.Z., Humbatova S.F., Zeynalov N.A. Spectroscopic Investigated Interaction Between Silver Nanocomposites Based of poly-N-vinylpyrrolidone and Doxorubucine for Drug Delivering. *Journal of Chemistry and Chemical Engineering*, 2014, vol. 8, pp. 800-804.
18. Tapdigov Sh.Z., Mammadova S.M., Taghiyev D.B., Zeynalov N.A. Investigation Chemical Interaction type of Polyacrylic acid based Hydrogel with Doxorubicin Hydrochloride. *American Chemical Science Journal,* 2016, vol.12(2), pp.1-9.

19. Mammadova S.M., Tapdigov Sh.Z., Humbatova S.F., Safaraliyeva S.F., Hasanova M.Kh., Zeynalov N.A. Immobilization of doxorubicin to polyacrylic acid-based hydrogel and the study of swelling ability. *Chemical Problems*, 2016, vol. 16, pp. 377-385.

20. Mammadova S.M., Tapdigov Sh.Z., Humbatova S.F., Safaraliyeva S.F., Hasanova M.Kh., Zeynalov N.A. Sorption of doxorubicin with polyacrylic acid based hydrogel and researching their structures. *Journal of Baku Engineering University, Chemistry and Biology*, 2017, vol.1, no. 1, pp. 35-43.

LEVOTİROKSİNİN XİTOZANIN ALKİL ƏVƏZLİ ŞİFF ƏSASLI HİDROGELİ İLƏ SORBSİYASI PROSESİNİN TƏDQİQİ

Samirə Səfərəliyeva[a], Dilqəm Tağıyev[a], Nizami Zeynalov[a], Şamo Tapdıqov[b], Mariya Rauççi[c]

[a]AMEA akad. M.Nağıyev adına Kataliz və Qeyri-üzvi Kimya İnstitutu,
AZ 1143, Bakı ş., H.Cavid pr.113, E-mail: safaraliyeva2017@mail.ru
[b]SOCAR Neftqazelmitədqiqatlayihə İnstitutu
[c]İtaliya Milli Tədqiqatlar Şurası, Polimerlər, Kompozitlər və Biomateriallar İnstitutu

Xülasə: *Qalxanabənzər vəzinin hormon əvəzedicisi olan Na-levotiroksin pentahidratın yan təsirlərini azaltmaq məqsədi ilə onun xitozanın yeni alkil törəməsinin kvaternizə olnmuş duzu ilə sorbsiyası öyrənilmişdir. Duzun (gelin) tərkibində preparatın miqdarı mkq tərtibdədir və gel-levotiroksin bioloji aktivlik göstərə bilən kompleks formasındadır. Bu məqsədlə levotiroksin-Na-un sulu məhluldan hidrogel daxilinə və səthinə statik şəraitdə sorbsiya prosesi həyata keçirilmişdir. Hidrogelin tutumunun mühitin pH-ı və ion qüvvəsi, hidrogelin miqdarı, preparatın qatılığı və temperaturdan asılılıqları müəyyən edilmişdir. Göstərilmişdir ki, xitozan əsaslı hidrogel ilə levotiroksinin effektiv sorbsiyası mühitin pH-nın 6-8.5 qiymətində, levotiroksinin 50 mq/L qatılığında 10-50 mq hidrogel iştirakında optimal olub, T=40 °C-dən sonra sorbsiya dərəcəsi azalmağa başlayır. Sorbsiya proseslərinin izoterm nəticələri əsasən Lənqmür və müəyyən qədər Freyndlix tənliklərinə tabe olması müəyyən edilmişdir. Göstərilmişdir ki, oksidləşdirici mühitində gelin deqradasiyası 2 həftə ərzində 70%, elastaza və PBS mühitində isə 17-20%-ə yaxın olur.*
Açar sözlər: *xitozan, kvaternizə, gel, qalxanabənzər vəzin hormonu, Na-levotiroksin pentahidrat, sorbsiya tutumu, izoterm.*

ИССЛЕДОВАНИЕ ПРОЦЕССОВ СОРБЦИИ ЛЕВОТИРОКСИНА ГИДРОГЕЛЕМ ХИТОЗАНА НА ОСНОВЕ АЛКИЛЗАМЕЩЕННОГО ОСНОВАНИЯ ШИФФА

Самира Сафаралиева[а], Дильгам Тагиев[а], Низами Зейналов[а], Шамо Тапдыгов[б], Мария Раччи[c]

[а]Институт Катализа и Неорганической Химии им. акад. М.Нагиева
Национальной АН Азербайджана
AZ1143, г. Баку, пр. Г.Джавида, 113, e-mail: safaraliyeva2017@mail.ru
[б]Научно-исследовательский и проектный институт нефти и газа SOCAR
[c]Национальный Исследовательский Совет Италии, Институт Полимеров, Композитов и Биоматериалов

Аннотация: *С целью снижения побочных эффектов заменителя тиреоидного гормона левотироксина натрия пентагидрата исследовали его сорбцию кватернизованной солью нового алкилпроизводного хитозана. Количество препарата в соли (геле) указано в мкг, а гель-левотироксин*

представлен в виде комплекса, способного проявлять биологическую активность. С этой целью был проведен процесс сорбции левотироксина натрия из водного раствора в объеме и на поверхности гидрогеля в статических условиях. Определена зависимость емкости гидрогеля от pH и ионной силы среды, количества гидрогеля, концентрации препарата и температуры. Показано, что эффективная сорбция левотироксина гидрогелем на основе хитозана оптимальна при pH 6-8,5, концентрации 50 мг/л в присутствии 10-50 мг левотироксина, а после температуры 40°C начинает снижаться степень сорбции. Установлено, что изотермические результаты сорбционных процессов подчиняются, в основном уравнениям Ленгмюра и в некоторой степени Фрейндлиха. Показано, что деградация геля в окислительной среде составляет около 70% за 2 недели, а в среде эластазы и PBS – около 17-20%.

Ключевые слова: *хитозан; кватернизация; гель; тиреоидный гормон; левотироксина натрия пентагидрат; сорбционная емкость; изотерма.*