

Sorption of medical preparations by chitosan

Anna Beliaeva^{1,*}, and Galina Nianikova¹

¹Saint-Petersburg State Institute of Technology, 190013, 26 Moskovsky prospect, St. Petersburg, Russia

Abstract. The article provides information about sorption properties of crab chitosan in relation to Analgin, Aspirin, Quamatel, Mydocalm, Paracetamol, Tsifran and Phtalazol. Quantitative determination of medicines' amount before and after sorption was performed by HPLC-MS method with the preliminary plotting of calibration curves. The sorption capacity of chitosan taken in different concentrations was determined. Sorption isotherms and kinetic curves of medications' sorption by chitosan were plotted. It has been shown that the maximum degree of sorption in static conditions for all studied medicines was achieved within an hour after the beginning of the sorption process.

1 Introduction

Chitosan still remains one of the most scientifically interesting biopolymers and, moreover, perspective for practical use. Chitosan is known for its characteristic sorption properties in relation to heavy and transition metals, radionuclides, some synthetic dyes and pesticides [1-5].

Due to such abilities, chitosan is used in medicine, cosmetics and crop production, textile, food and paper industries, as well as in the environmental measures [6-7].

Medicine should be highlighted as a particularly perspective sphere of chitosan use. It is used in ointments, wound coverings, targeted drug delivery, for the surgical sutures manufacturing, for the obesity and atherosclerosis treatment, and also as an enterosorbent [7-9].

Chitosan derivatives have also found an application in medicine. Thus, the use of 40% chitosan ascorbate in membrane dialysis accelerated healing of an experimental purulent wound by 5-7 days compared with the use of 33% polyvinylpyrrolidone [8].

Due to scientific studies, various biological effects of chitosan have been identified [8, 10]:

- the ability to bind and remove excess cholesterol and fats from the body (*hypcholesterolemic* and *hypolipidemic*);
- the ability to regulate the acidity of gastric juice (*antiulcer*);
- ability to neutralize toxic peroxides (*antioxidant*);
- the ability to reduce the load on the liver (*hepatoprotective*);
- the possibility of binding and further elimination of toxic elements from the human body (*antitoxic*);

* Corresponding author: belyaeva_any@mail.ru

- stimulation of the immune system functions, whereby the body's resistance to infections is increasing (*immunomodulating*);
- binding of radioactive isotopes and their subsequent elimination (*radioprotective*);
- the protection of human body from certain viral infections (*antiviral*);
- inhibition of a number of microorganisms (*antibacterial*);
- ability to stimulate the healing of ulcers, burns and wounds (*regenerating*);
- stimulation of normal human microflora (*prebiotic*).

Currently, there is an acute problem of the human body toxicosis caused by an excessive intake of medicines, for example, through negligence or intentionally – in the case of suicide. One of the most effective methods of detoxification is sorption. Chitosan is the first sorbent, due to its high sorption activity, selectivity, non-toxicity and compatibility with human tissues, to keep in mind for the use in detoxification.

2 Materials and methods

In this study, seven medical preparations (Analgin, Aspirin, Quamatel, Mydocalm, Paracetamol, Tsifran and Phtalazol) were selected on the basis of the data from the journal of accounting for chemical and toxicological tests of the toxic- and radiological laboratory of Clinic for Military Field Therapy of the Military Medical Academy named after S. M. Kirov of the Ministry of Defense of Russian Federation. The medicines' selection was based on the frequency of their detection during chemical and toxicological tests, as well as on their chemical structure and the ability to bind to chitosan.

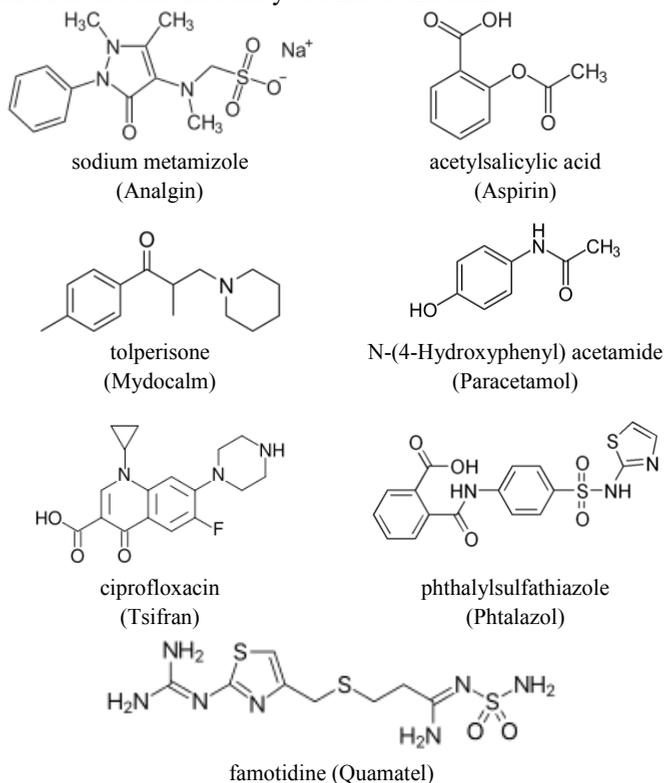


Fig.1. Structural formulas of selected medical preparations' active substances.

Food crab chitosan (in the form of powder), manufactured by Russian Federal Research Institute of fisheries and oceanography, Moscow, was used as a sorbent. The molecular weight of this chitosan is 83.7 kDa, the degree of deacetylation - 79.7%. It complies with sanitary rules according to SanPiN 2.3.2.1078-01 "Hygienic requirements for safety and nutritional value of food products".

To prepare medicine solutions, the tablets were ground in a mortar, then weighed on an analytical balance. Weighed samples were dissolved in a volumetric flask using distilled water and, if needed, an ultrasonic bath.

For the preparation of chitosan solutions, the required weights were dissolved in volumetric flasks in a 1% solution of acetic acid.

In the studies of the effect of chitosan concentration on the degree of sorption of medicines, chitosan was taken at concentrations of 0.125; 0.25; 0.5 and 1.0 mg/mL. The concentration of medical preparations was taken as 1.0 mg/mL.

For the sorption isotherms' plotting, the initial medicine concentrations were varied, and the chitosan concentration was taken as 1.0 mg/mL.

The sorption process was carried out in a stationary mode, at room temperature for 1 h, at pH = 6.5.

While studying the kinetics of medical preparations' sorption by chitosan, sampling was carried out after 15, 30, 45, 60, 120, 180 and 240 minutes from the beginning of the experiment.

Quantitative determination of the content of medicines before and after sorption was performed by HPLC-MS method with the preliminary plotting of calibration curves; using Agilent 1200, detector: Agilent 6120 LC/MS, Zorbax SB column - C18, 150 mm x 4.6 mm, 5 μm, at temperature of (25±1)°C. Composition of the mobile phase was taken as following: phosphoric acid: acetonitrile: deionized water = 2:400:600 (v/v/v).

For the implementation of the calibration curve plotting, solutions of medicines with known concentrations were prepared in triplicate and analyzed using the stated HPLC-MS method.

3 Results and discussion

The degree of medical preparations' sorption by chitosan was determined depending on their initial concentration. The concentration of chitosan was taken as 1 mg/mL. The results are presented in the Figure 2.

The degree of sorption of each medical preparation (X , %) was calculated according to the Formula 1:

$$X = \frac{(C_{init} - C_{equil})}{C_{init}} \times 100\% \quad (1)$$

where C_{init} – initial concentration of medical preparation, mg/mL;

C_{equil} – concentration of medical preparation after sorption, mg/mL.

It was determined that with an increase in the concentration of Analgin from 0.125 mg/mL up to 5.0 mg/mL the degree of sorption decreased from (89.4±0.7)% to (50.4±0.5)%. With an increase in the concentration of Aspirin from 0.125 mg/mL up to 5.0 mg/mL the degree of sorption decreased from (71.9±1.2)% to (51.1±1.1)%. With an increase in the concentration of Quamatel from 0.125 mg/mL up to 5.0 mg/mL the degree of sorption decreased from (75.3±0.9)% to (17.1±0.2)%. With an increase in the concentration of Mydocalm from 0.125 mg/mL up to 5.0 mg/mL the degree of sorption decreased from (24.2±0.8)% to (5.0±0.1)%. With an increase in the concentration of

Paracetamol from 0.125 mg/mL up to 5.0 mg/mL the degree of sorption decreased from $(99.9 \pm 0.4)\%$ to $(76.3 \pm 0.3)\%$. With an increase in the concentration of Tsifran from 0.125 mg/mL up to 5.0 mg/mL the degree of sorption decreased from $(47.02 \pm 0.47)\%$ to $(6.10 \pm 0.02)\%$. With an increase in the concentration of Phtalazol from 0.125 mg/mL up to 5.0 mg/mL the degree of sorption decreased from $(12.4 \pm 0.5)\%$ to $(2.4 \pm 0.1)\%$.

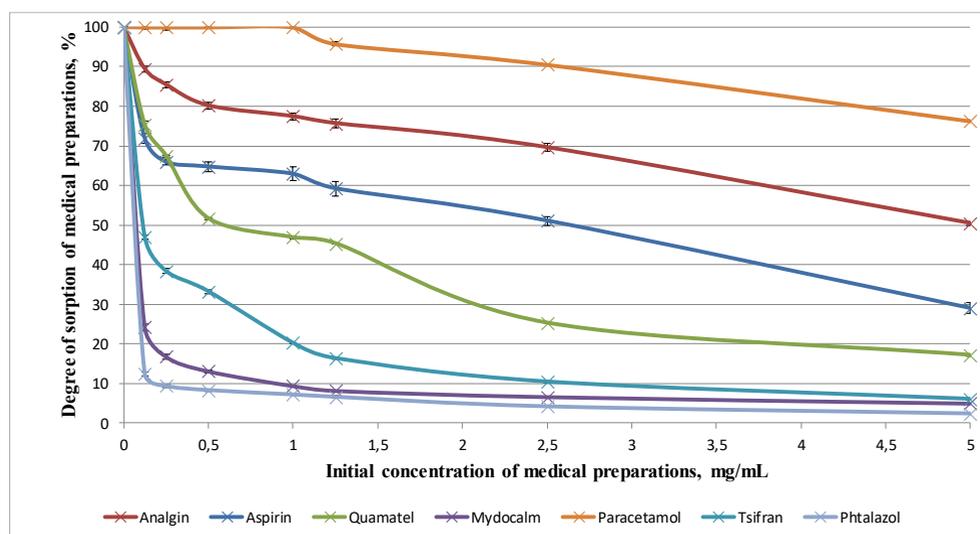


Fig.2. Study of the effect of medical preparations' concentration on the process of their sorption by chitosan.

Figure 2 shows that the degree of Paracetamol's sorption by chitosan is significantly higher compared to all other medicines.

With an increase in the concentration of medical preparations, the degree of sorption decreases due to saturation of the sorbent with an adsorbed substance.

Possible sorption mechanisms are presented in the Table 1. In addition, physical adsorption of the medical preparations in the pores of the sorbent is also a possible way of sorption.

Table 1. Possible mechanisms of medical preparations' sorption by chitosan [6, 9].

Functional group of medical preparation	Functional group of chitosan	Sorption mechanism
-OH	-NH ₂	Hydrogen bonding
=C=O	-NH ₂	Donor-acceptor mechanism
-A ⁻ *	-NH ₂ ⁺	Ionic bonding

Note: * -A⁻ – negatively charged ion

Hydrogen bonding is possible when chitosan is adsorbing Aspirin, Paracetamol, Tsifran, Phtalazol; donor-acceptor mechanism – Analgin, Aspirin, Mydocalm, Paracetamol, Tsifran, Phtalazol; ionic bonding – Analgin. Physical adsorption is possible for all the selected medical preparations.

The results of a study of the effect of sorbent concentration on the medical preparations' degree of sorption are shown in the Figure 3.

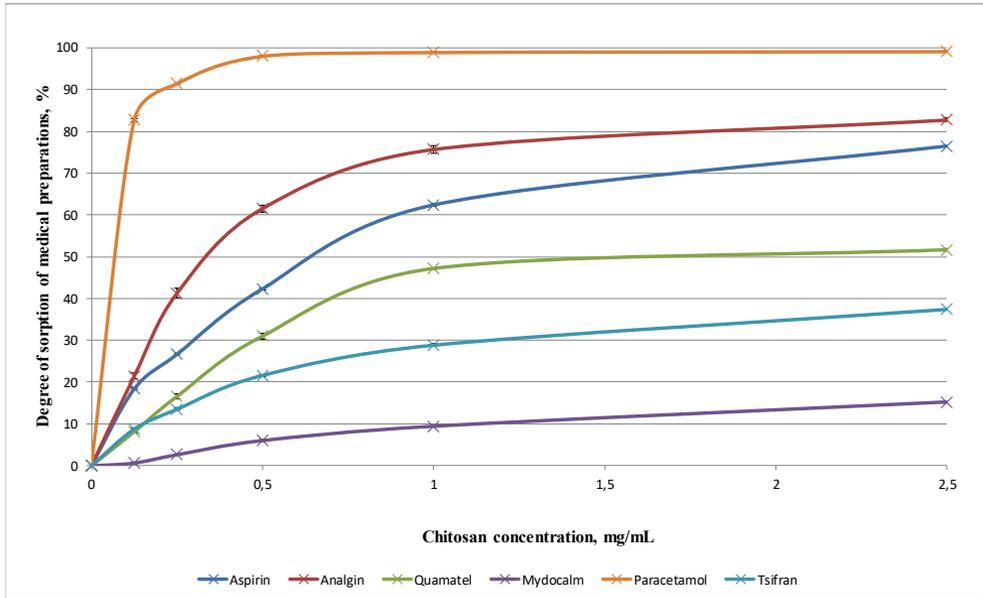


Fig.3. The effect of chitosan concentration on the degree of sorption of medical preparations.

Figure 3 shows that at the highest concentration of chitosan taken equal to 2.5 mg/mL the values of the degree of sorption of drugs were as follows: Analgin – (76.5±0.7)%, Aspirin – (82.7±0.5)%, Quamatel – (51.6±0.3)%, Mydocalm – (15.17±0.15)%, Paracetamol – (99.04±0.04)%, Tsifran – (37.43±0.12)%. No studies with Phtalazol were performed due to an extremely low degree of sorption of this medical preparation by chitosan.

It was of great interest to calculate the sorption capacity of chitosan for the subsequent comparison with other sorbents. Sorption capacity is the amount of substance that the sorbent can absorb per unit mass. The higher the value of sorption capacity, the more effective the sorbent.

Sorption capacity was calculated according to the Formula 2, sorption isotherms are shown in Figure 4.

$$SC = \frac{(C_{init} - C_{equil}) \times V_i}{m_{sorb}}, \quad (2)$$

where SC – sorption capacity, mg/g;
 C_{init} – initial concentration of medical preparation, mg/L
 C_{equil} – concentration of medical preparation after sorption, mg/L;
 V_i – sample volume, L;
 m_{sorb} – sorbent mass, g.

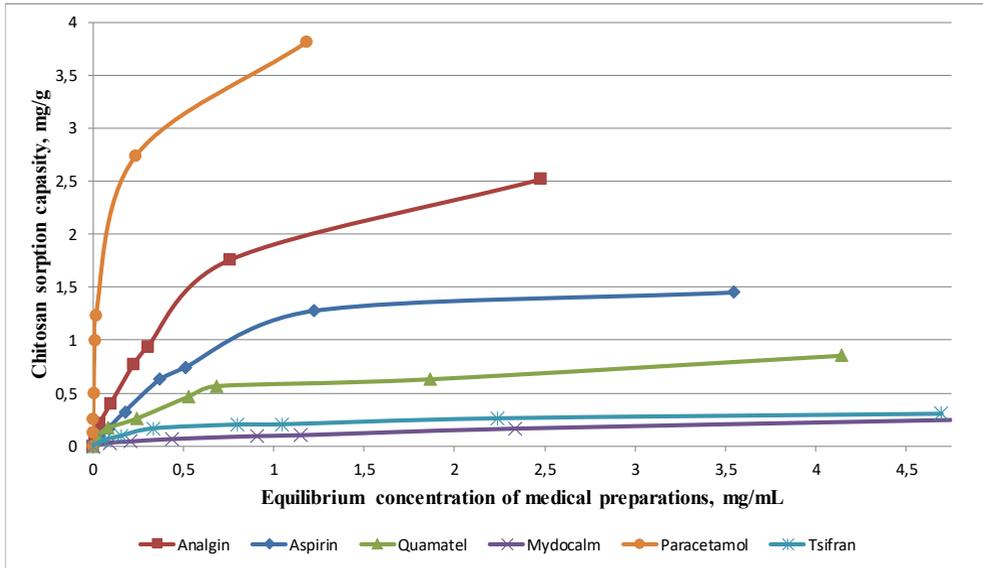


Fig.4. Sorption isotherms of the studied medical preparations by chitosan.

Figure 4 shows that the largest value of the sorption capacity of chitosan is achieved with sorption of Paracetamol, and the smallest – with sorption of Tsifran and Mydocalm.

Kinetics of the medical preparations' sorption by chitosan was studied. The results are presented in Figure 5.

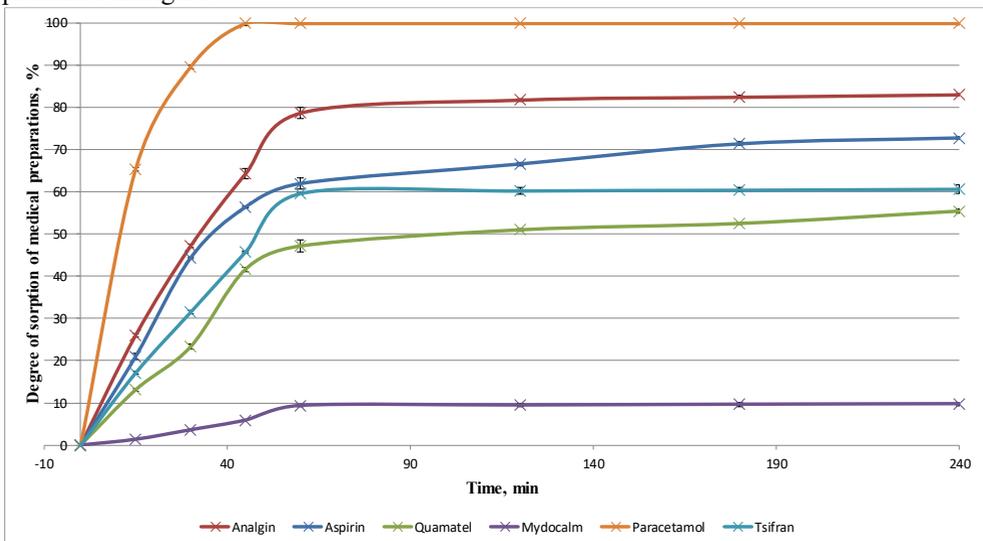


Fig.5. Kinetics of the medical preparations' sorption by chitosan.

It follows from the Figure 5 that the maximum degree of sorption for all medical preparations is achieved, on average, one hour after the start of the sorption process. This time is sufficient for the implementation of the hemosorption process, as well as the process of enterosorption, when it is necessary to adsorb the substances from the stomach or small bowel. Three hours after the beginning of sorption, desorption process did not occur.

4 Conclusion

The highest degree of sorption by crab chitosan at a concentration of 1.0 mg/mL was determined for Paracetamol ($99.5 \pm 0.2\%$), Analgin ($89.4 \pm 0.7\%$) and Aspirin ($71.9 \pm 1.2\%$). The maximum degree of sorption in static conditions for all studied medicines was achieved within an hour.

Considering the received data, it should be recommended to adjust the medicine regimen (single dose, time interval between doses of medicines, etc.) when combined with sorbents. In addition, it is necessary to take into account the sorption characteristics of chitosan in relation to various medicines while using it as a detoxification agent.

The usage of chitosan as a sorbent can be implemented in a complex of therapeutic measures to eliminate the consequences of poisoning the body with medicines, in particular, as a sorbent in such procedures as enterosorption, hemosorption, hemodialysis, hemofiltration, plasmapheresis and others, and also, possibly, for reinforcing the sorption properties of other enterosorbents.

The research was partially supported by FASIE.

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