

BEHAVIOUR OF TiO₂/CHITOSAN DISPERSION AS A FUNCTION OF SOLUTION pH

Agata Gozdecka, Agnieszka E. Wiącek*

*Department of Interfacial Phenomena, Faculty of Chemistry, Maria Curie-Skłodowska University, 20-031 Lublin, Poland
e-mail: a.wiacek@poczta.umcs.lublin.pl*

Abstract

This paper presents the physico-chemical characteristics of titanium dioxide/chitosan dispersion. The surface and electrostatic properties of TiO₂ particles in the electrolyte solution (NaCl) and in the presence of a biopolymer were determined by static and dynamic light scattering. The stability measurements were made under different conditions, where the variable was the dispersion pH. This paper mainly includes discussion of dispersion behaviour in neutral and alkaline environments. At each pH value (6–9), the addition of chitosan caused significant improvement in stability compared to the systems of base titanium dioxide. Of the tested systems, the most stable values of diameter and zeta potential for dispersion were found at pH 7. The study allowed the conclusion that the addition of chitosan to TiO₂ dispersion created the possibility of using such systems as a drug carrier for the controlled release of active substances sensitive to pH changes.

Keywords: *chitosan, titanium dioxide, pH, targeted therapy, adsorption*

Received: 15.02.2017

Accepted: 30.05.2017

1. Introduction

Recently, chitosan – a natural polymer – has been viewed as the most interesting compound of a commonly applied biopolymer, due to its valuable properties, relatively low cost and natural origin. It occurs naturally in the body armour of crustaceans, such as crabs, shrimp or krill, and in the cell walls of some fungi. However, on the industrial scale, it is obtained from chitin, largely by chemical deacetylation [1–2]. In recent years, the interest in this material has been continually increasing, due to its interesting properties that can be used in the creation of a variety of chemical bonds in a number of inorganic compounds as well as synergistic effects of some qualities between these compounds. Titanium dioxide is an example of such a compound. It is the most common and most durable of the titanium oxides. It exhibits amphoteric properties, which are more acidic than alkaline, and the pH value of its aqueous dispersion is similar to that of skin. TiO₂ powder is also characterised by high resistance and good chemical stability [3–4].

Both chitosan and TiO₂ have antibacterial, antifungal and non-toxic properties. In addition, these substances are biocompatible and biodegradable in the human body. These features have made them widely used products by pharmaceutical companies or medical care for many kinds of cosmetics, medicines and/or dressings with controlled release of active substances [5–10].

Dispersions of titanium (IV) oxide with the addition of chitosan can be used in the pharmaceutical industry and medicine. Therefore, it is essential to create optimal conditions for stabilising the dispersions of titanium dioxide by the chitosan solution, to meet the assumed functions in the complex systems. Finding the most favourable physicochemical parameters of TiO₂/chitosan dispersion in terms of their stability and biocompatibility was the main goal of this paper. The study analysed the size diameter, multimodal size distribution and zeta potential of the base dispersion of titanium dioxide and that of TiO₂/chitosan characterised by different pH values. The results of the tests conducted are expected to be important in the formation of tablets, controlled-release microcapsules and antibacterial covering.

2. Materials and Methods

2.1 Chitosan

Chitosan (Fig. 1) is a copolymer formed by two units: 2-acetamido-2-deoxy-β-D-glucopyranose and 2-amino-2-deoxy-β-D-pyranose. A large part of the second component is more soluble compared to chitin in many organic aqueous solutions and inorganic acids. Furthermore in contrast to chitin, polysaccharide chitosan which is formed, most often by chemical deacetylation of chitin in an alkaline medium, is dissolved in water, thereby increasing the interest of pharmaceutical companies [1, 2, 11]. In solutions of low ionic strength, chitosan takes the form of a stretched macromolecule, which is a result of mutual electrostatic repulsion between the segments of the chain. Increasing the ionic strength neutralises protonation, resulting in the loss of forces from the electrostatic repulsion, which, in turn, generates a compact structure of the chitosan molecules, regardless of the existing differences in molecular weight [11].

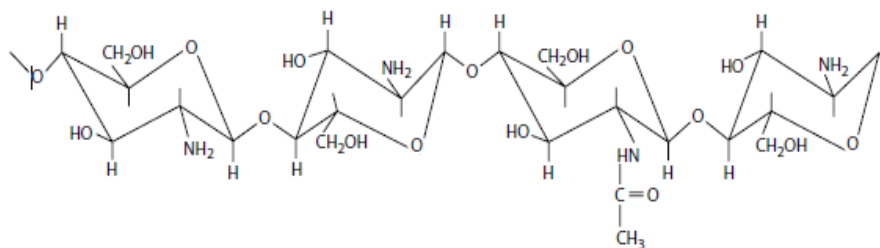


Figure 1. Structure of chitosan [1].

The most important characteristic of chitosan that has led to its widespread use is the presence of amino groups in the chain of the macromolecule. These are protonated under acidic conditions, and therefore the number of available groups may be the main parameter that allows overlapping of various processes in the chitosan molecule. Furthermore, in its structure it has primary or secondary hydroxyl groups located at the 3 and 6 carbon polysaccharide chains. These are responsible for the adsorption ability of the compound. This is very important for the creation of hybrid systems for the controlled release of active substances [2, 11–14]. Moreover, chitosan can help control the nanoparticle size and dispersion homogeneity due to its spreading on titanium oxide particles during system preparation. This is a consequence of the unique film-forming characteristics, the swellability in aqueous solution and gel forming properties of chitosan. These features have been exploited by us in the present study during the preparation of TiO₂/chitosan dispersion.

Chitosan is soluble in aqueous solutions of various acids. However, it does not have amphiphilic properties, so it cannot form micelles in water, but it can be moulded into various forms. Furthermore, it can form a porous structure by lyophilisation. With small amounts of acids, needed to dissolve chitosan, chitosan can be removed [5–6]. To summarise the above, it was found that chitosan can be used as a carrier sensitive to pH changes.

2.2 Titanium dioxide

Titanium is the tenth most prevalent element in the studied areas of the globe: according to estimates, its content is about 0.42%. It is a white, odourless powder. Despite high incidence, it is highly dispersed in nature and is unlikely to create large clusters of its own minerals. Titanium minerals are durable, resistant to water and atmospheric agents, and most of them are rutile (TiO₂), ilmenite (FeTiO₂) and titanite (CaTiSiO₅). Due to its high mechanical strength and low specific weight as well as corrosion resistance, titanium is suitable for aerospace or medicine. As an alloying addition to steel it improves its strength and flexibility. It is characterised by amphoteric properties: it reacts with concentrated sulfuric acid, it fuses with hydroxides, carbonates or oxides of other metals and it transforms into titanates. It does not dissolve in water.

2.3 Sample preparation

TiO₂ P25 Evonik (early Degussa), a fine-particulate, pure titanium dioxide (TiO₂ 99.9%), was used. For the treatment of the data, the refractive index of TiO₂ P25 was set at $n = 2.57$ (taking into account the ratio (80:20) of anatase ($n = 2.561$) and rutile ($n = 2.613$) in the mixture). To remove impurities, the following cleaning procedure described by Preočanin and Kallay was applied [15]. Additionally, dried oxide was

subjected to grinding in a mortar in order to obtain thorough homogeneity and dispersibility of molecules. The dispersions were prepared using 5 mg of the oxide for 50 cm³ of chitosan solution of suitable concentration.

For modification, chitosan (Acrōs Organics, ACRS34905) was used. The polysaccharide biopolymer (molecular weight 100,000–300,000) was applied without purification. The stock solution of chitosan (0.0001 mol/dm³) was prepared dissolving the weighed amounts of chitosan in a proper amount of acetic acid (1 M) at the ratio of 0.1 g of polymer in 1 mL of CH₃COOH, using Milli-Q water to fill to the required volume (50 cm³). Water used for preparation of all suspensions was purified in the Milli-Q Plus 185 system from Millipore (USA, the resistivity 18.2 MΩ cm). Next, concentrations of solutions were adjusted to suitable dilutions of stock solution, where the electrolyte solution (NaCl) of the concentration 10⁻³ mol/dm³ was the diluent.

The additional components NaCl, NaOH, HCl and CH₃COOH were analytical grade reagents (POCh S.A., Poland). The stability of the dispersion of titanium dioxide with chitosan depending on pH was studied using the chitosan solution of the concentration of 0.6x10⁻⁵ mol/dm³. The choice of this concentration was justified by determining stability in a concentration range of 0.4x10⁻⁶ mol/dm³ to 0.6x10⁻⁵ mol/dm³. The system of the chitosan concentration 0.6x10⁻⁵ mol/dm³ proved to be the most stable, as confirmed by the value of the stability coefficient, TSI = 5.9, the smallest value obtained for the systems in the series. Therefore, this system was accepted as the best for further investigation [16].

The series was elaborated according to the above scheme (look second paragraph in this section), changing the pH value using a small portion of the solutions of strong HCl acid (0.1 mol/dm³) or strong NaOH base (0.1 mol/dm³). The initial pH value (named in the text as natural pH) of the base titanium dioxide dispersion in the electrolyte solution was about 7, but the initial pH value (natural) of the TiO₂/chitosan dispersion was 3.2. Finally, the dispersions had the following pH values: 3; 4.8; 6; 7 and 9. The dispersions prepared in this way were subjected to the action of a homogeniser (5000 rpm) for 3 minutes. When the obtained pH value (after homogenization) was within the measurement error, the dispersion was investigated, which is described in the section 3.

2.4 Methods

The stability of the above systems was estimated based on two main measurement methods. In the first, dynamic light scattering was applied by the device Zeta Pals (Brookhaven, USA). Dispersion analysis is possible owing to the inbuilt laser whose action is based on light scattering. Its advantage is the possibility of measuring particle sizes and electrophoretic mobility (which is recalculated by the computer into the zeta potential based on the Smoluchowski or Hückel equation), using the same sample in both cases. Droplet or particle size distribution measurements are made, the polyacrylic cuvette with the studied solution is removed and, after putting an electrode into it, it is returned to the device to measure mobility by electrophoresis. The systems were investigated using a zetameter in the function of time, i.e. after 5 and 30 minutes and after 1, 2, 3 and 24 hours, when homogenization was over. Dispersions were studied at room temperature, i.e. 20±1 °C. The mean and effective diameters of the particles and electrophoretic mobility (calculated from this zeta potential) were measured.

The second measurements use the static light scattering method, and were made for each of the obtained titanium dioxide dispersions for two hours, which is sufficient to obtain equilibrium in a system of this type. The measurements of the percentage contribution of passing light, from which the value of the stability coefficient Turbiscan

stability index (TSI) was obtained, were taken at regular time intervals, i.e. every 15 minutes. Measurements of the stability coefficient (TSI) were made using a TurbiscanLab^{Expert} device. The analysis of dispersion stability is possible owing to the inbuilt electroluminescence diode emitting a light beam near infrared, which moves together with sensors along the whole height of the cell, from the bottom (0 mm) to the top (55 mm) at a fixed frequency, combined with the intensity of the passing light as well as that of the transmitted or backscattered light on the molecules. Based on these quantities, the program calculates the coefficient, TSI, which reflects the changes taking place in transmission and backward reflection of light in time. The kinetic measurements of destabilisation, determined by the stability coefficient, enable comparison of the samples with each other in a short period of time.

The main rule of Turbiscan measurements is that the lowest value of TSI reflects the highest stability in the system. The TSI gives values from 0 to 100. The larger the TSI, the greater the change occurs in the sample and therefore the lower the system stability. The coefficient TSI was calculated with the special computer program Turbiscan Easy Soft using the following equation:

$$TSI = \sqrt{\frac{\sum_{i=1}^n (x_i - x_{BS})^2}{n-1}}$$

where:

X_i – average transmission (T) or backscattering (BS) of light for each minute of measurement, X_T, X_{BS} – average X_i , n – number of scans (repetitions of single measurements during the total time of the experiment).

To eliminate noise measurements, the software automatically selects the most significant changes and matches the polynomial curve to the sample stability change trajectory. The calculation is performed directly in the zone between the bottom of the cell and the meniscus. The meniscus is automatically detected or its position can be changed manually.

The systems characterised by pH values 3 and 4.8 were described in our previous papers as the potential systems combining skin tissue and mucous membranes [16]. The measurements described in this paper will be devoted to a thorough discussion of similar systems, but at natural and alkaline pH (6–9).

In addition, resistance to solvents and the swelling capacity of chitosan and TiO₂/chitosan composites were examined, using the simple gravimetric method. Three different solvents (in the first case) were used, which are popular in the medical and pharmaceutical industry, i.e. water, ethanol and glycerol. Two kinds of beads were formed (of chitosan and of TiO₂/chitosan dioxide mixtures, respectively), which were immersed in solvents. The material for the beads was made by dissolving 0.1 g of chitosan and of TiO₂/chitosan (mix equilibrium) in 1 mL of 0.1 M HCl. Beads were immersed in 25 mL of solvents at 20 °C for 24 h. Then the beads were dried in a desiccator to a constant weight. In the second case, the beads of chitosan and TiO₂/chitosan were allowed to swell in redistilled water at 20 °C. The swollen samples were periodically weighed (every 5 minutes) until no weight increase or bead dissolution was observed.

3. Results and discussion

3.1 Stability of titanium dioxide and TiO₂/chitosan dispersion as a function of solution pH

The greatest changes of the effective diameter of titanium dioxide particles caused by the addition of chitosan (Fig. 2) were observed for the system at pH 9, which resulted in chitosan coagulation due to the concentration of hydroxyl ions being too high. Data on the TiO₂/chitosan dispersion graph are reduced 10 times because the values were too large to compare with the data for pure TiO₂ dispersion. As a result of the presence of the functional group originating from a weak base in the chitosan molecule, the structure behaved like a polybase in the environment of changeable ionic strength. In the acidic environment, the polymer was dissolved below the pK_a point (<6.3) of chitosan. However, in the environment characterised by high pH values, nonionised amino groups bind by means of the hydrogen bond, and the increasing forces of intra- and intermolecular interactions led to aggregation. Finally, after exceeding pH 7, the polymer precipitated from the solution.

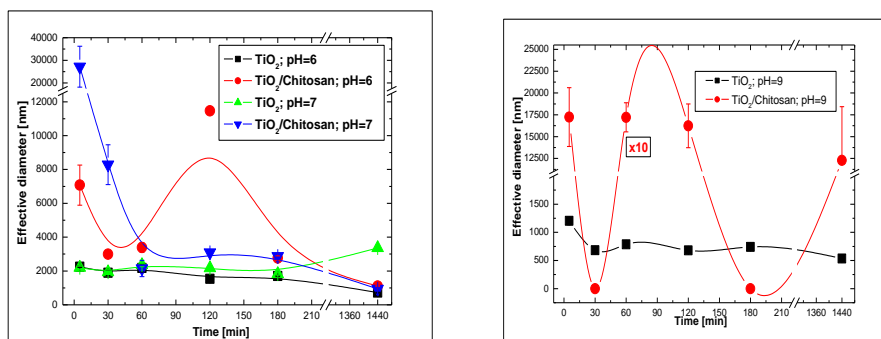


Figure 2. The effective diameter of titanium dioxide and titanium dioxide/chitosan dispersion as a function of time at the pH values of 6, 7 and 9.

In the systems at pH 6 and 7, chitosan addition caused a more than two-fold increase in particle diameter and slight fluctuations in the diameter compared to that containing only titanium dioxide. For the titanium (IV) oxide dispersion at pH 6, the effective particle diameter throughout the measurement cycle oscillated around 2000 nm and, after 24 hours, was about 700 nm. However, the addition of chitosan increased its initial value to about 7000 nm and then decreased to 3000 nm (30, 60 and 180 minutes), and finally became about 1000 nm. For the titanium (IV) oxide dispersion at pH 7, the effective particle diameter was about 2000 nm at all times, and after 24 hours it was about 3300 nm. After adding the polymer, the diameter was much higher at the beginning of the measurement and after 30 minutes (27000 and 8000 nm, respectively). For subsequent measurements, it was about 3000 nm.

In all original figures (Figs. 3, 4 and 6-9) from the Turbiscan measurements on the right scale, each selected time is shown in a different colour (start of measurements 0 min – pink; 15 min – dark green; 30 min – bottle green; 1 h and 1.30 min – different shades of green; 1.45 min – light green and 2 h – red, end of measurements). If the

measured suspensions are stable, these lines and colours are difficult to distinguish. The X-axis reflects the height of cuvette, from 0 mm (bottom of cuvette) to 55 mm (top of cuvette). Fluctuation at the bottom and/or top of the cuvette and extension of the band (each colour is visible in the figure as a separate line) can mean start of the destabilisation process.

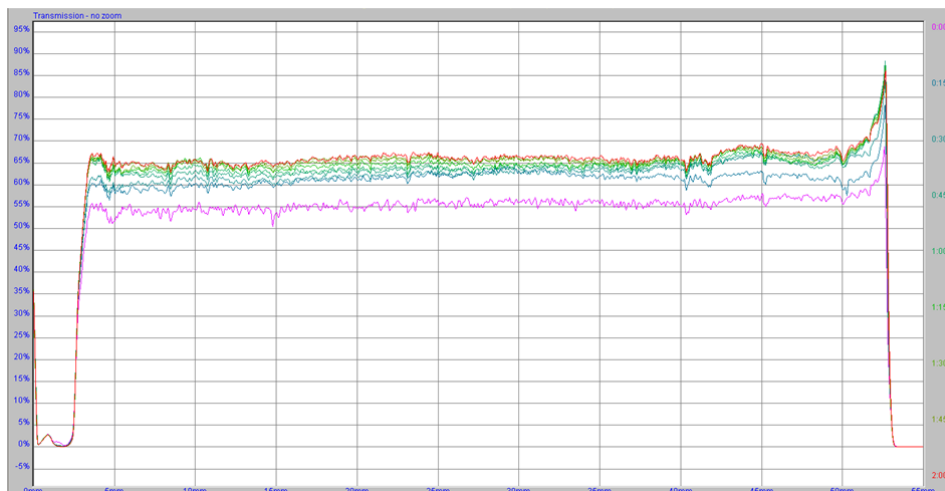


Figure 3. Transmission of light for the titanium dioxide dispersion as a function of time and height of cuvette at pH 9 (start of measurements 0 min – pink; 15 min – dark green; 30 min – bottle green; 1 h and 1.30 min – different shades of green; 1.45 min – light green and 2 h – red, end of measurements). The X-axis reflects the height of cuvette, from 0 mm (bottom of cuvette) to 55 mm (top of cuvette).

The original Turbiscan scans for the titanium dioxide particles with and without chitosan modification are presented in Figs. 3 and 4. On the basis of the obtained relationships, it can be stated that equilibrium is reached quickly and fluctuations are lower after chitosan modification. However, it is not largely a stable dispersion. The migration rates are the mean values estimated from the scans transported along 0–55 mm (bottom scale) of the calibrated cell. For the base titania suspensions, the migration rates are medium (about 10 $\mu\text{m}/\text{min}$, and transmission is in the range 50–85%). However, after the chitosan addition, curves more compact each other with time for a larger part of the system are observed (transmission in the range 40–55%). This indicates that the chitosan surface coverage of oxide particles is similar and the stabilisation of the suspension is achievable.

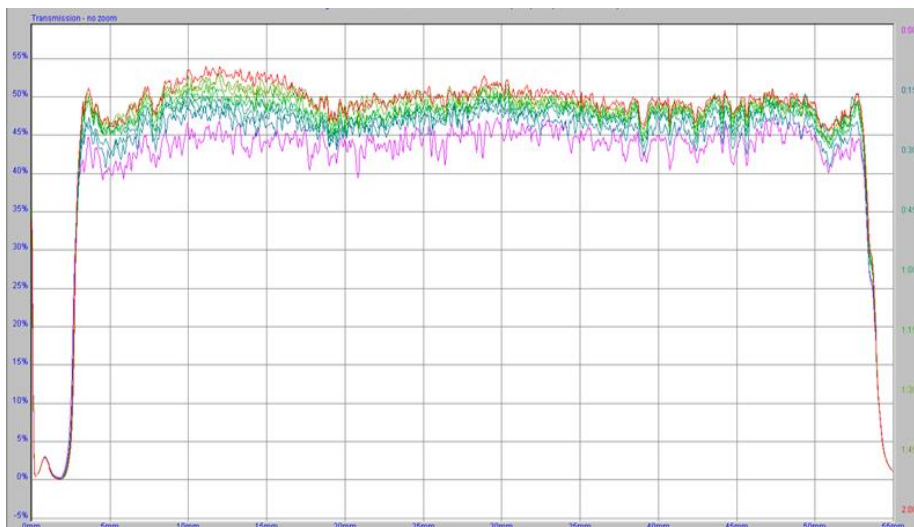


Figure 4. Transmission of light for the titanium dioxide/chitosan dispersion as a function of time and height of cuvette at pH 9. (start of measurements 0 min – pink; 15 min – dark green; 30 min – bottle green; 1 h and 1.30 min – different shades of green; 1.45 min – light green and 2 h – red, end of measurements). The X-axis reflects the height of cuvette, from 0 mm (bottom of cuvette) to 55 mm (top of cuvette).

Analysing the diagram of zeta potential changes in the system over time at pH 6, 7 and 9, it was found that in each of the three cases, the addition of a cationic polysaccharide induced more positive zeta potential for the titania particles, as a result of preferential adsorption of oppositely charged molecules (Fig. 5). Moreover, it was noticed that for all three dispersions containing chitosan, values of each of the above parameters were very similar. At the same time, its instability was reduced during the measurement cycle.

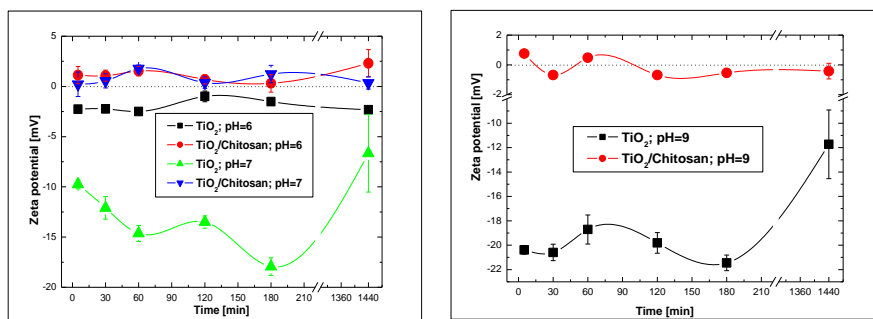


Figure 5. Zeta potential of the titanium dioxide and titanium dioxide/chitosan dispersion as a function of time at pH values of 6, 7 and 9.

Monotonic curves of changes in the effective diameter and the zeta potential after the addition of chitosan to the dispersion of TiO₂ at pH 6 and 7 showed an increase in stability for these systems. Major changes of particle diameter in the case of titanium dioxide dispersion of pH 6 and 7, contributed to a wide range of quantities of transmitted light which vary by 20 – 25 percentage points, as can be seen in Figs. 6 and 7.



Figure 6. Transmission of light for titanium dioxide dispersion as a function of time and height of cuvette at pH 6. (start of measurements 0 min – pink; 15 min – dark green; 30 min – bottle green; 1 h and 1.30 min – different shades of green; 1.45 min – light green and 2 h – red, end of measurements). The X-axis reflects the height of cuvette, from 0 mm (bottom of cuvette) to 55 mm (top of cuvette).

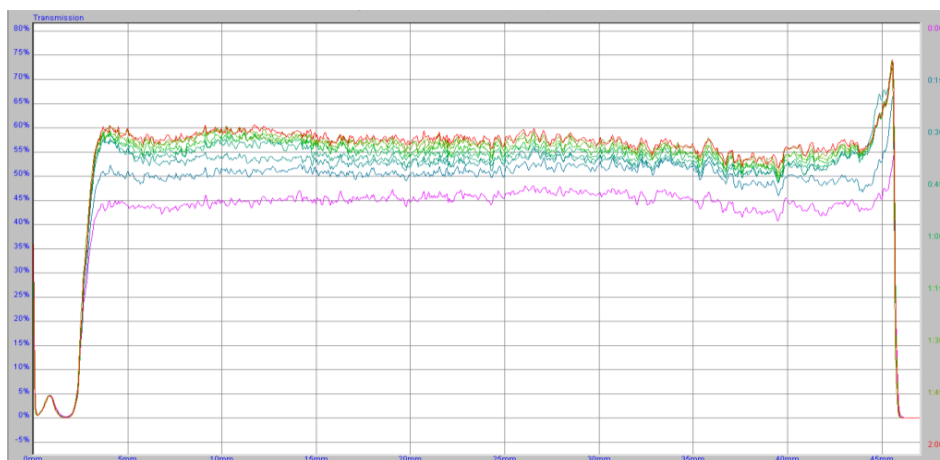


Figure 7. Transmission of light for the titanium dioxide dispersion as a function of time and height of cuvette at pH 7. (start of measurements 0 min – pink; 15 min – dark green; 30 min – bottle green; 1 h and 1.30 min – different shades of green; 1.45 min – light green and 2 h – red, end of measurements). The X-axis reflects the height of cuvette, from 0 mm (bottom of cuvette) to 55 mm (top of cuvette).

The addition of chitosan into the dispersion of titanium dioxide in each case (i.e. the dispersion at pH 6 and 7) had greatly improved stability. This is confirmed by the relationships of the amount of light transmitted as a function of time and the height of the cell for those systems (Figs. 8 and 9). As can be seen, there are much smaller fluctuations in the amount of light passing throughout the measuring cycle, which demonstrates the durability of the studied systems over time. In addition, the systems of TiO₂/chitosan attained thermodynamic equilibrium in a shorter time compared with the titanium dioxide dispersions.

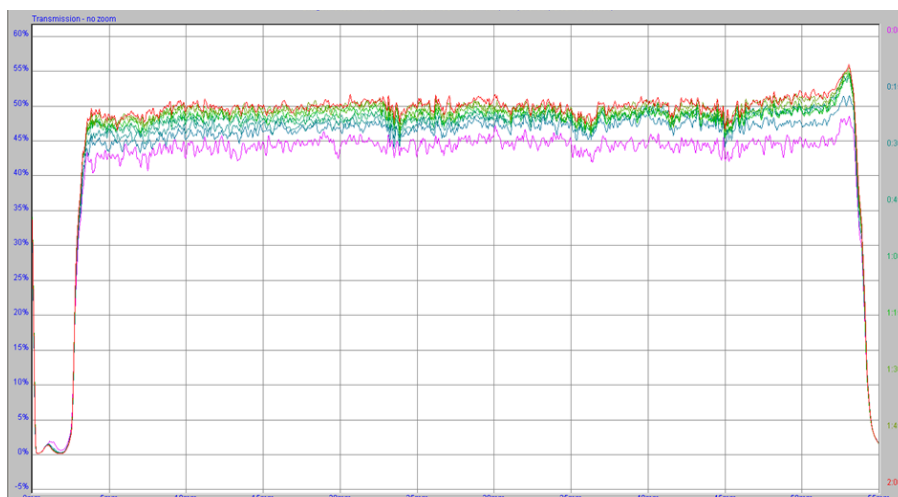


Figure 8. Transmission of light for the titanium dioxide/chitosan dispersion as a function of time and height of cuvette at pH 6. (start of measurements 0 min – pink; 15 min – dark green; 30 min – bottle green; 1 h and 1.30 min – different shades of green; 1.45 min – light green and 2 h – red, end of measurements). The X-axis reflects the height of cuvette, from 0 mm (bottom of cuvette) to 55 mm (top of cuvette).

In the presence of long-chain molecules, an effect of steric stabilisation can play a significant role. Additionally, at higher concentrations of chitosan, the process of gel forming is also possible due to its swelling properties. Considering the dispersions of TiO₂/chitosan at different pH values, i.e. 6, 7 and 9, it was found that the plot of the dependence of light passing the entire volume of the sample in the case of pH 6 (Fig. 8) showed a slightly lower transmittance, compared with the curve obtained for the dispersion of TiO₂/chitosan at pH 7 (Fig. 9).

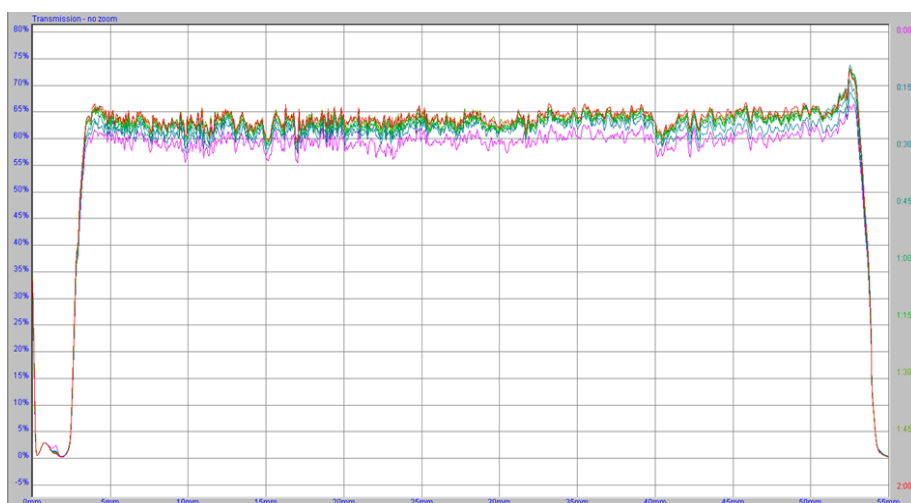


Figure 9. Transmission of the titanium dioxide/chitosan dispersion as a function of time and height of cuvette at pH 7. (start of measurements 0 min – pink; 15 min – dark green; 30 min – bottle green; 1 h and 1.30 min – different shades of green; 1.45 min – light green and 2 h – red, end of measurements). The X-axis reflects the height of cuvette, from 0 mm (bottom of cuvette) to 55 mm (top of cuvette).

However, the bandwidths in both systems were very close to each other (approx. 10 percentage points), as evidenced by the constant zeta potential values and the effective diameter of the particles. Large fluctuations in the amount of passing light and a lack of balance in the entire measurement cycle, in the case of TiO_2 /chitosan dispersion at pH 9 (Fig. 4), was due to the previously mentioned phenomenon of chitosan coagulation, which is evident in the huge measured values of effective diameter of particles (Fig. 2 – on the right).

3.2 Point of zero charge and TSI coefficient of titanium dioxide and TiO_2 /chitosan dispersions

The addition of chitosan into the dispersion of titanium dioxide of different pH values caused significant shifts of the electrokinetic properties of the systems by changing the position of the point of zero charge to a more acidic environment, from the initial pH of about 5.9 to a value near pH 4.9 (Fig. 10). However, stability in the zeta potential in the above systems when increasing the effective diameter of the dispersed particles suggests that chitosan is adsorbed onto the oxide particles, thus significantly increasing their stability by increasing repulsive forces between them. This is supported by the calculated three-fold lower rates of stability TSI values compared to that obtained for the pure TiO_2 dispersion (Fig. 10 – on the right).

The TiO_2 particles modified by chitosan are stable when the migration rates are about the same. After analysing all the systems of TiO_2 /chitosan, it was found that the highest stability was characterised by the dispersion at pH 7. Understanding the interactions of titanium dioxide with polysaccharides is an important step to obtain knowledge about biological effects. In combination with chitosan, the titanium dioxide dispersions are stable (regarding the zeta potential for the values in the range 6.5–8.5) as an effect of the

electrosteric stability, so that it can be used as a carrier for pharmaceuticals (e.g. anti-cancer drugs).

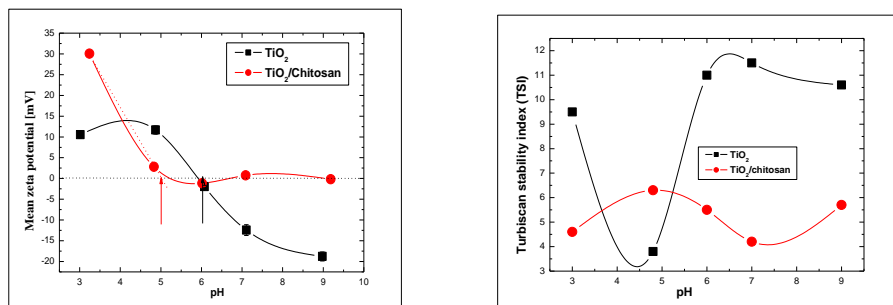


Figure 10. Zeta potential and Turbiscan stability index (TSI) of the titanium dioxide and titanium dioxide/chitosan dispersion as a function of the pH values.

As reported in the literature, the blood pH should be in the range of 7.35–7.41 [10]. At this pH value, lymphocytes responsible for the destruction of infected cells are the most effective. Below this pH value, the activity decreases, and such an environment is produced by tumours in the immediate vicinity. Polymeric systems are stable in the blood environment and are able to penetrate and pass through them to reach the infected cell and there release active medicinal substances. It can be concluded that the system at pH 7 examined by us, could provide such support as the mentioned earlier TiO₂/chitosan dispersion at this pH value exhibits. The best stability of those examined at this pH is confirmed by the calculated amount of reflected light passing and backwards – the TSI index – which in this case showed the minimum value (4.2) in the series.

The attention was focused on the systems of natural and alkaline pH, because finding a system that would be most stable in the blood environment was the goal of this study. The stability of control systems under such conditions would involve the maximum precision of the release of the drug substance during transport to the infected cell so that a larger amount would be delivered with no additional losses.

In the acidic environment, amine groups are present on the ionisable surface of chitosan, whereby the chain is loosened, leading to the transfer of polymer into solution (e.g. blood). In addition, the acidic environment is conducive to the survival and development of micro-organisms such as viruses, bacteria, fungi and yeast. It is known that chitosan has the ability to counteract these microorganisms. An additional advantage is the ability to act synergistically so that by combining the chitosan polymer with titanium dioxide (which also possesses such properties), this capability can be enhanced.

Analysing the changes in the zeta potential and the stability coefficient TSI due to the addition of chitosan to the dispersion of titanium (IV) oxide in the range of pH 6–9, it was found that despite the low zeta potential, these systems have a much better stability compared to the pure TiO₂ dispersions, for which the calculated TSI values were approximately twice as high (Table 1). The addition of chitosan in the case of pH 6 resulted in decreasing ratios of TSI from 11.0 to 5.5. At pH 7, the analogous value of 11.5 decreased to that of 4.2, and for the dispersion at pH 9, from 10.6 to 5.7.

The explanation is that in the first of these two cases, the particles of titanium (IV) oxide are stabilised not only by electrostatic, but also steric forces. Moreover, the surrounding molecules of chitosan are able to form a film on the oxide particle surfaces as evidenced by the increased effective diameter values. Adsorption of chitosan molecules onto the TiO₂ particles increases repulsive forces between them, thereby increasing the stability of the electrokinetic properties of dispersions. For all measured values of pH after the chitosan addition not high and satisfactory values of TSI for the TiO₂/chitosan composite were obtained. As previously stated, the lowest value of TSI reflects the highest stability in the system. These were lower than 10 units, and were even sometimes twice as low as for the unmodified titania (see Fig. 10 – on the right). Enhanced electrostatic repulsions help to diminish the flocculated system organisation. The addition of a cationic polysaccharide usually induces a more positive charge for the titania particles, according to the adsorption preference of the oppositely charged molecules, and thus the surface charge can be regulated.

3.3 Swelling properties of chitosan and TiO₂/chitosan beads

In the case of creating drug delivery systems, one should remember that biological processes occur in the aquatic environment. This requires hydrophilicity of the shell [10]. The possibility of crosslinking and the swelling capacity allow a gradual release of the matrix contained in the drug substance [12]. In this article, we have addressed the behaviour of beads in the water. The behaviour of these beads in other solvents has been more fully described in our previous paper [16]. The analysis of resistance to solvent demonstrated a non-linear relationship of the mass decrease for both kinds of beads after the treatment. It was observed that both types of beads are soluble in water and that after 24 h complete dissolution of beads was found in water. Water molecules strongly interact with the biopolymer (or TiO₂/chitosan) and could replace the hydrogen bonding between TiO₂/chitosan and their chains. However, the additional crosslinking effect between chitosan and TiO₂ moderately prevents the mass loss, and dissolution process is slower for TiO₂/chitosan beads.

Analysis of the swelling properties of both bead types demonstrated that the swelling ratio increased as an effect of enhanced acidity of the environment. This happens because in such an environment, the amine groups (present on the surface of chitosan molecules) have a positive charge and repel each other. Both bead types showed a high swelling ratio (more than 100%), but a moderately higher ratio was observed for base chitosan than for the TiO₂/chitosan beads. From the point of view of drug delivery, the TiO₂/chitosan systems are more beneficial, because a slower and more precise release of the drug is possible. This can be explained by the fact that the protonation of the free amino groups on the polymer surface is easier compared to the TiO₂/chitosan dispersion, where some of them can be blocked by the titanium dioxide particles (more specifically, titanium ions, Ti⁴⁺), which slightly inhibits the remarkable swelling behaviour of chitosan.

4. Conclusions

The present study has allowed the classification of the analysed TiO₂ systems in terms of stability, which has practical applications in everyday life. Finding a dispersion of titanium (IV) oxide with chitosan that has good stability and reproducibility is an important issue. This can provide the possibility of using the valuable characteristics of these substances, such as bactericidal or biocompatibility, which are highly valued mainly in the medical and pharmaceutical industries. In all tested systems of

TiO₂/chitosan, where the variable parameter was the pH, the polymer additive strengthened the stability, and the most promising system was the one characterised by the pH value of 7. However, comparing the levels of the zeta potential and the factors of the stability coefficient, TSI, it can be stated that the differences between the systems are rather small. Thus, both the titania systems at pH 6 and 7 can be of interest for the above-mentioned industries, considering different applications. Detailed wettability and biocompatibility tests of such systems are planned for the future.

5. References

- [1] Venugopal V; (2011) Marine polysaccharides food applications. CRC Press & Francis Group, United States of America 70–73
- [2] Norranattrakul P, Siralermukul K, Nuisin R; (2013) Fabrication of chitosan/titanium dioxide composites film for the photocatalytic degradation of dye. *Journal of Metals, Materials and Minerals* 23 (2): 9–22
- [3] Ozerin AN, Zelenetskii A, Akopova TA, Pavlova-Verevkin OB, Ozrina LA, Surin NM, Kechek'yan AS; (2006) Nanocomposites based on modified chitosan and titanium oxide. *Polymer Science* 48 (6): 638–643
- [4] Haldorai Y; (2013) Chitosan/titanium oxide composite: a photocatalyst and bacteriocide. *Society of Plastics Engineers*. DOI: 10.2417/spepro.005202
- [5] Peter M, Ganesh N, Selvamurugan N, Nair SV, Furuike T, Tamura H, Jayakumar R; (2010) Preparation and characterization of chitosan–gelatin/nanohydroxyapatite composite scaffolds for tissue engineering applications. *Carbohydrate Polymers* 80 (3) 687–694
- [6] Dev A, Binulal NS, Anitha A, Nair SV, Furuike T, Tamura H, Jayakumar R; (2010) Preparation of poly(lactic acid)/chitosan nanoparticles for anti-HIV drug delivery applications. *Carbohydrate Polymers* 80 (3) 833–838
- [7] Mazin C, Thanshif A, Anandapadmanabhan, Ashfaq, Mujeeb A, Lobo AG; (2015) Study on the effect of nano TiO₂ on mechanical properties of chitosan. *IOSR Journal of Mechanical and Civil Engineering* 12 (3) 48–54
- [8] Song W, Song X, Yang C, Gao S, Klausen LH, Zhang Y, Dong M, Kjems J; (2015) Chitosan/siRNA functionalized titanium surface via a layer-by-layer approach for in vitro sustained gene silencing and osteogenic promotion. *International Journal of Nanomedicine* 10: 2335–2346
- [9] Kavitha K, Prabhu M, Rajendran V, Manivasakan P, Prabu P, Jayakumar T; (2013) Optimization of nano-titania and titania-chitosan nanocomposite to enhance bio-compatibility. *Current Nanoscience* 9: 308–317
- [10] Kubiak T; (2014) The use of shells made of poly(ethylene glycol) and chitosan to ensure the biocompatibility of nanoparticles in biomedical applications. *Polimery w Medycynie* 44 (2): 119–127
- [11] Carreira AS, Gonçalves FAMM, Mendonça PV, Gil MH, Coelho JFJ; (2010) Temperature and pH responsive polymers based on chitosan: Applications and new graft copolymerization strategies based on living radical polymerization. *Carbohydrate Polymers*. 80 (3): 618–630
- [12] Zarzycki R, Modrzejewska Z, Nawrotek K, Skwarczyńska A; (2009) Adsorption processes in forming of hybrid structures for controlled release of pharmaceuticals. *Chemia, Dydaktyka, Ekologia, Metrologia* 14 (1–2): 85–94

- [13] Yazdani M, Bahrami H, Arami M; (2014) Feldspar/titanium dioxide/chitosan as a biophotocatalysts hybrid for removal of organic dyes from aquatic phases. *Journal of Applied Polymer Science*. **DOI:** 10.1002/APP.40247
- [14] Tiyaboonchai W; (2003) Chitosan nanoparticles: A promising system for drug delivery. *Naresuan University Journal* 11 (3): 51–66
- [15] Preočanin T, Kallay N; (2006) Point of zero charge and surface charge density of TiO₂ in aqueous electrolyte solution as obtained by potentiometric mass titration. *Croatica Chemica Acta* 79: 95–106
- [16] Wiącek AE, Gozdecka A; (2017) Physicochemical characteristics of chitosan/TiO₂ composites Part I. Stability and swelling. *Chemical Engineering Science*, under review.