Coordinative interaction of microcrystalline chitosan with oxovanadium (IV) ions in aqueous solution

Marta E Lichawska¹, Kazimiera H Bodek², Julia Jezierska³ and Aleksander Kufelnicki¹*

Abstract

Background: Chitosan, a non-toxic, biodegradable and biocompatible polysaccharide has attained great interest in pharmaceutical applications, as versatile drug delivery agent. Chitosan has been already shown to serve as vehicle for sustained drug release by chitosan-vanadium(IV) complex from a chitosan gel matrix. Therefore, chitosan gel proved to retain vanadium and preserve its insulin-mimetic efficacy. Nevertheless, there is a lack of reports concerning complexing equilibria in aqueous solution, in particular when using the more advantageous microcrystalline form of chitosan (MCCh). Microcrystalline chitosan shows a number of valuable features as compared with unmodified chitosan.

Results: Experimental studies on complexing interaction between a special form of biomaterial - microcrystalline chitosan as ligand, L = MCCh, of two exemplary degrees of deacetylation DD (lower 79.8%; higher 97.7%) with M = oxovanadium (IV) ions have been carried out potentiometrically at four ligand-to-metal concentration ratios (2:1, 5:1, 8:1, 10:1). Among the five hydrolysis equilibria of VO²⁺ reported up to now in the literature, under the conditions of the present work i.e. aqueous solutions of ionic strength I = 0.1 (KNO₃) and temperature 25.0 ± 0.1°C, the predominating one was (VO)₂(OH)₂⁺ formation: log β₂₀⁻² = −7.01(2). Analysis of potentiometric results permitted to note that degree of deacetylation does not essentially influence the coordination mode of the complexes formed. In the case of both the two DD values, as well as for all the ligand-to-metal ratios, formation of hydroxyl deprotonated MLH⁻₁ and ML²H⁻₂ moieties has been confirmed potentiometrically (log β₁₁⁻¹ = −0.68(2) for DD = 79.8% and −0.68(2) for DD = 97.7%, log β₁₂⁻² = −7.64(6) for DD = 79.8% and −5.38(7) for DD = 97.7%).

Conclusion: Microcrystalline chitosan coordinates the vanadyl ions by the hydroxyl groups. Interaction of MCCh with VO²⁺ ions in aqueous solution occurs within pH 5–7. Amounts of alkali excessive towards -NH₂ are needed to deprotonate the OH groups. Deprotonation occurring at the chitosan hydroxyl groups permits a “pendant” or “bridge” model of coordination with VO(IV). Lack of complexation via deprotonation of amine groups, typical for simple cations and the molybdenum anion, has been indicated also by FTIR spectroscopy and EPR.

Keywords: Biomaterial, Microcrystalline chitosan, Vanadium (IV), Metal-polymer complexes, Equilibria in aqueous solution

* Correspondence: aleksander.kufelnicki@umed.lodz.pl
¹Department of Physical and Biocoordination Chemistry, Faculty of Pharmacy, Medical University of Łódź, 90-151 Łódź, Poland
Full list of author information is available at the end of the article

© 2014 Lichawska et al; licensee Chemistry Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.
Background

Chitosan is a polysaccharide composed of D-glucosamine (2-amino–2-deoxy–β-D-glucose) and N-acetyl-D-glucosamine (2-acetamido–2-deoxy–β-D-glucose) (Figure 1). This biopolymer is formed by partial deacetylation of chitin, the most widespread natural polysaccharide, found in shells of crustaceans. The molar D-glucosamine to N-acetyl-D-glucosamine ratio in the chitosan sample is an estimate of the so-called degree of deacetylation (DD). The term chitosan is referred to chitin of DD > 60% [1-3]. The degree of deacetylation of the copolymer is usually within the range of 70.0% - 95.0% [4-5].

This non-toxic, biodegradable and biocompatible material has attained great interest in pharmaceutical applications, as versatile drug delivery agent [1-3]. A valuable physicochemical modification of chitosan, used among others as excipient in drug formulations, is microcrystalline chitosan (MCCh), obtained in form of suspension, powder or granules [6-7]. A polymer of desired chemical properties is prepared by appropriate aggregation of the macromolecules from aqueous solutions of organic acids (via neutralization, coagulation and then precipitation of microcrystalline chitosan) [8]. During this process the polymer is also refined from low-molecular side products. Microcrystalline chitosan shows a number of valuable features as compared with unmodified chitosan: higher absorptivity, chelating capability, higher bioactivity, as well as ability of forming polymer films directly from water slurry. Similarly as it was the case with the previous forms of chitosan, MCCh may be proposed as an effective vehicle for the controlled vanadium release [3].

Vanadium (IV) plays a number of roles in the physiology of living systems. It is responsible for a number of processes, e.g. the inhibition of phosphate–metabolising enzymes such as phosphatases, ribonuclease and ATP-ases. The interaction of VO²⁺ with phosphates and nucleotides is of special interest in vanadate biochemistry [9]. The insufficiency of vanadium may, among other effects, lead to lowering the level of erythrocytes and pathologic increase of lipid level in blood. Recently, the medical significance of this element focuses on enhancing the treatment of type I diabetes mellitus (insulin-dependent) and also of type II (noninsulin-dependent) [10]. However, direct application of vanadium by vanadyl sulphate has several undesired side-effects, such as gastrointestinal symptoms, anorexia and weight loss. Hence, it is necessary to elaborate a delivery mechanism suitable to be used in therapy. The most successful clinical trials were carried out with bis(maltolato)oxovanadium(IV) compounds (BMOV - bis-3-hydroxy-4-pyronato)oxovanadium(IV) – and BEOV - bis(2-ethyl)-3-hydroxy-4-pyronato)oxovanadium(IV) but also with corresponding complexes of kojic acid (Hkoj - 3-hydroxy-6-hydroxymethyl-4-pyrone) and tropolone (Htrop - 2-hydroxy-2,4,6-cycloheptatrien-1-one) [11-15]. The first of them, BMOV, proved to be three times more effective than vanadyl sulfate as a glucose lowering agent. Recently also a number of other synthetic imidazole and pyridine based compounds of potential insulin-mimetic activity have been studied in solution [16-17]. Vanadium (IV) compounds mimic most of the biological effects of insulin in various cell types. They have been shown to increase glucose transport and oxidation (by that lowering glucose level in blood), to stimulate glycogen synthesis and to inhibit hepatic gluconeogenesis [18]. The anti-diabetic effect is probably attained via irreversible strong inhibition of the insulin receptor – one of the large class of tyrosine kinase receptors.

Unmodified chitosan has been already shown to serve as vehicle for sustained drug release by controlling the diffusion of chitosan-vanadium complex from a chitosan gel matrix. Therefore, chitosan gel proved to retain vanadium and preserve its insulin-mimetic efficacy [10]. Some earlier, kinetic and equilibrium studies on adsorption of VO²⁺ by chitosan were performed as well [19]. Up to now, the spectroscopic (only FTIR) investigation of the VO²⁺ - unmodified chitosan interaction was carried out for the final solid complex in comparison with pure chitosan [2]. Nevertheless, there is a lack of reports concerning complexing equilibria in aqueous solution, in particular when using the more advantageous microcrystalline form of chitosan (MCCh). Corresponding reactions of MCCh have been studied with other metals in our previous papers [20-22]. It would be also interesting to investigate the DD influence on VO²⁺ - MCCh complex formation. This effect has already been discussed in our latest paper with Mo(VI) [23].

Results and discussion

Analysis of potentiometric data and speciation models

The pH potentiometric data were elaborated in order to obtain appropriate speciation models and to determine the stability constants of complexes.

Hydrolysis of VO²⁺

The potentiometric studies of the vanadyl solution under exactly the same conditions as they were used in the potentiometric measurements with MCCh, described
in later section, confirmed predomination of only the (VO)$_2$(OH)$_2$ $^{2+}$ hydroxo complex from among the species mentioned in the literature:

$$2\text{VO}^{2+} + 2\text{H}_2\text{O} \leftrightarrow (\text{VO})_2(\text{OH})_2^{2+} + 2\text{H}^+ \quad \log\beta_{20-2} = -7.01$$

(1)

The hydrolysis constant obtained was in good agreement with the corresponding corrected values reported recently: $-6.95$ [16, 17], and in fairly agreement with the elder data: $-6.67$ [24], $-6.72$ [25], $-6.88$ [26]. On the other hand the simplest VO(OH)$^+$ hydroxo complex has been shown to occur in minor share up to pH $\sim 5$, just like it was indicated in ref. [19]. The remaining hydroxo species reported in the literature: $[\text{VO(OH)}_3]^{2-}$ and $[(\text{VO})_2(\text{OH})_5]^{2-}$ occur at pH $> 8$ [16], that is to say beyond the pH range of complexation with MCCh.

**Complex formation with VO$^{2+}$**

The potentiometric titrations in presence and absence of $L = \text{MCCh}$ corresponded to neutralization of the hydrogen ions in dependence of base equivalent $a$ ($a = \text{mmole of base/mmole of ligand}$). Measurements started with neutralization of the excessive mineral acid ($a = -0.1 - 0$) and then were continued by further alkalinization of the $-\text{NH}_3^+$ chitosan groups up to $a > 1$ (Figure 2). As it follows also from Figure 2, the use of alkali needed to reach the end point in the samples with chitosan increased in presence of VO$^{2+}$ - starting from ligand to metal ratio 10:1 up to 2:1. The values of pH were lower than for MCCh in absence of vanadyl ions. The parts of curves after $a \sim 1$ (end point of MCCh), the longer the higher is the part of vanadyl ion, are evidently connected with VO(IV) – MCCh complexation via the deprotonated hydroxyl groups but not the amine groups. This result is not surprising because it is known that the affinity of V$^{IV}$O$^{2+}$ ion is much higher towards ligands with oxygen donors [27-29]. Coordinative interaction of oxido V$^{IV}$O$^{2+}$ ion towards only nitrogen donors is very low and results in hydrolytic processes in acid and neutral solution. In turn, the titration curve corresponding to VO$^{2+}$ in absence of ligand, showed a disturbance not far after the end point ($a > \text{ca 1.3}$), due to poor solubility of the forming aquo-hydroxo products.

Owing to the potentiometric results the proposed coordination reactions in the $M = \text{VO}^{2+} - L = \text{MCCh}$ system are shown in Equations (2) and (3) – charges omitted for clarity.

$$M + L = MLH_{-1} + H$$

$\beta_{11-1} = \frac{[MLH_{-1}][H]}{[M][L]}$ (2)

$$M + 2L = ML_2H_2 + 2H$$

$\beta_{12-2} = \frac{[ML_2H_2][H]^2}{[M][L]^2}$ (3)

where: $\beta_{\text{mlh}} = [M_{m+l}H_h]/[M]^m[L]^l[H]^h$ – cumulative stability constant; $m$, $l$, $h$ – number of metals (central ions), ligands and protons, respectively; concentrations in square bracket are equilibrium concentrations.

Except of the hydrolysis reaction mentioned in Equation 1, the calculations involved the protonation constant of MCCh under the same conditions as in the present experiments with VO$^{2+}$ ($\log \beta_{011} = 6.50$, that is in accordance with our previous data [23] and also with the literature [30]).

![Figure 2](image)  
**Figure 2** Titration of the H$^-$ - VO(IV) – MCCh (DD = 0.977) system at various ligand to metal ratio. $C_{\text{MCCh}}$ (mol L$^{-1}$) = 7.0 $\times$ 10$^{-3}$. The value of base equivalent $a = -0.1$ corresponds to HNO$_3$ in excess as related to ligand.
The next plot (Figure 3), directly originating from Hyperquad refinements, shows that the significant share of the accepted deprotonated species MLH$_{1-}$ as well as lower share of the twice deprotonated ML$_{2}$H$_{-2}$ complex occurs at pH 5–7. At lower pH the refinements indicate a small contribution (up to 10%) of the M$_{2}$H$_{-2}$ = (VO)$_{2}$OH)$_{2}$$^{2+}$ hydroxo complex (Figure 3). In turn, at pH higher than ca 7–7.5, the increasing aggregation of chitosan makes impossible further accurate pH measurements. Finally, the present refinement results indicate donation via the deprotonated hydroxyl groups (Figure 4) just following –$\text{NH}_3^+$ deprotonation. On the other hand, the specific structure of chitosan as polymer chain with a long distance between consecutive monomers suggests that the higher accessibility of coordination sites occurs for hydroxyl donors from two neighbouring polymer chains in the ML$_{2}$H$_{-2}$ complex (Figure 4b). The above mentioned pattern involving deprotonated OH groups bonded to the VO$^{2+}$ cation has already been described for VO$_{2}$/carbohydrate complexes [9].

It is worthy to note that for the MLH$_{1-}$ species the coordination mode does not essentially depend on the DD of chitosan (Table 1). However, at DD 97.7% the stability constant of the ML$_{2}$H$_{-2}$ species is somewhat higher (less negative) than for DD 79.8%. The latter difference is difficult to be interpreted because at pH > 7, i.e. at the end of the pH range used in calculations (and where the ML$_{2}$H$_{-2}$ species becomes predominating) as the titrations are evidently disturbed by increasing aggregation of MCCh of both DD’s.

**Infrared spectra**

The FTIR spectra of free MCCh and of related MCCh samples in presence of VO$^{2+}$ and at various pH are shown exemplary in Figures 5a and b for the lower DD value – 79.8%.

In free chitosan the broad band (due to hydrogen bond interaction) visible from the high wavenumber side of spectrum (~3400 cm$^{-1}$) is assignable to the O-H and N-H stretching vibrations [2]. Moreover, the C-H stretching bands could be identified as doublets at 2900/2850 cm$^{-1}$ (Figure 5a). In presence of VO(IV) the spectra become poorly unresolved within this range, most probably as a result of overlapping by the vanadyl ion line and also due to the lower thickness and higher fragility of the films obtained in presence of VO$^{2+}$.

In the medium IR range 600 – 1800 cm$^{-1}$ the region 1400–1800 cm$^{-1}$ is of particular interest. Our spectra of pure MCCh derived from thin films, much more distinct that the ones recorded from KBr pellets, showed both the so called amide I band at ca 1630 cm$^{-1}$ (which is essentially the C = O stretching vibration of the –NHOC-CH$_3$ group) [2] as well as the amide II band of the secondary amide groups and the deformation scissoring mode, δ(NH$_2$), of the primary amine groups –NH$_2$ – ca 1530 cm$^{-1}$. As can be observed the two bands are well splitted and free of noise up to pH at least 5.5. In presence of VO(IV) the rise of pH resulted in lowering and deformation of the latter bands, also probably due to progressive deprotonation of the –$\text{NH}_3^+$ and following aggregation of the MCCh chains – (ref. Figure 4b). The bands are only remaining in lowering intensity only at pH 3.54 – 6.44. Characteristic that in presence of VO(IV) the spectra do not show any visible shift of the amide II band nor of the scissoring mode of the primary amine groups, δ(NH$_2$). Such shifts towards higher wavenumbers have been already described for interaction of chitosan with other metals, like Cu(II), Hg(II) and Ni (II) [31-32]. Hence, this observation may be evidently connected with our previously discussed potentiometric titrations confirming rather complexation via the hydroxyl oxygens than the amine nitrogens.

An additional spectral IR line of pure VO$^{2+}$ was shown in Figure 5b. Its special feature may be assigned to the low intensive, scarcely splitted band at ca 1000 cm$^{-1}$, due to
the characteristic $V = O$ stretching vibration [3-9]. The visible disappearance of this band in presence of MCCh (starting from the lowest pH 3.54, where potentiometry shows already the share of complexation) may be explained by strong hydrogen-bond interactions between free hydroxyl groups of the carbohydrate ligand and the oxo group of the metal center thus leading to diminution of the $V = O$ bond strength.

**Indications of EPR spectroscopy**

The EPR spectra of water frozen solutions of VOSO$_4$ – chitosan system (Figure 6), exhibit eight line hyperfine splitting due to $I(^{51} V) = 7/2$. The parallel hyperfine lines are located symmetrically around $g_{||} = 1.933$ (with $A_{||} \sim 180 \times 10^{-4}$ cm$^{-1}$) whereas the perpendicular lines around $g_{\perp} = 1.977$ (with $A_{\perp} \sim 70 \times 10^{-4}$ cm$^{-1}$). The EPR parameters, $g_{||} < g_{\perp}$ correspond to axial symmetry of compressed tetragonal geometry of VO$_{2}^{+}$ complexes. On the other hand the relation $g_{||} < g_{\perp} < 2.0023$ is an unambiguous proof of $d^{1}$ electron configuration of vanadium ion. The EPR $g$ and $A$ tensor components corresponding to $H = \beta S g B$ and $H = S A I$ spin Hamiltonians of the VO(IV) complexes formed at various pH are almost similar to those observed for water solution of VOSO$_4$. This indicates that amine nitrogen atoms of chitosan are not involved in VO (IV) coordination and supports that only oxygen donors are located symmetrically around $g_{||} = 1.933$ (with $A_{||} \sim 180 \times 10^{-4}$ cm$^{-1}$) whereas the perpendicular lines around $g_{\perp} = 1.977$ (with $A_{\perp} \sim 70 \times 10^{-4}$ cm$^{-1}$). The EPR parameters, $g_{||} < g_{\perp}$ correspond to axial symmetry of compressed tetragonal geometry of VO$_{2}^{+}$ complexes. On the other hand the relation $g_{||} < g_{\perp} < 2.0023$ is an unambiguous proof of $d^{1}$ electron configuration of vanadium ion. The EPR $g$ and $A$ tensor components corresponding to $H = \beta S g B$ and $H = S A I$ spin Hamiltonians of the VO(IV) complexes formed at various pH are almost similar to those observed for water solution of VOSO$_4$. This indicates that amine nitrogen atoms of chitosan are not involved in VO (IV) coordination and supports that only oxygen donors are located symmetrically around $g_{||} = 1.933$ (with $A_{||} \sim 180 \times 10^{-4}$ cm$^{-1}$) whereas the perpendicular lines around $g_{\perp} = 1.977$ (with $A_{\perp} \sim 70 \times 10^{-4}$ cm$^{-1}$). The EPR parameters, $g_{||} < g_{\perp}$ correspond to axial symmetry of compressed tetragonal geometry of VO$_{2}^{+}$ complexes. On the other hand the relation $g_{||} < g_{\perp} < 2.0023$ is an unambiguous proof of $d^{1}$ electron configuration of vanadium ion. The EPR $g$ and $A$ tensor components corresponding to $H = \beta S g B$ and $H = S A I$ spin Hamiltonians of the VO(IV) complexes formed at various pH are almost similar to those observed for water solution of VOSO$_4$. This indicates that amine nitrogen atoms of chitosan are not involved in VO (IV) coordination and supports that only oxygen donors are located symmetrically around $g_{||} = 1.933$ (with $A_{||} \sim 180 \times 10^{-4}$ cm$^{-1}$) whereas the perpendicular lines around $g_{\perp} = 1.977$ (with $A_{\perp} \sim 70 \times 10^{-4}$ cm$^{-1}$). The EPR parameters, $g_{||} < g_{\perp}$ correspond to axial symmetry of compressed tetragonal geometry of VO$_{2}^{+}$ complexes. On the other hand the relation $g_{||} < g_{\perp} < 2.0023$ is an unambiguous proof of $d^{1}$ electron configuration of vanadium ion. The EPR $g$ and $A$ tensor components corresponding to $H = \beta S g B$ and $H = S A I$ spin Hamiltonians of the VO(IV) complexes formed at various pH are almost similar to those observed for water solution of VOSO$_4$. This indicates that amine nitrogen atoms of chitosan are not involved in VO (IV) coordination and supports that only oxygen donors

**Table 1 Cumulative stability constants log$\beta_{mlh}$ of the VO(IV) - MCCh complexes**

| Value of DD | $C_{l}/C_{M}$ | log$\beta_{11-1}^{b}$ | log$\beta_{11-1}^{c}$ | log$\beta_{12-2}^{b}$ | log$\beta_{12-2}^{c}$ | pH range |
|------------|---------------|----------------------|----------------------|----------------------|----------------------|-----------|
| 79.8%      | 2:1           | -0.39 (5)            | -4.48 (23)           |                     |                     |           |
|            | 5:1           | -0.26 (5)            | -4.18 (24)           |                     |                     |           |
|            | 8:1           | -0.09 (5)            | -7.81 (16)           |                     |                     |           |
|            | 10:1          | -0.09 (6)            | -7.59 (8)            |                     |                     |           |
| 97.7%      | 2:1           | -0.53 (4)            | -8.11 (10)           | -7.64 (6)           | 2.53-7.34           |           |
|            | 5:1           | -0.56 (3)            | -7.43 (10)           |                     |                     |           |
|            | 8:1           | -0.09 (6)            | -7.83 (26)           |                     |                     |           |
|            | 10:1          | -0.09 (6)            | -8.06 (11)           |                     |                     |           |
| 2:1        | -0.71 (4)     | -4.41 (9)            |                     |                     |                     |           |
| 5:1        | -0.68 (4)     | -4.45 (9)            |                     |                     |                     |           |
| 8:1        | -0.08 (6)     | -4.45 (9)            |                     |                     |                     |           |
| 10:1       | -1.29 (8)     | -4.59 (14)           |                     |                     |                     |           |

$^{a}$results from individual titrations.
$^{b}$results from comprehensive files of all titrations.
$^{c}$results from calculations of all titrations.

$T = 25.0^\circ C$, $I = 0.1$ mol L$^{-1}$ (KNO$_3$). Standard deviations in parentheses. $C_{l}$ = total concentration of ligand; $C_{M}$ = total concentration of VO$_{2}^{+}$.
of hydroxyl groups participate in VO(IV) complexation, as it has been already shown by the potentiometric results.

**Conclusions**
The studies show that MCCh interacts with oxovanadium (IV) in aqueous solution starting from pH 5. Then, the deprotonation of amine groups is followed by deprotonation of the hydroxyl groups, which leads to a higher use of alkali in the pH-potentiometric titration with respect to chitosan alone, proportional to the part of vanadyl ion in the sample. Thus, the refinements based on potentiometric data confirm coordination via oxygen atoms from the deprotonated hydroxyl groups.

From the coordination modes accepted: OH deprotonated MLH$^{-1}$ and twice OH deprotonated ML$_2$H$_2$$^{-2}$ species, the second one involves a moiety with one vanadyl binding two adjacent chitosan mers, most probably of two neighbouring polymer chains. Lack of complexation via deprotonation of amine groups, typical for simple cations and the molybdenum anion, has been indicated also by FTIR spectroscopy and EPR. It seems then quite understandable that the degree of deacetylation has no essential influence on the thermodynamical stability of the MLH$^{-1}$ species predominating within the main range of complexation. On the other hand the second deprotonated species i.e. ML$_2$H$_2$$^{-2}$ is formed when the

---

**Figure 5** FTIR spectra obtained in thin polymer films of a) pure MCCh (DD 79.8%) and b) MCCh in presence of VO$^{2+}$ ions at various pH. Comparative spectrum for VO$^{2+}$ taken in KBr pellets.
titrations are evidently disturbed by increasing aggregation of MCCh regardless DD.

**Methods**

**Materials**

MCCh (weight-average molecular weight $M_w = 2 \times 10^5$ Da, Institute of Biopolymers and Chemical Fibers, Łódź, Poland) was used in the form of hydrogel of definite polymer content (2.55 and 2.56 wt%) at two different average degrees of DD: 79.8, 97.7%. The degree of DD, necessary to estimate the content of $\text{–NH}_2$ groups in the samples, was determined by the method of first derivative UV-spectrophotometry (1DUVS) according to Khor and co-workers [33]. Vanadium(IV) stock solution was prepared from VOSO$_4$ × H$_2$O (Alfa Aesar GmbH & Co KG). Carbonate-free 0.1000 ± 0.0003 M NaOH solution (Mallinckrodt Baker B.V.) was used as titrant. Other reagents, i.e., nitric acid and potassium nitrate were from grade pro analysis (P.A.).

**Potentiometric titrations**

A Molspin instrument (Newcastle upon Tyne, England) equipped with an OSH-10-10 combined electrode (METRON, Poland), and autoburette was used for EMF measurements. All titrations were run at least in duplicate to ensure reliability of the data. The total volume of the Hamilton microsyringe in the autoburette amounted to 500 μL. The number of up to 100 titration points was attained by volume increments 5.0 μL. The titration course was controlled by MOLSPIN software. All the measurements were carried out at 25.0 ± 0.1°C and ionic strength 0.1 mol L$^{-1}$ (KNO$_3$). The cell was standardized according to IUPAC recommendations with two buffers: pH = 3.926 (potassium hydrogen phthalate 0.05 M + 0.05 M KNO$_3$) and pH = 9.10 (disodium tetraborate 0.01 M + 0.07 M KNO$_3$) [34]. It follows then, that the buffer solutions were of the same ionic strength, medium and temperature as in the tested solutions. In addition, prior to each titration the electrode system had been calibrated in the $–\log [H^+]$ scale by strong acid-strong base titrations, according to the procedure recommended by Irving et al. [35]. In particular, 0.005 M HNO$_3$ (adjusted to $I = 0.1$ mol L$^{-1}$ by adding KNO$_3$) was neutralized with carbonate-free 0.1 M NaOH at temperature 25.0 ± 0.1°C. The ionization product of water ($pK_w$) under these conditions was 13.77 in our study and was in accordance with the references [36]. The values of standard electromotive force ($E_0$), which also comprises the liquid junction potential, and slope ($s$) from the equation $E = E_0 - s \cdot 59.16(–\log [H^+])$ were evaluated by Superquad and Hyperquad 2008 [37-39]. The parameters, that were different from the ones obtained from the two-point cell standardization on pH, were then inserted into the input files of the programs Superquad and Hyperquad 2008 to evaluate the overall, concentration formation constants: $\beta_{mlh} = [M_mL_lH_h]/[M][L][H]^s$, where: $M = VO^{2+}$, $L =$ microcrystalline chitosan (MCCh), $H =$ hydrogen (proton). Goodness-of-fit was tested by two parameters: $\sigma$ (connected with the objective function $U = \sum_{i=1}^{n} W_i r_i^2$, where $W_i$ - weight of the $i$-th experimental point of $n$ and $r_i = i$-th residual in EMF ($E_{exp} - E_{theoret}$)) as well as by the $\chi^2$ statistics (test of randomness).

**FTIR spectrophotometric measurements**

Polymer films in absence and presence of the vanadyl ion were prepared for the use in IR studies. In the latter case the optimum L:M ratio was 5:1 just as in the potentiometric measurements. Initially a portion of 0.075 mmol of nitric (V) acid was added to 0.070 mmol of MCCh to dissolve the ligand. By using 0.1 M NaOH each sample was brought to definite pH within the range 3.0 - 6.8. The formed water slurry was put on a teflon plate and left drying at room temperature. Then the polymer film was removed and used in the FTIR measurements on a Perkin Elmer FT-IR System Spectrum BX spectrophotometer. A total of 10 scans were accumulated. Spectral resolution was ±4 cm$^{-1}$. For comparison polymer membranes with chitosan in absence of the metal were prepared as well. Separately, the IR spectra of VO$^{2+}$ ion were taken in KBr pellets.
EPR measurements

The EPR spectra were measured using a Bruker Elexys E500 spectrometer equipped with NMR telesmeter (ER 036TM) and frequency counter (E 41 FC) at X-band. The simulations of the experimental spectra were performed using computer program WIN-EPR Simfonia, version 1.26 beta and the program written by Dr Andrew Ozarowski from NHMFL, University of Florida, with resonance field calculated by diagonalization of energy matrix. The spectra were measured with a modulation frequency 100 kHz, modulation amplitude of 7 gauss and microwave power of 10 mW. The MCCh ligand (L) and VO$^{2+}$ concentrations were $C_L = 7.0 \times 10^{-3}$ M and $C_{VO_2^+} = 8.75 \times 10^{-4}$ M, respectively. In order to avoid aggregation of VO(IV) complexes in water 10% (v/v) of ethyl glycol was added to the studied solutions.

Abbreviations

DD: Degree of deacylation; FTIR: Fourier-transform infrared spectroscopy; EPR: Electron paramagnetic resonance; L = MCCh: Microcrystalline chitosan as ligand; M: Oxovanadium (IV) ion as metal; L/M: The ligand-to-metal concentration ratio; $\beta_{\text{eff}} = [M(LH)_2]/[ML]^2[H]^3$: Cumulative stability constant; $m$, $l$, $h$: Number of metals (central ions), ligands and protons, respectively; concentrations in square brackets are equilibrium concentrations.

Competing interests

The authors declare that they have no competing interest.

Authors' contributions

All authors contributed equally for the development of the manuscript. MEL approved the final manuscript. AK carried out and interpreted the EPR data. AK proposed the research idea and coordinated final formulation. The authors read and approved the final manuscript. JJ carried out the potentiometric and FTIR spectroscopic analysis, participated in the results discussion. KHB interpreted the spectral data and revised the manuscript. All authors contributed equality for the development of the manuscript. MEL is kindly acknowledged.

Acknowledgements

Financial support of this work by the Medical University of Łódź (Project 502-03/3-014-02/503-34-005) – M.E. Lichawska and Statute Funds. No. 503/3-014-02/503-01 – A. Kufelnicki, No. 503/3-021-01/503-01 – K.H. Bodek is kindly acknowledged.

Author details

1Department of Physical and Biocoordination Chemistry, Faculty of Pharmacy, Medical University of Łódź, 90-151 Łódź, Poland. 2Chair of Applied Pharmacy, Faculty of Pharmacy, Medical University of Łódź, 90-151 Łódź, Poland. 3Faculty of Chemistry, University of Wrocław, 50-383 Wrocław, Poland.

Received: 8 May 2014 Accepted: 31 July 2014

Published online: 09 September 2014

References

1. Ravi Kumar MNV, Muzzarelli RA, Muzzarelli A, Sachwa CH, Domb A: Chitosan Chemistry and Pharmaceutical Perspectives. Chem Rev 2004, 104:6017–6084.
2. Baran EJ: Spectroscopic investigation of the VO$^{2+}$/chitosan interaction. Carbohydr Polym 2008, 74:704–706.
3. Baran EJ: Oxovanadium(IV) complexes of carbohydrates: A brief overview. J Inorg Biochem 2009, 103:547–553.
4. Rowe RC, Sheasley PJ, Quinn ME: Handbook of Pharmaceutical Excipients. 6th edition. London UK: Pharmaceutical Press, 2009.
5. Roberts GA: Chitin Chemistry. Hongkong: Macmillan Publishers Limited; 1992:203.
6. Säkkinen M, Marvola J, Kanerva H, Lindell K, Lipponen M, Kekki T, Ahonen A, Manola M: Gamma scintigraphic evaluation of the fate of microcrystalline chitosan granules in human stomach. Eur J Pharm Biopharm 2004, 57:133–143.
7. Säkkinen M, Marvola J, Kanerva H, Lindell K, Ahonen A, Kekki T, Manola M: Are chitosan formulations mucoadhesive in the human small intestine? An evaluation based on gamma scintigraphy. Int J Pharm 2006, 307:285–291.
8. Struszczyk H: Microcrystalline chitosan. Preparation and properties of microcrystalline Chitosan. J. Appl Polym Sci 1987, 33:177–189.
9. Baran EJ: Review: Spectroscopic studies of oxovanadium coordination compounds. J Coord Chem 2001, 54:215–238.
10. Kofugi K, Qian Cj, Murata Y, Kawashima S: The controlled release of insulin-mimetic metal ions by the multification of chitosan. J Inorg Biochem 2005, 99:1329–1334.
11. Thomson KH, Orvig C: Vanadium in diabetes: 100 years from Phase 0 to Phase I. J Inorg Biochem 2006, 100:1925–1935.
12. Thomson KH, Lichter J, Lebel C, Scliffe MC, McNeill H, Orvig C: Vanadium treatment of type 2 diabetes: a view to the future. J Inorg Biochem 2009, 103:554–558.
13. Parajón-Costa BS, Baran EJ: Vibrational spectra of bis(maltolato)oxovanadium(IV): A potent insulin mimetic agent. Spectrochim Acta A Mol Biomol Spectrosc 2011, 78:133–135.
14. Sanna D, Biró L, Buglyó P, Micera G, Garibba E: Transport of the anti-diabetic VO$^{2+}$ complexes formed by pyrone derivatives in the blood serum. J Inorg Biochem 2012, 115:857–861.
15. Sanna D, Biró L, Buglyó P, Micera G, Garibba E: Coordinating Properties of Pyrone and Pyridinone Derivatives, Tropolone and Catechol toward the VO$^{2+}$ Ion: An Experimental and Computational Approach. Eur J Inorg Chem 2012, 1079–1092.
16. Várnagy K, Csorba T, Kiss D, Garibba E, Micera G, Sanna D: VIVO Complexes of Bis[imidazol-2-yl] Derivatives: A Potentiometric, Spectroscopic and DFT Study. Eur J Inorg Chem 2007, 4884–4896.
17. Pisano L, Dávay K, Várnagy K, Sanna D, Micera G, Garibba E: Potentiometric, Spectroscopic and DFT Study of the VIVO Complexes Formed by Di(pyridin-2-yl) Ligands. Eur J Inorg Chem 2009, 2362–2374.
18. Kiss T, Kiss E, Garibba E, Sakurai H: Speciation of insulin-mimetic VO(IV)-containing drugs in blood serum. J Inorg Biochem 2000, 80:65–73.
19. Jansson-Chantier M, Guibal E, Roussi J, Delanghe B, Le Clarei P: Vanadium (IV) sorption by chitosan: kinetics and equilibrium. Water Res 1996, 30:465–475.
20. Bodek KH, Kufelnicki A: Protolytic and Complexing Properties of Microcrystalline Chitosan with Co(II), Zn(II), and Cu(II) Ions. J Appl Polym Sci 1995, 57:645–651.
21. Bodek KH, Kufelnicki A: Interaction of microcrystalline chitosan with Ni(II) and Mn(II) ions in aqueous solution. J Appl Polym Sci 2005, 98:2572–2577.
22. Lichawska ME, Kufelnicki A, Bodek KH: Coordinative interaction of microcrystalline chitosan (MCCh) with Ca(II) and Mg(II) in aqueous solution. Clin Exp Med Lett 2010, 5:4169–73.
23. Kufelnicki A, Lichawska M, Bodek KH: Interaction of Microcrystalline Chitosan (MCCh) with Mo(VI) in Aqueous Solution. J Appl Polym Sci 2009, 114:1619–1625.
24. Henry RP, Mitchell PCH, Prue JE: Hydrolysis of the Oxovanadium(IV) Ion and the Stability of its Complexes with the 1,2-Dihydroxybenzenato(2-) Ion. J Chem Soc Dalton Trans 1973, 1156–1159.
25. Komura A, Hayashi M, Imanaga H: Hydrolytic Behavior of Oxovanadium(IV) Ions. Bull Chem Soc Jpn 1977, 50:2927–2931.
26. Rossotti FJ, Rossotti HS: Studies on the Hydrolysis of Metal Ions, XII. The Hydrolysis of the Vanadium(IV) Ion. Acta Chem Scand 1955, 9:1177–1192.
27. Berto S, Giuseppe PD, Diana E, Lauretani F, Preneist E: Thermodynamic, spectroscopic and DFT description of oxovanadium(IV) complexes with malate and tartrate in aqueous solution. Inorg Chim Acta 2014, 414:105–114.
28. Lodya-Chruscińska E, Sanna D, Garibba E, Micera G: Potentiometric, spectroscopic, electrochemical and DFT characterization of oxovanadium(IV) complexes formed by citrate and tartrates in aqueous solution at high ligand to metal molar ratios: the effects of the trigonal bipyramidal distortion in bis-chelated species and biological implications. Dalton Trans 2008, 36:4903–4916.
29. Lodya-Chruscińska E, Sanna D, Garibba E, Micera G: Potentiometric, spectroscopic, electrochemical and DFT characterization of oxovanadium(IV) complexes formed by citrate and tartrates in aqueous solution at high ligand to metal molar ratios: the effects of the trigonal bipyramidal distortion in bis-chelated species and biological implications. Dalton Trans 2008, 36:4903–4916.
31. Taboada E, Cabrera G, Cardenas G: Retention Capacity of Chitosan for Copper and Mercury Ions. J Chilean Chem Soc 2003, 48:7–12.
32. Hadi AG: Adsorption of Nickel Ions By Synthesized Chitosan. Brit J Sci 2012, 6:109–113.
33. Tan SC, Khor E, Tan Teck K, Wong Sek M: The degree of deacetylation of chitosan: advocating the first derivative UV-spectrophotometry method of determination. Talanta 1998, 45:713–719.
34. Buck RP, Rondinini S, Covington AK, Baucke FGK, Brett CMA, Camões MF, Milton MJT, Mussini T, Naumann R, Pratt KW, Spitzer P, Wilson GS: Measurement of pH. Definition, standards, and procedures. Pure Appl Chem 2002, 74:2169–2200.
35. Irving HM, Miles MG, Pettit LD: A study of some problems in determining the stoichiometric proton dissociation constants of complexes by potentiometric titrations using a glass electrode. Anal Chim Acta 1967, 38:475–488.
36. Zekany L, Nagypal: PSEQUAD: A Comprehensive Program for the Evaluation of Potentiometric and/or Spectrophotometric Equilibrium Data Using Analytical Derivatives. In Computational Methods for the Determination of Stability Constants. Plenum Press; New York: David J. Leggett; 1985:352.
37. Gans P, Sabatini A, Vacca A, SUPERQUAD: an improved general program for computation of formation constants from potentiometric data. Journal of the Chemical Society, Dalton Transactions 1985, 1195–1200.
38. Sabatini A, Vacca A, Gans P: Mathematical algorithms and computer programs for the determination of equilibrium constants from potentiometric and spectrophotometric measurements. Coord Chem Rev 1992, 120:389–405.
39. Gans P, Sabatini A, Vacca A: Investigation of equilibria in solution. Determination of equilibrium constants with the HYPERQUAD suite of programs. Talanta 1996, 43:1739–1753.

doi:10.1186/s13065-014-0050-7

Cite this article as: Lichawska et al. Coordinative interaction of microcrystalline chitosan with oxovanadium (IV) ions in aqueous solution. Chemistry Central Journal 2014 8:50.