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Transport Properties of Carbohydrates: Towards the Minimization Toxicological Risks of Cobalt and Chromium Ions

Ana C. V. Trindade ¹, Sónia I. G. Fangaia ^{1,2,*} , Pedro M. G. Nicolau ^{1,3} , Ana C. F. Ribeiro ^{2,*} , Daniela S. A. Silva ² , Artur J. M. Valente ² , M. Melia Rodrigo ⁴  and Miguel A. Esteso ^{4,5} 

- ¹ Faculty of Medicine, CIROS, Institute of Implantology and Prosthodontics, University of Coimbra, Av. Bissaya Barreto, Blocos de Celas, 3000-075 Coimbra, Portugal; anavargastrindade@hotmail.com (A.C.V.T.); pgnicolau@mail.telepac.com (P.M.G.N.); ana.messias@uc.pt (A.M.)
- ² CQC-IMS, Department of Chemistry, University of Coimbra, 3004-535 Coimbra, Portugal; danielasilva178@gmail.com (D.S.A.S.); avalente@ci.uc.pt (A.J.M.V.)
- ³ Center of Mechanical Engineering Materials and Processes (CEMMPRE), Departamento de Engenharia Mecânica Pinhal de Marrocos, University of Coimbra, 3030-788 Coimbra, Portugal
- ⁴ U.D. Química Física, Universidad de Alcalá de Henares, 28805 Alcalá de Henares, Spain; mmelia.rodrigo@uah.es (M.M.R.); mangel.esteso@ucavila.es (M.A.E.)
- ⁵ Faculty of Health Sciences, Universidad Católica de Ávila, Calle Los Canteros s/n, 05005 Ávila, Spain
- * Correspondence: sfangaia@fmed.uc.pt (S.I.G.F.); anacfrib@ci.uc.pt (A.C.F.R.)

Abstract: The influence of oligosaccharides (α -cyclodextrin, β -cyclodextrin and γ -cyclodextrin), and a polysaccharide, sodium hyaluronate (NaHy), on the diffusion of aqueous solutions of cobalt and chromium chlorides has been investigated. Cobalt and chromium are constituents of metal alloys for biomedical use, including dental prostheses. Thus, the release of these ions in the human body can lead to harmful biological effects. The interaction of metal ions with saccharides might have information on the role of mouthwashes in preventing these effects. This interaction has been assessed by measuring multicomponent intermolecular diffusion coefficients at 298.15 K. It has been found that β -cyclodextrin has the highest interaction towards cobalt and chromium ions. This work will contribute to unveiling the mechanisms responsible for transport by diffusion in aqueous solutions, and, therefore, mitigating the potential toxicity inherent to those metal ions.

Keywords: cobalt; chromium; Co-Cr alloys; cyclodextrins; hyaluronic acid; diffusion coefficient; Taylor dispersion; transport properties



Citation: Trindade, A.C.V.; Fangaia, S.I.G.; Nicolau, P.M.G.; Messias, A.; Ribeiro, A.C.F.; Silva, D.S.A.; Valente, A.J.M.; Rodrigo, M.M.; Esteso, M.A. Transport Properties of Carbohydrates: Towards the Minimization Toxicological Risks of Cobalt and Chromium Ions. *Processes* **2023**, *11*, 1701. <https://doi.org/10.3390/pr11061701>

Academic Editor: Alexander Novikov

Received: 5 April 2023

Revised: 20 May 2023

Accepted: 23 May 2023

Published: 2 June 2023



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1. Introduction

The toxicity of heavy metals is an issue of growing concern in the scientific community. Although some of these metals such as cobalt (Co) and chromium (Cr) are essential nutrients, used in various biochemical and physiological functions [1] at high doses, regardless of their different oxidation states, they exhibit high toxicity [2].

Heavy metal-induced toxicity and carcinogenicity involve many mechanistic aspects, some of which are not clearly elucidated [1,3]. Human exposure to cobalt and chromium can occur for a short time or by prolonged exposure through inhalation, ingestion, or skin contact [4,5]. In human primary cells and experimental systems, cobalt metal seems to induce oxidative stress, chronic inflammation, changes in cell proliferation and death [6]; cobalt metal has also recently been classified as a C1B, M2, and R1B substance by the EU REACH Regulation, which has a significant and a direct impact on the application of Co-Cr biomedical alloys [7,8], despite the fact that metal cobalt presents physicochemical properties different from Co-based biomedical alloys [9].

It also should be stressed that chromium in its +6 oxidation state is also classified as human carcinogenic by the International Agency for Research on Cancer (IARC) [10]. It

should be stressed that this oxidation state is in equilibrium with chromium in the trivalent state, coexisting both in vivo [8,11]. Nevertheless, a recent in vitro study by Bellouard et al. showed that Cr^{3+} has cytotoxic effects on human HepaRG hepatocyte cells, even in low concentrations, similar to the concentrations found in prosthesis-wearing patients [3].

Co-Cr biomedical alloys are composed of approximately 60% and 30% of cobalt and chromium, respectively. These alloys have been the material of choice for fixed and removable dental prostheses, and are also used in orthodontic components [7,8]; although these oral devices are not implanted in the body, when located in the oral cavity, they are subject to corrosion phenomena and mechanical wear, with the release of the corresponding metallic ions in the oral environment [12–15].

With the high concern about chromium and cobalt [7,8,13,16], in this study, we intend to investigate the interaction between the following metal ions and saccharides frequently used in the pharmaceutical industry: cyclodextrins and hyaluronic acid. It should be stressed that metal salt solutions were used in previous studies of cytotoxicity of dental alloys, as reported elsewhere [17,18].

Cyclodextrins (CDs) are defined as cyclic oligomers, composed of glucopyranose units linked to each other, giving the molecule a truncated cone conformation with a hydrophilic outer surface and a hydrophobic inner cavity [19,20]. The most common CDs are α , β , and γ cyclodextrins with 6, 7 and 8 units, respectively [19]. The hydrophobic cavity allows CDs to form inclusion complexes [21] with hydrophobic molecules by the process of molecular complexation [19,22], and act as a molecular carrier [20]. Additionally, it is known that cyclodextrins can also form adducts with inorganic salts and are able to complex with cations, in particular, metal ions with high stability constants (i.e., $10 \text{ mol}^{-1} \text{ dm}^3 < K < 1000 \text{ mol}^{-1} \text{ dm}^3$) [23–27]. Due to this property, CDs offer a wide range of benefits in many industries (pharmaceutical, cosmetics, textile, food industry, etc.) [28].

Hyaluronic acid (HA) is a macromolecular mucopolysaccharide, composed of molecules of D-glucuronic acid and N-acetylglucosamine united by glycosides links [29]. HA has diagnostic and therapeutic potential, acting as a combinative agent with the encapsulation of different drugs and biomolecules or in the form of a nanocarrier [30].

Either cyclodextrins or hyaluronic acid are also present in some mouthwash formulations; CDs have solubilizing and anti-odor properties [31], while HA has anti-inflammatory and antioxidant properties [20,32,33], and act to prevent dental plaque and demineralization [31]. Additionally, cyclodextrins (in particular, β -cyclodextrin) are part of mouthwash formulations due to their recognized anti-viral properties [34,35].

By using a simple and reliable method, based on the evaluation of ternary interdiffusion diffusion coefficients obtained by using a Taylor dispersion technique, the interaction between cobalt and chromium salts and α -, β -, γ -cyclodextrins and sodium hyaluronate was evaluated. This represents the first step in understanding how the carrier carbohydrate molecules can most efficiently be used, e.g., in the formulations of mouthwashes, for reducing toxicological effects in organisms.

2. Materials and Methods

2.1. Materials

Table 1 describes all the reagents used as received in the present work, including cobalt chloride, chromium chloride, α -cyclodextrin, β -cyclodextrin and γ -cyclodextrin, and sodium hyaluronate. All chemicals were used without further purification.

All solutions were prepared using ultrapure water (Millipore, Germany, Milli-Q Advantage A10, specific resistance = $1.82 \times 105 \Omega \text{ m}$, at 298.15 K). The weighing was performed using a Radwag AS 220C2 balance (Radwag, Radom, Poland), with an accuracy of $\pm 0.0001 \text{ g}$. The concentrations of cyclodextrins were computed by correcting their water content.

Table 1. Description of materials.

Chemical Name	Source	CAS Number	Mass Fraction Purity ¹
Cobalt(II) chloride hexahydrate	Panreac	7791-13-1	>0.98
Chromium (III) chloride hexahydrate	Sigma-Aldrich	10060-12-5	>0.98
Sodium hyaluronate ²	Contipro Ltd. (Dolní Dobrouč, Czech Republic)	9067-32-7	
α -Cyclodextrin	Sigma-Aldrich	10016-20-3	
β -Cyclodextrin ³	Sigma-Aldrich	7585-39-9	>0.97
γ -Cyclodextrin	Sigma-Aldrich	17465-86-0	
H ₂ O	Millipore-Q water ($\rho = 1.82 \times 10^5 \Omega \text{ m at } 298.15 \text{ K}$)	7732-18-5	

¹ Values provided by the suppliers. ² In this work, we used two samples of NaHy with different molecular weights (i.e., Mw = 124 kDa and 243 kDa). ³ β -Cyclodextrin with water mass fraction 0.131.

2.2. Experimental Techniques

2.2.1. pH Measurements

The pH values were obtained using a Radiometer PHM 240 pH meter (Radiometer, Copenhagen, Denmark) coupled to a pH conjugate electrode (Ingold U457-K7). The pH measurements were obtained in recently prepared solutions, at 298.15 K, and after previous calibration of the electrode using, for this purpose, pH 4, 7 and 10 buffer solutions. The measurement sensitivity was greater than 98.7% and zero pH was equal to 6.11 ± 0.03 .

2.2.2. Taylor Dispersion Technique

The Taylor diffusion technique allows the measurement of diffusion coefficients in multicomponent systems and, as the name implies, is based on the work carried out by G.I. Taylor in the 1950s of the last century, being profusely described in the literature [36–39]. A summary of the most relevant issues related to the technique will be described in the following section. As a common feature of all chromatographic-based techniques, a disperse profile is obtained by injecting a volume equal to 0.063 mL of solution, at the beginning of the experiment, into a Teflon tube with a length and internal diameter of 3048.0 (± 0.1) cm and $0.06440 \pm (0.00006)$ cm, respectively, where a solution of defined concentration and composition flows in laminar flow. All equipment is thermostated at a temperature of 298.15 (± 0.01) K. The dispersion obtained in the sequence of different flows, of the different species, is registered using a differential refractometer (Waters model 2410). This equipment measures the electric potential as a function of time, $V(t)$, by coupling a digital voltmeter (Agilent 34401 A).

The dispersion profiles for these ternary solutions {CoCl₂ (or CrCl₃) + cyclodextrins (or sodium hyaluronate)} were analyzed by fitting the Equation (1) to the obtained dispersion profile [40–42].

$$V(t) = V_0 + V_1 + V_{\max}(t_R/t)^{1/2} \left[W_1 \exp\left(-\frac{12D_1(t-t_R)^2}{r^2t}\right) + (1 - W_1) \exp\left(-\frac{12D_2(t-t_R)^2}{r^2}\right) \right] \quad (1)$$

In Equation (1), V_{\max} is the dispersion peak height, V_0 and V_1 are the baseline voltage and baseline slope, respectively, W_1 is the normalized pre-exponential factor, D_1 and D_2 are the eigenvalues of the ternary diffusion coefficient matrix, r is the internal radius of the dispersion tube and t_R is the mean sample retention time.

The values of the tracer diffusion coefficients, D_T , for NaHy in aqueous solutions of cobalt chloride and chromium chloride were also measured. For these pseudo-binary

systems, $\text{CoCl}_2(1)/\text{NaHy}(2)$ and $\text{CrCl}_3(1)/\text{NaHy}(2)$, the previous dispersion equation (Equation (1)) can be simplified, and can be described as

$$V(t) = V_0 + V_1 t + V_{\max} (t_R/t)^{1/2} \exp\left(-\frac{12D_T(t-t_R)^2}{r^2 t}\right) \quad (2)$$

In fact, these systems can be considered as pseudo-binary, considering that the concentration of the salt under study (component 1) is significantly higher than the concentration of NaHy (component 2), ensuring the occurrence of tracer diffusion of the latter and the concentrations of CoCl_2 (or CrCl_3) in the injection and carrier solutions can be assumed as equal.

More details on how the binary and ternary diffusion coefficients can be calculated can be found in the following references [43–45].

3. Results

pH measurements were taken for the solutions containing cobalt chloride and chromium chloride, at 0.010 M, without and with cyclodextrins (α -CD, β -CD or γ -CD) or NaHy, to assess the state of metal ion species (Table 2). It can be observed that for the Co(II)-containing solutions, the pH is lower than ca. 6 and for Cr(III), the solutions have a pH lower than 4. At these pH values, we can say that the cobalt ion species are essentially in a non-hydrolyzed form [46]. Concerning the Cr^{3+} ions, the presence of hydrolyzed species cannot be ruled out.

Table 2. pH measurements for 0.010 M CoCl_2 or CrCl_3 solutions without and with cyclodextrins (CDs) 0.005 M or sodium hyaluronate, NaHy 0.1% (*w/v*).

Aqueous System	pH	Aqueous System	pH
CoCl_2	5.59	CrCl_3	3.45
$\text{CoCl}_2/\alpha\text{-CD}$	5.67	$\text{CrCl}_3/\alpha\text{-CD}$	3.25
$\text{CoCl}_2/\beta\text{-CD}$	5.92	$\text{CrCl}_3/\beta\text{-CD}$	3.20
$\text{CoCl}_2/\gamma\text{-CD}$	5.75	$\text{CrCl}_3/\gamma\text{-CD}$	3.15
NaHy ¹	6.09	$\text{CrCl}_3/\text{NaHy}$ ¹	3.90
NaHy ²	6.45	$\text{CrCl}_3/\text{NaHy}$ ²	3.80
$\text{CoCl}_2/\text{NaHy}$ ¹	5.46		
$\text{CoCl}_2/\text{NaHy}$ ²	5.30		

¹ Mw(NaHy) = 124 kDa. ² Mw(NaHy) = 234 kDa.

Tables 3 and 4 summarize the mean values of the D_{ik} diffusion coefficients for the solutions of different compositions and concentrations for six aqueous systems, involving two salts (CoCl_2 and CrCl_3) and three cyclodextrins (α -CD, β -CD and γ -CD). The values were calculated by fitting Equation (1) to dispersion curves; the number of replicas is always greater than four. The main diffusion coefficients (D_{11} and D_{22}) have an uncertainty value smaller than ($\pm 0.015 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$), whilst the cross-diffusion coefficients (D_{12} and D_{21}) have an uncertainty value smaller than ($\pm 0.030 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$).

At the limiting situations of $X_1 = 0$ and $X_1 = 1$, the values of D_{11} correspond to the tracer diffusion coefficient of CoCl_2 (or CrCl_3) in CDs and the binary mutual diffusion coefficient of aqueous CoCl_2 (or CrCl_3) at 0.001 and 0.01 M, respectively. Regarding these latter values for D_{11} , a good agreement is observed between them and the binary diffusion coefficient values reported in previous works [47,48]. For example, for aqueous CrCl_3 solutions at 0.01 M, the deviations are equal to or less than 0.8% between the binary value $D = 1.170 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ [47] and the D_{11} values shown in Table 3 ($D_{11} = 1.172 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$, $D_{11} = 1.180 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ and $D_{11} = 1.160 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$).

Table 3. Ternary diffusion coefficients ($D_{11}, D_{12}, D_{21}, D_{22}$)¹ of aqueous $\text{CrCl}_3(\text{C}_1) + \text{CDs}(\text{C}_2)$ solutions.

C_1^2	C_2^2	X_1	$D_{11} \pm S_D^3$	$D_{12} \pm S_D^3$	$D_{21} \pm S_D^3$	$D_{22} \pm S_D^3$
CrCl ₃ (C ₁) + α-CD (C ₂) solutions						
0.001	0.000	1.000	1.267 ± 0.010	−0.013 ± 0.004	−0.019 ± 0.015	0.467 ± 0.020
0.000	0.010	0.000	1.285 ± 0.010	−0.007 ± 0.004	−0.030 ± 0.015	0.470 ± 0.015
0.010	0.000	1.000	1.172 ± 0.019	−0.016 ± 0.009	0.014 ± 0.004	0.499 ± 0.021
CrCl ₃ (C ₁) + β-CD (C ₂) solutions						
0.001	0.000	1.000	1.210 ± 0.020	−0.183 ± 0.020	−0.020 ± 0.010	0.408 ± 0.007
0.000	0.007	0.000	1.270 ± 0.020	−0.023 ± 0.014	−0.070 ± 0.010	0.401 ± 0.010
0.007	0.000	1.000	1.180 ± 0.020	−0.092 ± 0.020	−0.025 ± 0.010	0.418 ± 0.005
CrCl ₃ (C ₁) + γ-CD (C ₂) solutions						
0.001	0.000	1.000	1.232 ± 0.014	−0.019 ± 0.012	0.019 ± 0.010	0.458 ± 0.001
0.000	0.010	0.000	1.242 ± 0.011	−0.007 ± 0.010	0.019 ± 0.010	0.450 ± 0.001
0.010	0.000	1.000	1.160 ± 0.017	−0.020 ± 0.008	0.009 ± 0.003	0.460 ± 0.002

¹ Averaged result for $n = 8$ experiments. ² C_1 and C_2 in mol dm^{−3}. ³ $D_{ij} \pm S_D$ in 10^{−9} m² s^{−1}, and at T = 298.15 K.

Table 4. Ternary diffusion coefficients ($D_{11}, D_{12}, D_{21}, D_{22}$)¹ of aqueous $\text{CoCl}_2(\text{C}_1) + \text{CDs}(\text{C}_2)$ solutions.

C_1^2	C_2^2	X_1	$D_{11} \pm S_D^3$	$D_{12} \pm S_D^3$	$D_{21} \pm S_D^3$	$D_{22} \pm S_D^3$
CoCl ₂ (C ₁) + α-CD (C ₂) solutions						
0.001	0.000	1.000	1.201 ± 0.010	−0.070 ± 0.024	−0.010 ± 0.020	0.471 ± 0.026
0.000	0.010	0.000	1.300 ± 0.007	−0.010 ± 0.018	0.008 ± 0.0001	0.469 ± 0.014
0.010	0.000	1.000	1.258 ± 0.007	−0.030 ± 0.018	0.0001 ± 0.0001	0.479 ± 0.034
CoCl ₂ (C ₁) + β-CD (C ₂) solutions						
0.001	0.000	1.000	1.219 ± 0.021	−0.268 ± 0.024	0.010 ± 0.010	0.435 ± 0.010
0.000	0.007	0.000	1.268 ± 0.020	−0.015 ± 0.013	−0.040 ± 0.010	0.438 ± 0.016
0.007	0.000	1.000	1.235 ± 0.021	−0.190 ± 0.014	+0.002 ± 0.010	0.435 ± 0.029
CoCl ₂ (C ₁) + γ-CD (C ₂) solutions						
0.001	0.000	1.000	1.260 ± 0.010	−0.030 ± 0.043	−0.010 ± 0.010	0.479 ± 0.019
0.000	0.010	0.000	1.289 ± 0.015	−0.011 ± 0.013	−0.010 ± 0.010	0.440 ± 0.020
0.010	0.000	1.000	1.256 ± 0.004	−0.040 ± 0.016	+0.003 ± 0.002	0.480 ± 0.023

¹ Averaged result for $n = 8$ experiments. ² C_1 and C_2 in mol dm^{−3}. ³ $D_{ij} \pm S_D$ in 10^{−9} m² s^{−1}, and at T = 298.15 K.

Tables 5 and 6 show the average values of the binary and ternary diffusion coefficients of NaHy in different aqueous solutions containing CoCl_2 (or CrCl_3) at the following two different concentrations: 0.001 and 0.010 M. These values were calculated from, at least, six independent measurements. Once the high viscosity of sodium hyaluronate strongly affects the measurement of the diffusion coefficients, these measurements were only carried out at tracer concentrations (Section 2.2.2). While the main diffusion coefficients D_{11} and D_{22} were generally reproducible within $\pm (0.020 \times 10^{-9} \text{ m}^2 \text{ s}^{-1})$, the cross-coefficients were in general reproducible within about $\pm (0.040 \times 10^{-9} \text{ m}^2 \text{ s}^{-1})$.

From Table 6, we can observe that whereas the limiting values for cross-coefficients D_{21} at the infinitesimal concentration are practically zero, within the experimental error, the cross-coefficients D_{12} differ from zero. In the other words, $D_{12} < 0$ indicates that the gradient in the concentration of NaHy produces counter-current coupled flows of CoCl_2 and CrCl_3 .

Table 5. Tracer diffusion coefficients, ${}^{\text{app}}D_T^0$, for NaHy¹ in aqueous solutions of CoCl₂ and CrCl₃ at 0.001 and 0.010 M, and T = 298.15 K.

Aqueous System	${}^{\text{app}}D_T^0 \pm S_D / (10^{-9} \text{ m}^2 \text{ s}^{-1})^1$	$(\Delta {}^{\text{app}}D_T^0 / D^0)\% ^4$
CoCl ₂ (0.001 M)	0.081 ± 0.008 ²	−86
CoCl ₂ (0.001 M)	0.082 ± 0.006 ³	−85
CoCl ₂ (0.010 M)	0.296 ± 0.030 ²	−49
CoCl ₂ (0.010 M)	0.312 ± 0.020 ³	−44
CrCl ₃ (0.001 M)	0.092 ± 0.010 ²	−84
CrCl ₃ (0.001 M)	0.099 ± 0.025 ³	−82
CrCl ₃ (0.010 M)	0.192 ± 0.009 ²	−67
CrCl ₃ (0.010 M)	0.125 ± 0.010 ³	−78

¹ Averaged result for $n = 8$ experiments. ² $M(\text{NaHy}) = 124 \text{ kDa}$. ³ $M(\text{NaHy}) = 234 \text{ kDa}$. ⁴ $D_L = 0.583 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ and $D_L = 0.562 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ for $M_w(\text{NaHy}) = 124 \text{ kDa}$ and $M_w(\text{NaHy}) = 234 \text{ kDa}$, respectively [47].

Table 6. Tracer ternary diffusion coefficients¹, D_{11} , D_{12} , D_{21} and D_{22} , for NaHy (component 2) in salt (component 1) solution, at $C_2 = 0.001$ and $0.010 \text{ mol dm}^{-3}$ and T = 298.15 K.

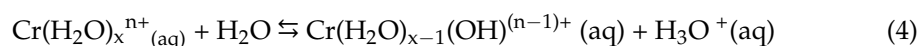
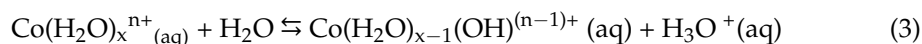
Salt	C_1 $/(\text{mol dm}^{-3})$	$D_{11} \pm S_D$ $/(10^{-9} \text{ m}^2 \text{ s}^{-1})$	$D_{12} \pm S_D$ $/(10^{-9} \text{ m}^2 \text{ s}^{-1})$	$D_{21} \pm S_D$ $/(10^{-9} \text{ m}^2 \text{ s}^{-1})$	$D_{22} \pm S_D$ $/(10^{-9} \text{ m}^2 \text{ s}^{-1})$
COCl ₂	0.001 ²	1.281 ± 0.025	−0.318 ± 0.030	0.058 ± 0.039	0.162 ± 0.019
	0.001 ³	1.255 ± 0.010	−0.124 ± 0.030	0.040 ± 0.019	0.065 ± 0.013
COCl ₂	0.010 ²	1.276 ± 0.020	−0.265 ± 0.035	0.008 ± 0.011	0.172 ± 0.013
	0.010 ³	1.215 ± 0.010	−0.205 ± 0.060	0.010 ± 0.019	0.192 ± 0.013
CrCl ₃	0.010 ²	1.136 ± 0.008	−0.195 ± 0.038	0.012 ± 0.015	0.157 ± 0.010
	0.010 ³	1.137 ± 0.012	−0.182 ± 0.040	−0.050 ± 0.029	0.302 ± 0.017

¹ Averaged result for $n = 8$ experiments. ² NaHy 124 kDa. ³ NaHy 234 kDa. $u_r(c) = 0.02$; $u_r(T) = 0.01 \text{ K}$ and $u(p) = 2.03 \text{ kPa}$; u and u_r represent the standard uncertainty and the relative standard uncertainty, respectively.

4. Discussion

From Tables 2 and 3, it can be observed that the limiting values for the infinitesimal concentration of cross-coefficients D_{21} can be considered null, taking into account the experimental error. This arises, most probably, due to the similarity of the mobilities of CD free species and eventual aggregates of CoCl₂ (or CrCl₃) and CDs. However, $D_{12} < 0$; that is, the gradient in the concentration of CD (α -CD, β -CD and γ -CD) produces counter-current coupled flows of these salts, which are the most significant in highly concentrated solutions of β -CD. These observations can readily be explained by the following two phenomena: the hydrolysis of cobalt and chromium ions and association between CoCl₂ (or CrCl₃) and these cyclodextrin molecules, leading to the formation of complexes in solution. This phenomenon will lead to a decrease in free cobalt (or chromium ions), and, consequently, to compensate for that loss, a counterflow of these salts will occur.

In fact, the diffusion of these salts can be affected by Co(II) and Cr(III) hydrolysis. As cobalt chloride and chromium chloride aqueous solutions are acidic if unbuffered (Table 2), when these salts diffuse in water, the hydronium ions produced by hydrolysis of the cobalt and chromium ions (as shown in Equations (3) and (4)) should diffuse ahead of the less-mobile cobalt (or chromium ions), producing a counter flow of chloride acid in addition to the main flow of partially hydrolyzed cobalt chloride (or chromium chloride) [47–49].

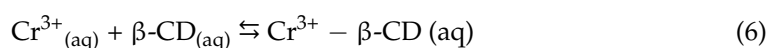
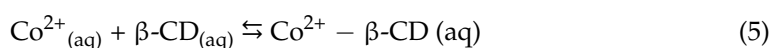


In other words, once the H_3O^+ ion has much higher mobility than Cl^- from the anomalous mechanism for H^+ proton transport in water, a strong electric field is generated, slowing down the H_3O^+ ions driving the large counter-current fluxes of Cr(III) (or Co(II)) species, free or associated with CD molecules and, thus, $D_{12} < 0$. Despite the diffusion of

aqueous cobalt chloride (or chromium chloride) being a ternary process because there is a small but additional flow of chloride acid, we can consider that if corrections for chloride acid diffusion are not made, the apparent binary diffusion coefficients of CoCl_2 (or CrCl_3) can only be 1–3%, which is too large. Support for this observation is given in the literature where the negligible effect of the hydrolysis of the beryllium ion on the diffusion of BeSO_4 is analyzed [50].

However, for aqueous systems containing CoCl_2 (or CrCl_3) plus β -CD, the D_{12} values are significantly more negative when compared with those obtained for the systems containing α -CD and γ -CD. The formation of aggregates between Co^{2+} and Cr^{3+} ions, and β -CD molecules can be other phenomenon that also occur, therefore justifying this difference in thermodynamic behavior between them.

Assuming the formation of a 1:1 supramolecular complex between these cations (Co^{2+} and Cr^{3+}) and β -CD (Equations (5) and (6)), and considering the values indicated in Table 7 for the limiting diffusion coefficients of the free and complexed species, the values for these binding constants K (Equations (7) and (8)) can be computed [45] and are equal to $40 (\pm 0.9) \text{ M}^{-1}$ and $30 (\pm 0.6) \text{ M}^{-1}$.



$$K = \frac{C_{(\text{Co}^{2+} - \beta\text{-CD})}}{C_{\text{Co}^{2+}} \cdot C_{\beta\text{-CD}}} \quad (7)$$

$$K = \frac{C_{(\text{Cr}^{3+} - \beta\text{-CD})}}{C_{\text{Cr}^{3+}} \cdot C_{\beta\text{-CD}}} \quad (8)$$

Table 7. Limiting diffusion coefficients, D_s , of species at $T = 298.15 \text{ K}$.

Species	$D_s / (10^{-9} \text{ m}^2 \text{ s}^{-1})$
CrCl_3	1.266 ¹
CoCl_2	1.272 ²
$\beta\text{-CD}$	0.400 ³
$\text{CoCl}_2\text{-}\beta\text{-CD}$	0.396 ³
$\text{CoCl}_3\text{-}\beta\text{-CD}$	0.395 ³

¹ [47]. ² [48]. ³ $D = (D_{(\text{CoCl}_2 \text{ or } \text{CrCl}_3)}^{-3} + D_{\beta\text{-CD}}^{-3})^{-1/3}$ [51].

From the values of these constants, we can consider that this interaction between these species is not negligible, and thus, some amounts of $\text{Co}(\text{II})$ (or $\text{Cr}(\text{III})$) and β -CD molecules can be transported as $\text{Co}^{2+}\text{-}\beta\text{-CD}$ (or $\text{Cr}^{3+}\text{-}\beta\text{-CD}$) complexes. In the range of higher β -CD concentrations, a high percentage of chromium chloride (or cobalt chloride) is in complexed form (i.e., associated with cyclodextrin). Consequently, the β -CD concentration gradient is responsible for a gradient in the opposite direction for the concentration of chromium (or cobalt) cations. This justifies the occurrence of a countercurrent to the main flow of chromium chloride and, consequently, the D_{12} values are negative for these solutions at the molar fraction of salt $X_1 = 1$ (Tables 2 and 3).

In relation to other CDs, at which $D_{12} \approx 0$, the interaction with these metal ions might be considered negligible. One possible explanation for the anomalous and unexpected diffusion behavior of β -CD in the presence of these salts may be attributed to its peculiar, less flexible molecular structure [52] and to the reduced number of hydroxyl groups capable of establishing hydrogen bonds with surrounding water molecules, as a consequence of the intramolecular hydrogen bonds between their secondary hydroxyl groups (that is, between a hydroxyl group at C-2 and a glucose unit and a hydroxyl group at C-2 of another adjacent glucose unit [53]). The presence of ions Co^{2+} and Cr^{3+} in these solutions will

perturb the dynamic structure of the water molecules surrounding β -CD and the intra cavity water molecules, as a consequence of the strong electrostatic interactions between their available hydroxyl groups and these ions, leading to the formation of complexes in solution, which are expected to demonstrate lower mobility than free species. Support for this observation is pointed out by Coleman et al. [54], and Poulson et al. [55] when they verified that multivalent cations lead to a significant alteration in β -cyclodextrin solubility, in aqueous solutions. This evidence demonstrates that this phenomenon is a result of the modification of the structure of water and leads to more favorable interactions with the β -CD supramolecular complexes.

Relative to the effect of the presence of NaHy on the diffusion behavior of CoCl_2 (or CrCl_3), we can say that this carbohydrate also significantly affects this parameter, as shown by the $D_{12} < 0$ values. (Table 6). This fact is not unexpected, bearing in mind the different mobilities of the sodium cation and the hyaluronate anions; that is, $\lambda^0(\text{Na}^+) = 50.10 \times 10^{-4} \Omega^{-1} \text{ m}^2 \text{ mol}^{-1}$ and $\lambda^0(\text{Hy}^- \text{ monomer}) = 40.05 \times 10^{-4} \Omega^{-1} \text{ m}^2 \text{ mol}^{-1}$ [56]. Once the Na^+ ion has much higher mobility than Hy^- , when there is a gradient of NaHy in solution, a strong electric field is generated, slowing down the Na^+ ions and driving large counter-current fluxes of Cr^{3+} (or Co^{2+}) species, free or associated and $D_{12} < 0$.

Information about coupled diffusion can be also inferred by the calculated values of the ratio D_{12}/D_{22} (Table 8). The higher negative ratio values for $\text{CoCl}_2/\text{NaHy}$ and $\text{CrCl}_3/\text{NaHy}$ systems, when compared with others, permits us to conclude that one mole of diffusing NaHy counter-transport up to 2 mol of CoCl_2 (or up to 1.2 mol of CrCl_3).

Table 8. Estimation of the moles of CoCl_2 and CrCl_3 transported for each mol of α -CD, β -CD, γ -CD, and NaHy 0.1%, obtained from D_{ij} data shown in Tables 2 and 3.

[CoCl ₂]/(M)	Aqueous System	D_{12}/D_{22}	[CrCl ₃]/(M)	D_{12}/D_{22}	
0.001	CoCl ₂ /(α -CD)	−0.15	0.001	CrCl ₃ /(α -CD)	−0.08
	CoCl ₂ /(β -CD)	−0.62		CrCl ₃ /(β -CD)	−0.45
	CoCl ₂ / γ -CD	−0.06		CrCl ₃ (γ -CD)	−0.02
	CoCl ₂ /NaHy ¹	−1.96			
	CoCl ₂ /NaHy ²	−1.91			
0.010	CoCl ₂ /(α -CD)	−0.12	0.010	CrCl ₃ /(α -CD)	−0.03
	CoCl ₂ /(β -CD)	−0.44		CrCl ₃ /(β -CD)	−0.22
	CoCl ₂ / γ -CD	−0.08		CrCl ₃ / γ -CD	−0.04
	CoCl ₂ /NaHy ¹	−1.54		CrCl ₃ /NaHy ¹	−1.24
	CoCl ₂ /NaHy ²	−1.07		CrCl ₃ /NaHy ²	−0.60

¹ NaHy 124 kDa. ² NaHy 234 kDa.

5. Conclusions

Sodium hyaluronate and one of the studied cyclodextrins, β -cyclodextrins, present a greater interaction with cobalt and chromium ions, which is why we consider them to be the best carrier agents for these metal ions.

D_{12} negative and K ($40 (\pm 0.9) \text{ M}^{-1}$ and $30 (\pm 0.6) \text{ M}^{-1}$) values show that β -CD interacts with both cobalt and chromium ions. This complexation prevents the occurrence of the hydrolysis of metal ions. It can be concluded that the interaction of ions with only β -CD probably arises from the perturbation of the structure of water and leads to less unfavorable interactions with the β -CD aggregates.

The present work shows that cyclodextrins and hyaluronic acid interact with cobalt and chromium ions once a significant amount of these salts per each mol of these carbohydrates (at most 2 mol of CoCl_2 per mol of NaHy) is transported. It can be hypothesized that the presence of these carbohydrates into mouthwash formulation might mitigate the toxicity inherent to the presence of metal ions.

We believe that the data obtained can be of great value to the entire scientific and technological community that works with these metals.

Author Contributions: Conceptualization, S.I.G.F., A.C.F.R., A.J.M.V., P.M.G.N. and M.A.E.; Methodology, S.I.G.F. and A.C.F.R.; Software, A.C.V.T., S.I.G.F., A.C.F.R., D.S.A.S. and M.M.R.; Validation, S.I.G.F., A.C.F.R., A.J.M.V., A.M., P.M.G.N. and M.A.E.; Formal Analysis, S.I.G.F., A.C.F.R., A.J.M.V., A.M., P.M.G.N. and M.A.E.; Investigation, A.C.V.T., S.I.G.F., P.M.G.N., A.M., A.C.F.R., D.S.A.S., A.J.M.V., M.M.R. and M.A.E.; Resources, A.C.V.T., S.I.G.F., P.M.G.N., A.M., A.C.F.R., D.S.A.S., A.J.M.V., M.M.R. and M.A.E.; Data Curation, S.I.G.F., A.C.F.R., A.J.M.V., A.M., P.M.G.N. and M.A.E.; Writing—Original Draft Preparation, A.C.V.T., S.I.G.F., A.C.F.R., A.J.M.V. and M.A.E.; Writing—Review and Editing, S.I.G.F., P.M.G.N., A.M., A.C.F.R., A.J.M.V., M.M.R. and M.A.E.; Visualization, A.C.V.T., S.I.G.F., P.M.G.N., A.M., A.C.F.R., D.S.A.S., A.J.M.V., M.M.R. and M.A.E.; Supervision, S.I.G.F. and A.C.F.R.; Project Administration, S.I.G.F. and A.C.F.R.; Funding Acquisition, S.I.G.F., A.C.F.R., A.J.M.V. and P.M.G.N. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Coimbra Chemistry Centre, which is supported by the Fundação para a Ciência e a Tecnologia (FCT), Portuguese Agency for Scientific Research, through the projects UID/UI0313/2013 and COMPETE Programme (Operational Programme for Competitiveness) and CIROS, Centro de Investigação e Inovação em Ciências Dentárias da FMUC.

Data Availability Statement: All data are presented in this paper.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Tchounwou, P.B.; Yedjou, C.G.; Patlolla, A.K.; Sutton, D.J. Heavy Metal Toxicity and the Environment. *Exp. Suppl.* **2012**, *101*, 133–164. [[PubMed](#)]
2. Vareda, J.P.; Valente, A.J.M.; Durães, L. Assessment of Heavy Metal Pollution from Anthropogenic Activities and Remediation Strategies: A Review. *J. Environ. Manag.* **2019**, *246*, 101–118. [[CrossRef](#)] [[PubMed](#)]
3. Bellouard, M.; Gasser, M.; Lenglet, S.; Gilardi, F.; Bararpour, N.; Augsburger, M.; Thomas, A.; Alvarez, J.-C. Toxicity and Metabolomic Impact of Cobalt, Chromium, and Nickel Exposure on HepaRG Hepatocytes. *Chem. Res. Toxicol.* **2022**, *35*, 807–816. [[CrossRef](#)] [[PubMed](#)]
4. Hariyani, N.; Berniyanti, T.; Setyowati, D. Effects of Occupational Environmental Controls on the Level of Co, Ni and Cr among Dental Technicians. *Int. J. Environ. Sci. Dev.* **2015**, *6*, 643–647. [[CrossRef](#)]
5. Lison, D.; van den Brule, S.; Van Maele-Fabry, G. Cobalt and Its Compounds: Update on Genotoxic and Carcinogenic Activities. *Crit. Rev. Toxicol.* **2018**, *48*, 522–539. [[CrossRef](#)]
6. Karagas, M.R.; Wang, A.; Dorman, D.C.; Hall, A.L.; Pi, J.; Sergi, C.M.; Symanski, E.; Ward, E.M.; Arrandale, V.H.; Azuma, K.; et al. Carcinogenicity of Cobalt, Antimony Compounds, and Weapons-Grade Tungsten Alloy. *Lancet Oncol.* **2022**, *23*, 577–578. [[CrossRef](#)]
7. Grosogoeat, B.; Vaicelyte, A.; Gauthier, R.; Janssen, C.; Le Borgne, M. Toxicological Risks of the Cobalt–Chromium Alloys in Dentistry: A Systematic Review. *Materials* **2022**, *15*, 5801. [[CrossRef](#)]
8. Vaicelyte, A.; Janssen, C.; Le Borgne, M.; Grosogoeat, B. Cobalt–Chromium Dental Alloys: Metal Exposures, Toxicological Risks, CMR Classification, and EU Regulatory Framework. *Crystals* **2020**, *10*, 1151. [[CrossRef](#)]
9. Eichenbaum, G.; Wilsey, J.T.; Fessel, G.; Qiu, Q.-Q.; Perkins, L.; Hasgall, P.; Monnot, A.; More, S.L.; Egnot, N.; Sague, J.; et al. An Integrated Benefit-Risk Assessment of Cobalt-Containing Alloys Used in Medical Devices: Implications for Regulatory Requirements in the European Union. *Regul. Toxicol. Pharmacol.* **2021**, *125*, 105004. [[CrossRef](#)]
10. Deng, Y.; Wang, M.; Tian, T.; Lin, S.; Xu, P.; Zhou, L.; Dai, C.; Hao, Q.; Wu, Y.; Zhai, Z.; et al. The Effect of Hexavalent Chromium on the Incidence and Mortality of Human Cancers: A Meta-Analysis Based on Published Epidemiological Cohort Studies. *Front. Oncol.* **2019**, *9*, 24. [[CrossRef](#)]
11. Meek, R.M.D.; Afolaranmi, G.A.; Tettey, J.; Grant, M.H. Release of Chromium from Orthopaedic Arthroplasties. *Open Orthop. J.* **2008**, *2*, 10–18. [[CrossRef](#)]
12. Haugli, K.H.; Syverud, M.; Samuelsen, J.T. Ion Release from Three Different Dental Alloys—Effect of Dynamic Loading and Toxicity of Released Elements. *Biomater. Investig. Dent.* **2020**, *7*, 71–79. [[CrossRef](#)]
13. Fangaia, S.I.G.; Nicolau, P.M.G.; Guerra, F.A.D.R.A.; Rodrigo, M.M.; Utzeri, G.; Cabral, A.M.T.D.P.V.; Valente, A.J.M.; Estes, M.A.; Ribeiro, A.C.F. Effect of Cobalt and Chromium Ions on the Chlorhexidine Digluconate as Seen by Intermolecular Diffusion. *Int. J. Mol. Sci.* **2021**, *22*, 13266. [[CrossRef](#)]
14. Affatato, S.; Grillini, L. Topography in Bio-Tribocorrosion. In *Bio-Tribocorrosion in Biomaterials and Medical Implants*; Elsevier: Amsterdam, The Netherlands, 2013; pp. 1–22.
15. Arregui, M.; Latour, F.; Gil, F.J.; Pérez, R.A.; Giner-Tarrida, L.; Delgado, L.M. Ion Release from Dental Implants, Prosthetic Abutments and Crowns under Physiological and Acidic Conditions. *Coatings* **2021**, *11*, 98. [[CrossRef](#)]
16. Golgovici, F.; Prodana, M.; Ionascu, F.G.; Demetrescu, I. A Comparative Electrochemical and Morphological Investigation on the Behavior of NiCr and CoCr Dental Alloys at Various Temperatures. *Metals* **2021**, *11*, 256. [[CrossRef](#)]

17. Schmalz, G.; Langer, H.; Schweikl, H. Cytotoxicity of Dental Alloy Extracts and Corresponding Metal Salt Solutions. *J. Dent. Res.* **1998**, *77*, 1772–1778. [[CrossRef](#)]
18. Milheiro, A.; Nozaki, K.; Kleverlaan, C.J.; Muris, J.; Miura, H.; Feilzer, A.J. In Vitro Cytotoxicity of Metallic Ions Released from Dental Alloys. *Odontology* **2016**, *104*, 136–142. [[CrossRef](#)]
19. Sharma, N.; Baldi, A. Exploring Versatile Applications of Cyclodextrins: An Overview. *Drug Deliv.* **2016**, *23*, 729–747. [[CrossRef](#)]
20. Fangaia, S.I.G.; Cabral, A.M.T.D.P.V.; Nicolau, P.M.G.; Guerra, F.A.D.R.A.; Rodrigo, M.M.; Ribeiro, A.C.F.; Valente, A.J.M.; Estes, M.A. Diffusion of Vanadium Ions in Artificial Saliva and Its Elimination from the Oral Cavity by Pharmacological Compounds Present in Mouthwashes. *Biomolecules* **2022**, *12*, 947. [[CrossRef](#)]
21. Bellia, F.; La Mendola, D.; Pedone, C.; Rizzarelli, E.; Saviano, M.; Vecchio, G. Selectively Functionalized Cyclodextrins and Their Metal Complexes. *Chem. Soc. Rev.* **2009**, *38*, 2756–2781. [[CrossRef](#)]
22. Valente, A.J.M.; Söderman, O. The Formation of Host–Guest Complexes between Surfactants and Cyclodextrins. *Adv. Colloid Interface Sci.* **2014**, *205*, 156–176. [[CrossRef](#)] [[PubMed](#)]
23. Ribeiro, A.C.F.; Estes, M.A.; Lobo, V.M.M.; Valente, A.J.M.; Simões, S.M.N.; Sobral, A.J.F.N.; Ramos, L.; Burrows, H.D.; Amado, A.M.; Amorim da Costa, A.M. Interactions of Copper (II) Chloride with β -Cyclodextrin in Aqueous Solutions. *J. Carbohydr. Chem.* **2006**, *25*, 173–185. [[CrossRef](#)]
24. Norkus, E.; Grincien, G.; Vaitkus, R. Interaction of Lead(II) with β -Cyclodextrin in Alkaline Solutions. *Carbohydr. Res.* **2002**, *337*, 1657–1661. [[CrossRef](#)] [[PubMed](#)]
25. Buvári, Á.; Barcza, L. Complex Formation of Inorganic Salts with β -Cyclodextrin. *J. Incl. Phenom. Mol. Recognit. Chem.* **1989**, *7*, 379–389. [[CrossRef](#)]
26. Buvári, Á.; Barcza, L. β -Cyclodextrin Complexes of Different Type with Inorganic Compounds. *Inorg. Chim. Acta* **1979**, *33*, L179–L180. [[CrossRef](#)]
27. Ribeiro, A.C.F.; Lobo, V.M.M.; Valente, A.J.M.; Simões, S.M.N.; Sobral, A.J.F.N.; Ramos, M.L.; Burrows, H.D. Association between Ammonium Monovanadate and β -Cyclodextrin as Seen by NMR and Transport Techniques. *Polyhedron* **2006**, *25*, 3581–3587. [[CrossRef](#)]
28. Hedges, A.R. Industrial Applications of Cyclodextrins. *Chem. Rev.* **1998**, *98*, 2035–2044. [[CrossRef](#)]
29. Salwowska, N.M.; Bebenek, K.A.; Żądło, D.A.; Wcisło-Dziadecka, D.L. Physicochemical Properties and Application of Hyaluronic Acid: A Systematic Review. *J. Cosmet. Dermatol.* **2016**, *15*, 520–526. [[CrossRef](#)]
30. Vasvani, S.; Kulkarni, P.; Rawtani, D. Hyaluronic Acid: A Review on Its Biology, Aspects of Drug Delivery, Route of Administrations and a Special Emphasis on Its Approved Marketed Products and Recent Clinical Studies. *Int. J. Biol. Macromol.* **2020**, *151*, 1012–1029. [[CrossRef](#)]
31. Radzki, D.; Wilhelm-Węglarz, M.; Pruska, K.; Kusiak, A.; Ordyniec-Kwaśnica, I. A Fresh Look at Mouthwashes—What Is Inside and What Is It For? *Int. J. Environ. Res. Public Health* **2022**, *19*, 3926. [[CrossRef](#)]
32. Rodrigues, S.V.; Acharya, A.B.; Bhadbhade, S.; Thakur, S.L. Hyaluronan-Containing Mouthwash as an Adjunctive Plaque-Control Agent. *Oral Health Prev. Dent.* **2010**, *8*, 389–394.
33. Boccalari, E.; Tadakamadla, S.K.; Occhipinti, C.; Lanteri, V.; Maspero, C. Evaluation of the Effectiveness of a Novel Mouth Rinse Containing Hyaluronic Acid and Hydrogen Peroxide on Gingivitis: A Randomized Pilot Controlled Trial. *Clin. Exp. Dent. Res.* **2022**, *8*, 673–679. [[CrossRef](#)]
34. Carrouel, F.; Gonçalves, L.S.; Conte, M.P.; Campus, G.; Fisher, J.; Fraticelli, L.; Gadea-Deschamps, E.; Ottolenghi, L.; Bourgeois, D. Antiviral Activity of Reagents in Mouth Rinses against SARS-CoV-2. *J. Dent. Res.* **2021**, *100*, 124–132. [[CrossRef](#)]
35. Carrouel, F.; Valette, M.; Gadea, E.; Esparcieux, A.; Illes, G.; Langlois, M.E.; Perrier, H.; Dussart, C.; Tramini, P.; Ribaud, M.; et al. Use of an Antiviral Mouthwash as a Barrier Measure in the SARS-CoV-2 Transmission in Adults with Asymptomatic to Mild COVID-19: A Multicentre, Randomized, Double-Blind Controlled Trial. *Clin. Microbiol. Infect.* **2021**, *27*, 1494–1501. [[CrossRef](#)]
36. Tyrrell, H.J.V.; Harris, K.R. *Diffusion in Liquids*; Butterworths: London, UK, 1984.
37. Faro, M.P.R.T.; Barros, M.C.F.; Santos, C.I.A.V.; Ribeiro, A.C.F. Coupled Mutual Diffusion in Aqueous Calcium Sulphate + Sulphuric Acid Solutions. *J. Chem. Thermodyn.* **2022**, *165*, 106659. [[CrossRef](#)]
38. Ribeiro, A.C.F.; Santos, C.I.A.V.; Lobo, V.M.M.; Cabral, A.M.T.D.P.V.; Veiga, F.J.B.; Estes, M.A. Diffusion Coefficients of the Ternary System (2-Hydroxypropyl- β -Cyclodextrin+caffeine+water) at T = 298.15K. *J. Chem. Thermodyn.* **2009**, *41*, 1324–1328. [[CrossRef](#)]
39. Ribeiro, A.C.F.; Barros, M.C.F.; Verissimo, L.M.P.; Estes, M.A.; Leaist, D.G. Coupled Mutual Diffusion in Aqueous Sodium (Salicylate + sodium Chloride) Solutions at 25 °C. *J. Chem. Thermodyn.* **2019**, *138*, 282–287. [[CrossRef](#)]
40. Callendar, R.; Leaist, D.G. Diffusion Coefficients for Binary, Ternary, and Polydisperse Solutions from Peak-Width Analysis of Taylor Dispersion Profiles. *J. Solut. Chem.* **2006**, *35*, 353–379. [[CrossRef](#)]
41. Loh, W. A Técnica de Dispersão de Taylor Para Estudos de Difusão Em Líquidos e Suas Aplicações. *Quim. Nova* **1997**, *20*, 541–545. [[CrossRef](#)]
42. Barthel, J.; Gores, H.J.; Lohr, C.M.; Seidl, J.J. Taylor Dispersion Measurements at Low Electrolyte Concentrations. I. Tetraalkylammonium Perchlorate Aqueous Solutions. *J. Solut. Chem.* **1996**, *25*, 921–935. [[CrossRef](#)]
43. Filho, C.M.C.; Verissimo, L.M.P.; Valente, A.J.M.; Ribeiro, A.C.F. Limiting Diffusion Coefficients of Sodium Octanoate, and Octanoic Acid in Aqueous Solutions without and with α -Cyclodextrin. *J. Chem. Thermodyn.* **2016**, *94*, 234–237. [[CrossRef](#)]

44. Romero, C.M.; Trujillo, G.P.; Verissimo, L.M.P.; Estesó, M.A.; Ramos, M.L.; Ribeiro, A.C.F. Limiting Diffusion Coefficients of α,ω -Amino Acids in Water and in Sodium Chloride Aqueous Solutions at 298.15 K. *Eur. Phys. J. E* **2019**, *42*, 94. [[CrossRef](#)] [[PubMed](#)]
45. Musilová, L.; Mráček, A.; Azevedo, E.F.G.; Valente, A.J.M.; Cabral, A.M.T.D.P.V.; Ribeiro, A.C.F.; Estesó, M.A. Interactions between Sodium Hyaluronate and β -Cyclodextrin as Seen by Transport Properties. *Int. J. Mol. Sci.* **2023**, *24*, 2889. [[CrossRef](#)]
46. Baes, C.F., Jr.; Mesmer, R.E. *The Hydrolysis of Cations*; John Wiley & Sons, Inc.: New York, NY, USA, 1976.
47. Ribeiro, A.C.F.; Lobo, V.M.M.; Oliveira, L.R.C.; Burrows, H.D.; Azevedo, E.F.G.; Fangaia, S.I.G.; Nicolau, P.M.G.; Guerra, F.A.D.R.A. Diffusion Coefficients of Chromium Chloride in Aqueous Solutions at 298.15 K and 303.15 K. *J. Chem. Eng. Data* **2005**, *50*, 1014–1017. [[CrossRef](#)]
48. Ribeiro, A.C.F.; Lobo, V.M.M.; Natividade, J.J.S. Diffusion Coefficients in Aqueous Solutions of Cobalt Chloride at 298.15 K. *J. Chem. Eng. Data* **2002**, *47*, 539–541. [[CrossRef](#)]
49. Valente, A.J.M.; Ribeiro, A.C.F.; Lobo, V.M.M.; Jiménez, A. Diffusion Coefficients of Lead (II) Nitrate in Nitric Acid Aqueous Solutions at 298 K. *J. Mol. Liq.* **2004**, *111*, 33–38. [[CrossRef](#)]
50. Hao, L.; Lu, R.; Leaist, D.G. Diffusion with Hydrolysis and Ion Association in Aqueous Solutions of Beryllium Sulfate. *J. Solut. Chem.* **1996**, *25*, 231–242. [[CrossRef](#)]
51. Musilová, L.; Mráček, A.; Azevedo, E.F.G.; Rodrigo, M.M.; Valente, A.J.M.; Estesó, M.A.; Ribeiro, A.C.F. Dependence of Viscosity and Diffusion on β -Cyclodextrin and Chloroquine Diphosphate Interactions. *Processes* **2021**, *9*, 1433. [[CrossRef](#)]
52. Sandilya, A.A.; Natarajan, U.; Priya, M.H. Molecular View into the Cyclodextrin Cavity: Structure and Hydration. *ACS Omega* **2020**, *5*, 25655–25667. [[CrossRef](#)]
53. Cai, W.; Sun, T.; Shao, X.; Chipot, C. Can the Anomalous Aqueous Solubility of β -Cyclodextrin Be Explained by Its Hydration Free Energy Alone? *Phys. Chem. Chem. Phys.* **2008**, *10*, 3236–3243. [[CrossRef](#)]
54. Coleman, A.W.; Nicolis, I. Inorganic Salt Modulation of the Aqueous Solubility of β -Cyclodextrin. *Supramol. Chem.* **1993**, *2*, 93–97. [[CrossRef](#)]
55. Poulson, B.G.; Alsulami, Q.A.; Sharfalddin, A.; El Agammy, E.F.; Mouffouk, F.; Emwas, A.-H.; Jaremko, L.; Jaremko, M. Cyclodextrins: Structural, Chemical, and Physical Properties, and Applications. *Polysaccharides* **2021**, *3*, 1–31. [[CrossRef](#)]
56. Verissimo, L.M.P.; Valada, T.I.C.; Sobral, A.J.F.N.; Azevedo, E.E.F.G.; Azevedo, M.L.G.; Ribeiro, A.C.F. Mutual Diffusion of Sodium Hyaluronate in Aqueous Solutions. *J. Chem. Thermodyn.* **2014**, *71*, 14–18. [[CrossRef](#)]

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