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Interaction between lactose and cadmium chloride in aqueous solutions as seen by diffusion coefficients measurements

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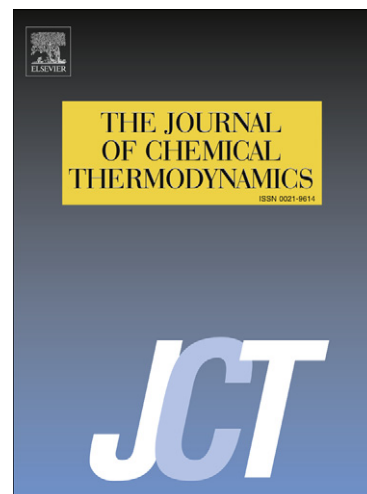
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ABSTRACT

Diffusion coefficients of an aqueous system containing cadmium chloride $0.100 \text{ mol}\cdot\text{dm}^{-3}$ and lactose at different concentrations at $25 \text{ }^\circ\text{C}$ have been measured, using a conductimetric cell and an automatic apparatus to follow diffusion. The cell relies on an open-ended capillary method and a conductimetric technique is used to follow the diffusion process by measuring the resistance of a solution inside the capillaries, at recorded times. From these results and by *ab initio* calculations, it was possible to obtain a better understanding of the effect of lactose on transport of cadmium chloride in aqueous solutions.

Keywords: Diffusion Coefficient; Lactose; Cadmium Chloride ; Solutions; Transport Properties.

1. Introduction

Lactose (disaccharide derived from the condensation of galactose and glucose, behaving as a typical non-electrolyte) is technologically a relevant compound and it is often used in medical, pharmaceutical, food and biological biomedical applications. The interactions of these compounds with metal ions are of major biological interest, having in mind that these systems play a dominant role in many biochemical interactions. Among them, we are particularly interested on systems containing this carbohydrate and cadmium ions, justified by the exposure of the population to these metal ions through different sources (*e.g.*, drinking water, food, excipients, and dental casting alloys) (*e.g.*, [1,2] and also, by their possible adverse effects on human health (*e.g.*, carcinogenic effects, toxic, and allergic ones) [3]. In fact, as a result of long-term exposure to cadmium in contaminated food and water (*e.g.*, from agricultural soils, where cadmium compounds are readily taken up by plants, and accumulated in edible parts due to their high solubility, and, consequently entering into the food chain), some research is ongoing regarding the estrogen mimicry that may induce breast cancer [3,4]. However, the understanding of these complex systems has not yet been well established, and consequently, their characterization is very important, helping us to understand better their structure, and to model them for practical applications. While numerous studies have been carried out on the thermodynamic properties of aqueous lactose solutions (*e.g.*, [5,6]), few have taken into account the transport behaviour of these systems (*e.g.*, [7-9]). We have been particularly interested in data on these properties for chemical systems, particularly on the diffusion of the systems containing lactose and cadmium ion as cadmium chloride.

A few diffusion coefficients for binary aqueous systems containing lactose and cadmium, respectively, have been reported (*e.g.*, [9,10]) but, as far as the authors know, after careful literature search, no data on diffusion coefficients are available in literature for systems containing cadmium salts and lactose at $t = 25\text{ }^{\circ}\text{C}$.

Thus, we have measured the diffusion (interdiffusion) coefficients D , for aqueous solutions of cadmium chloride $0.100\text{ mol}\cdot\text{dm}^{-3}$ plus lactose in the concentration range from $(0.005\text{ to }0.200)\text{ mol}\cdot\text{dm}^{-3}$, using the open-ended conductimetric capillary cell, at $t = 25\text{ }^{\circ}\text{C}$.

1 To better understand the structure of the chemical species formed and the main
2 biochemical mechanisms involved, we have complemented these studies using *ab initio*
3 calculations.
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7 **2. Experimental**

10 **2.1 Materials**

11 The solutes used in this study were lactose monohydrate and cadmium chloride
12 (table 1). They were used as received without further purification. The solutions for the
13 diffusion measurements were prepared in calibrated volumetric flasks using bi-distilled
14 water. The solutions (concentration in molarity) were freshly prepared and de-aerated
15 for about 30 minutes before each set of runs.
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25 **2.2 Mutual diffusion coefficients, D , measured by the open-ended conductimetric 26 capillary cell**

27 The open-ended capillary cell, which has been used to obtain mutual diffusion
28 coefficients for a wide variety of electrolytes (*e.g.* [11-14]) is described in great detail in
29 paper [13]. Basically, it consists of two vertical capillaries, each closed at one end by a
30 platinum electrode, and positioned one above the other with the open ends separated by
31 a distance of about 14 mm. The upper and lower tubes, initially filled with solutions of
32 concentrations $0.75 c$ and $1.25 c$, respectively, are surrounded with a solution of
33 concentration c . This ambient solution is contained in a glass tank ($200 \times 140 \times 60$) mm
34 immersed in a thermostat bath at $25\text{ }^{\circ}\text{C}$. Perspex sheets divide the tank internally and a
35 glass stirrer creates a slow lateral flow of ambient solution across the open ends of the
36 capillaries. Experimental conditions are such that the concentration at each of the open
37 ends is equal to the ambient solution value c , that is, the physical length of the capillary
38 tube coincides with the diffusion path. This means that the required boundary conditions
39 described in the literature [13] to solve Fick's second law of diffusion are applicable.
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41 Therefore, the so-called Δl effect [13] is reduced to negligible proportions. In our
42 automatic apparatus, diffusion is followed by measuring the ratio $w = R_t/R_b$ of
43 resistances R_t and R_b of the upper and lower tubes by a Solartron digital voltmeter
44 (DVM) 7061 with 6 1/2 digits. A power source (Bradley Electronic Model 232)
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1 supplies a 30 V sinusoidal signal at 4 kHz (stable to within 0.1 mV) to a potential
2 divider that applies a 250 mV signal to the platinum electrodes in the top and bottom
3 capillaries. By measuring the voltages V' and V'' from top and bottom electrodes to a
4 central electrode at ground potential in a fraction of a second, the DVM calculates w .
5

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7 In order to measure the differential diffusion coefficient D at a given concentration c ,
8 the bulk solution of concentration c molarity is prepared by mixing 1 dm³ of “top”
9 solution with 1 dm³ of “bottom” solution, accurately measured. The glass tank and the
10 two capillaries are filled with c solution, immersed in the thermostat, and allowed to
11 come to thermal equilibrium. The resistance ratio $w = w_{\infty}$ measured under these
12 conditions (with solutions in both capillaries at concentration c accurately gives the
13 quantity $\tau_{\infty} = 10^4 / (1 + w_{\infty})$.
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16 The capillaries are filled with the “top” and “bottom” solutions, which are then allowed
17 to diffuse into the “bulk” solution. Resistance ratio readings are taken at various
18 recorded times, beginning 1000 min after the start of the experiment, to determine the
19 quantity $\tau = 10^4 / (1 + w)$ as τ approaches τ_{∞} . The diffusion coefficient is evaluated using a
20 linear least-squares procedure to fit the data and, finally, an iterative process is applied
21 using 20 terms of the expansion series of Fick’s second law for the present boundary
22 conditions. The theory developed for the cell has been described previously [13].
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35 **2.3 Methods: *ab initio* studies**

36 Calculations were performed in a HP Z620 workstation using the HyperChemv7.5
37 software package from Hypercube Inc., 2000, USA. The geometry optimization used a
38 Polak-Ribiere conjugated gradient algorithm for energy minimization in vacuum, with a
39 final gradient of 4.18 kJ·nm⁻¹·mol⁻¹. The potential surfaces were calculated after an *ab*
40 *initio* geometry minimization using a RHF method with a small (3-21G) basis set.
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3. Results and discussion

3.1 Measurements of diffusion coefficients

Diffusion coefficients, D , and their respective standard deviations, S_D , of CdCl_2 $0.100 \text{ mol}\cdot\text{dm}^{-3}$ in aqueous solutions of lactose ($0.005 \text{ mol}\cdot\text{m}^{-3}$, $0.010 \text{ mol}\cdot\text{dm}^{-3}$, $0.025 \text{ mol}\cdot\text{dm}^{-3}$, $0.050 \text{ mol}\cdot\text{dm}^{-3}$, $0.100 \text{ mol}\cdot\text{dm}^{-3}$ and $0.200 \text{ mol}\cdot\text{dm}^{-3}$) at $25 \text{ }^\circ\text{C}$ are shown in table 2 and figure 1. For brevity, we will indicate as 1 and 2 (not including the solvent, component 0), the lactose and CdCl_2 species, respectively. D is the mean value of, at least, three independent measurements, and the error limits of our results should be close to the imprecision, therefore giving an experimental uncertainty of (1 to 3) per cent.

The following polynomial in $c_1^{1/2}$ was used to fit our data by a least squares procedure (table 2),

$$\begin{aligned} D/(10^{-9} \text{ m}^2\cdot\text{s}^{-1}) &= 0.892 + 0.991 c_1^{1/2} - 5.426 c_1 \\ R^2 &= 0.999 \end{aligned} \quad 1)$$

where c_1 and D represent the molarity concentration of lactose and the diffusion coefficients of cadmium chloride in different aqueous solutions containing this carbohydrate, respectively. The goodness of the fit (obtained with a confidence interval of 98 %) was assessed by the excellent correlation coefficient, R^2 , and the low standard deviation (< 1 %). Moreover, the deviation between the limiting D^0 value calculated by extrapolating experimental results to $c_1 \rightarrow 0$ ($D^0 = 0.892 \times 10^{-9} \text{ m}^2\cdot\text{s}^{-1}$) and the measured D value for solutions containing only CdCl_2 for $c = 0.100 \text{ mol}\cdot\text{dm}^{-3}$ ($D = 0.902 \times 10^{-9} \text{ m}^2\cdot\text{s}^{-1}$) is also acceptable (-1.1 %).

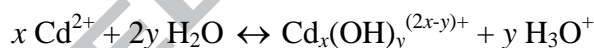
From our results (table 2), we can verify that the diffusion behaviour of cadmium chloride in aqueous solutions at $25 \text{ }^\circ\text{C}$ is affected by the presence of the lactose molecules. In fact, under the present experimental conditions, the decrease of the diffusion coefficients of cadmium chloride with the increasing of concentration of lactose in these media, may be interpreted on the basis of the formation of new species

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resulting, mainly, from the interactions of Cd^{2+} cations with lactose (as suggested by our *ab initio* calculations) which will lead to greater resistance to the motion through the liquid and, consequently, a lower diffusion coefficient.

The difference between the diffusion measurements on CdCl_2 in aqueous solutions in the presence and absence of lactose (measured as the percentage difference, $\Delta D/D$ %) strongly suggests that lactose at concentrations in the region $0.005 \text{ mol}\cdot\text{dm}^{-3}$, $0.010 \text{ mol}\cdot\text{dm}^{-3}$ and $0.025 \text{ mol}\cdot\text{dm}^{-3}$ did not significantly change the diffusion coefficient of CdCl_2 . However, when the lactose concentration is increased up to $0.200 \text{ mol}\cdot\text{dm}^{-3}$, the observed diffusion coefficients are lower than those obtained in aqueous solutions, reaching a maximum difference at a lactose/ CdCl_2 ratio 2:1 (*i.e.*, $\Delta D/D = -69.6$ %), and, estimating that, in those circumstances, about 30 % of the CdCl_2 are found under the form of aggregates with lactose.

The diffusion of cadmium chloride in aqueous solutions containing lactose may be affected by the eventual presence of new different species resulting from various equilibria. For example, we know that small amount of hydrolysis of cadmium ion can occur in concentrated solutions, that is,



and the most prominent hydrolysed species are $\text{Cd}(\text{OH})^+$, $\text{Cd}_2(\text{OH})^{3+}$ and $\text{Cd}_4(\text{OH})_4^{4+}$. The decrease of $D_{(\text{CdCl}_2)}$ with increasing concentration, may be explained assuming those species have a lower mobility than Cd^{2+} due to its size. The eventual formation of ion pairs, increasing with concentration, also may contribute to the decrease of $D_{(\text{CdCl}_2)}$ with concentration. On the other hand, from *ab initio* calculations (section 3.2), we conclude that the diffusion of cadmium chloride in aqueous solutions of lactose at $T = 298.15 \text{ K}$ is strongly affected, may be the aggregates between lactose and Cd^{2+} responsible for that behaviour. So, when the lactose concentration is increased up to $0.200 \text{ mol}\cdot\text{dm}^{-3}$, the free lactose component is reduced because about 30 % of the CdCl_2 are found under the form of aggregates. Thus, the decrease of D with increasing concentration, may be explained assuming those aggregates have a lower mobility than Cd^{2+} due to its size.

In fact, the contribution of all species for the influence on this transport property may eventually be difficult to make. In fact, clarifying the nature of these interactions is not an easy task. However, we could say that what eventually can be more important for

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some areas of interest (*e.g.* pharmaceutical applications) is the thermodynamic behaviour of the involved species, not so much the complex question of the nature of their internal binding forces. However, diffusion coefficients measured for aqueous solutions of CdCl₂ and lactose provide transport data necessary to model diffusion in practical applications.

3.2 *ab initio* studies

Lactose is a disaccharide derived from the condensation of galactose and glucose, by a β -1 \rightarrow 4 glycosidic linkage. It has an anomeric carbon in the C1 that present mutarotation due to axial to equatorial changes in the hydroxyl at C1 position, through an open form. Hence, it is not relevant to do the calculation starting from the alpha or the beta stereoisomer, but since the beta isomer corresponds to near 60 % of the natural lactose at room temperature, it was chosen as the starting structure of our calculations.

To evaluate the docking points for the Cd²⁺ on the lactose molecules we performed a detailed vacuum energy minimization in 3 different conditions: a) lactose alone (as a reference) b) lactose and Cd²⁺ (assuming the Cd²⁺ is the main interacting specie with lactose) and c) lactose and Cd²⁺ and 2 Cl⁻ ions (assuming that some CdCl₂ may not be fully dissociated and the chlorine anions may be near the lactose and the Cd²⁺). All those calculated structures were later used to calculate a charge potential surface in order to identify probable points of interaction between lactose and Cd²⁺.

Figure 2 shows that as expected the total charge density surface presents higher density near the oxygen atoms of the hydroxyl residues, pointing clearly to be those atoms that will interact with the Cd²⁺ cations. However, two other observations come from the calculation of this surface: despite lactose having a folded structure which conceals some of the oxygen's from cation interaction, the ether oxygen's have a similar density charge than the hydroxyl oxygens, what may indicate that in similar steric exposure the cations can bind to both ether and hydroxyls oxygen's leading to significant overall interactions between lactose and Cd²⁺ cations.

After vacuum energy minimization of lactose and Cd²⁺, we observe a noticeable change in the conformation of the lactose molecule approaching one of the hydroxyl groups to the Cd²⁺ at a distance of just 0.26 nm what is a clear indication of lactose/Cd²⁺ interactions. The total charge density surface shows a significant modification with

1 most of the charge density being transferred from the lactose to the Cd^{2+} cation,
2 pointing again to a strong interaction between those two chemical species in vacuum.

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4 Despite all those *ab initio* calculations were made in the absence of water, which
5 can dramatically change some of the observed trends, we can conclude from this initial
6 studies that the Cd^{2+} cations will interact strongly with the lactose molecule. These
7 finding support the observed experimental results, which behaviour may be explained
8 by the presence of the strong interactions in solution between lactose and Cd^{2+} species.
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16 **4. Conclusions**

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20 We have measured diffusion coefficients for cadmium chloride at 0.100 mol·
21 dm^{-3} in different aqueous solutions of lactose at 25 °C. From these results, we observed
22 that the diffusion coefficients of cadmium chloride in mixtures with this carbohydrate
23 decreased significantly with an increase of concentration. This fact, together with our *ab*
24 *initio* calculations, leads us to conclude that the diffusion of cadmium chloride in
25 aqueous solutions of lactose at 25 °C is strongly affected. It may be that the aggregates
26 between lactose and Cd^{2+} are responsible for that behaviour.
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Table 1

Provenance and purity of the materials studied .

Chemical name	Source	Mass fraction purity
Cadmium chloride	Merck	> 0.970
Lactose monohydrate	BDH	> 0.970

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Table 2

Experimental diffusion coefficients, D , of systems containing lactose, c_1 , and cadmium chloride ($c_2 = 0.100 \text{ mol}\cdot\text{dm}^{-3}$) at $25 \text{ }^\circ\text{C}$.^a

$c_1 /$ $\text{mol}\cdot\text{dm}^{-3}$ ^b	$D \pm S_D /$ $10^{-9} \text{ m}^2\cdot\text{s}^{-1}$ ^c	$(\Delta D/D) /$ $\%$ ^b
0.200	0.274 ± 0.022	-69.6
0.100	0.669 ± 0.015	-25.8
0.050	0.847 ± 0.010	-6.1
0.025	0.915 ± 0.010	+1.4
0.010	0.931 ± 0.015	+3.2
0.005	0.924 ± 0.010	+2.4
0.000	0.902 ± 0.028^c	0.0

^a $u(T) = 0.01 \text{ K}$. ^b $u(c) = 0.001 \text{ mol}\cdot\text{dm}^{-3}$. ^c D is the mean diffusion coefficient of 3 experiments and S_D is the standard deviation of that mean.

^b $(\Delta D/D) / \%$ represent the deviation between the diffusion coefficients of system (Lactose + $\text{CdCl}_2 + \text{H}_2\text{O}$) and the diffusion coefficients, D , of system ($\text{CdCl}_2 + \text{H}_2\text{O}$) [9].

^c Experimental value of the diffusion coefficient of aqueous solutions of cadmium chloride at $c_2 = 0.100 \text{ mol}\cdot\text{dm}^{-3}$ for $c_1 = 0$ [9].

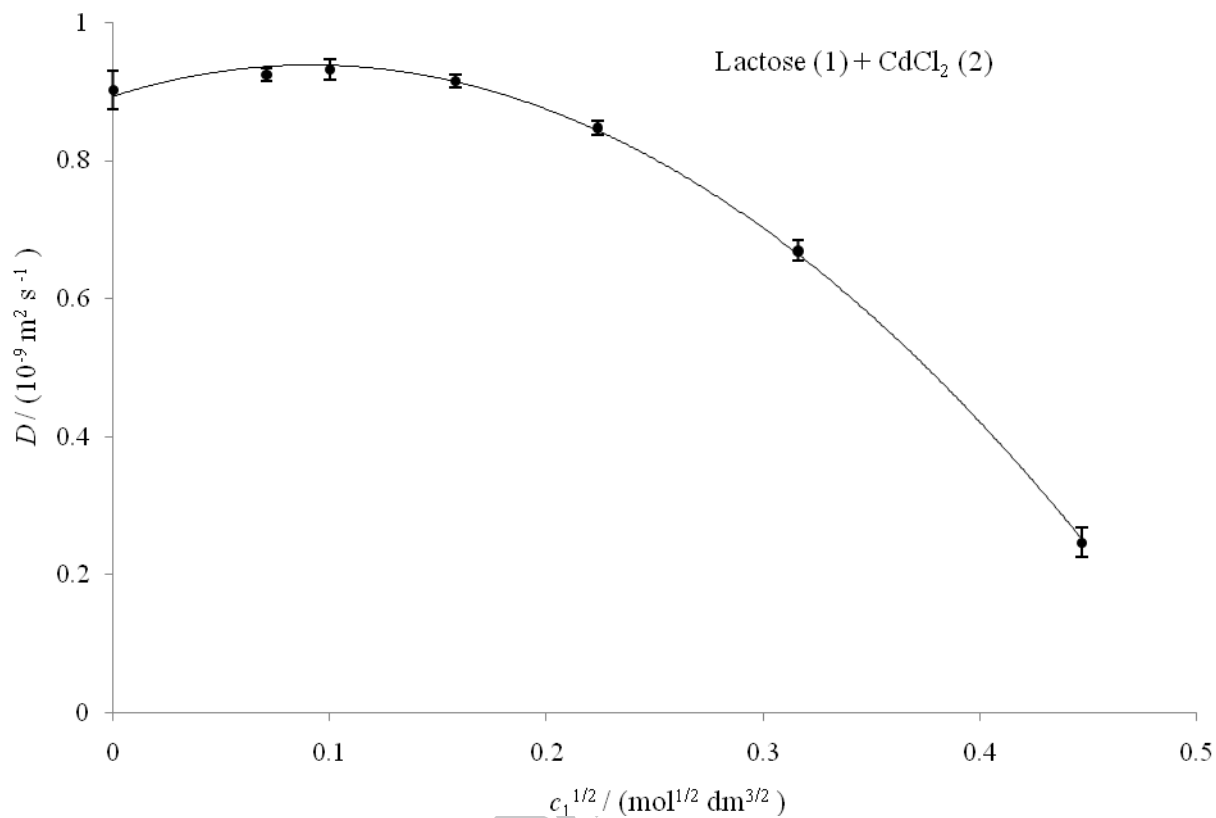


Figure 1. Diffusion coefficients, D , of aqueous lactose (c_1) + cadmium chloride (c_2) solutions at 25 °C plotted against the solute concentration of lactose, c_1 . (●) Measured values of D (table 2). — Adjustment curve applied to our diffusion coefficients of cadmium chloride in aqueous solutions containing lactose at different concentrations (equation 1).

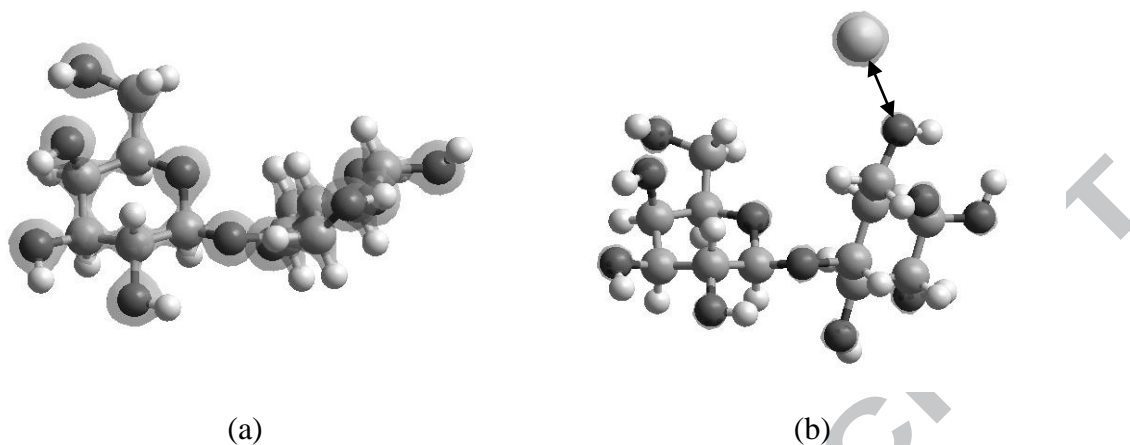


Figure 2. Total charge density surfaces (in light grey) for lactose alone (a) and lactose with Cd²⁺ (b), and conformational perturbation ((a) → (b)) induced by with Cd²⁺ on the lactose molecule.

Research Highlights

Diffusion coefficients of aqueous systems containing lactose and cadmium chloride.

Influence of the lactose on the diffusion of cadmium chloride.

Interactions between Cd^{2+} and lactose.

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