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Glass transition effects on the molecular transport of caffeine from condensed k-carrageenan/polydextrose systems

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ABSTRACT

We investigate the effect of added KCl on the glass transition of potassium-κ-carrageenan/polydextrose and molecular transport of caffeine. Samples were prepared with 2% (w/w) κ-carrageenan, 82% (w/w) polydextrose and 1% (w/w) caffeine to a total solids level of 85% (w/w). KCl was added at 0, 50, 100 and 200 mM to induce a dependence of structural properties on the potassium ion concentration. High-resolution spectral data over a wide spectral range for the tertiary system were collected using Fourier transform infrared spectroscopy (FTIR), which were complemented by tangible evidence of its morphology with scanning electron microscopy (SEM). Work then focused on the estimation of the mechanical (T_{gm}) and calorimetric (T_{gc}) glass transition temperature using in-shear dynamic oscillation and modulated differential scanning calorimetry (MDSC). Molecular transport of caffeine in the condensed polysaccharide/co-solute system was followed with UV–*vis* spectroscopy over a wide temperature range (−20 to 30 °C) and modelled with extended diffusion theory. Time-dependent mass transport of the diffusant was correlated to the structural relaxation of the polymeric matrix seen in increasing values of the mechanical glass transition temperature with higher additions of potassium counterions to κ-carrageenan. It was concluded that the mechanical glass transition temperature has a prominent effect on the release kinetics of caffeine in these materials, as compared to the calorimetric glass transition temperature.

Authorship contribution statement

Diah Ikasari: Methodology, Data modeling, Writing - original draft. **Vilia Darma Paramita:** Supervision, Data modeling, Writing - review & editing. **Stefan Kasapis:** Funding acquisition, Conceptualization, Supervision, Writing - review & editing.

1. Introduction

Caffeine is a popular bioactive compound naturally found in many plant crops, including coffee, tea and chocolate. It is known to have advantages as a pain reliever and psychotherapeutic by producing vasoconstricting, anti-inflammatory and stimulating effects (Temple et al., 2017). As a hydrophilic bioactive compound, it has been investigated in drug delivery systems in several forms, including tablet/powders, chewing gum, topical gel, solid lipid nanoparticles, nano-emulsion and hydrogel beads (Shakeel, 2017). The use of excipients to entrap/encapsulate caffeine is essential to control its release and preserve its bioavailability in the human GI tract. Hydrocolloids have been proposed as good carriers (e.g. tablets of spray-dried casein powder) for the bioactive compound especially *via* chemical or physical crosslinking that can slow down its release in the surrounding media over several hours/days according to the requirements of the therapeutic dose (Tan, Ebrahimi, & Langrish, 2019).

κ-Carrageenan is a sulphated linear polysaccharide made from D-galactose as well as 3,6-anhydro D-galactose units (Evageliou, Ryan, & Morris, 2019). As an ionic polysaccharide is highly affected by the presence of cations in solution that can induce a disorder-to-order transition. It is sensitive, in particular, to potassium ions that form bridges with the D-galactose sulfate group supporting the formation of double helices upon cooling, which at high enough concentrations of the polysaccharide create aggregated gels with extensive thermal hysteresis (Viebke, Piculell, & Nilson, 1994; Stenner, Matubayasi, & Shimizu, 2016). The effect of potassium and other cations (sodium and calcium) on the thermal stability and aggregation of κ-carrageenan has been studied by differential scanning calorimetry (Evageliou et al., 2019) and compressive elastic modulus analysis (Wang, Yuan, Cui, & Liu, 2018).

It has further been shown that the degree of aggregation is also

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determined by the concentration of the prevalent cations (potassium, sodium and calcium) found in most preparations of the polysaccharide with industrial interest (Morris, Rees, & Robinson, 1980; Nickerson, Paulson, & Hallet, 2004). The effect of temperature is to partially disturb the fine network structure leading to the formation of ordered super-strands that align in parallel or compactly pack together upon cooling (Núñez-Santiago, Tecante, Garnier, & Doublier, 2012; Rochas & Rinaudo, 1984). Such reorientations in the ordered conformation control the mechanism of bioactive compound release in advanced delivery vehicles. In this respect, the rubber-to-glass transformation of condensed materials becomes of importance in the optimisation of drug release (Jiang & Kasapis, 2011; Slade & Franks, 2002).

Polydextrose is a massively branched low-molecular weight polymer of glucose comprising random glycosidic bonds, which are α and β (1–2), (1–3), (1–4) and (1–6) arrangements (Stowell, 2009). The polymer has an average degree of polymerisation (DP) of 10 with the molecular weight ranging from 162 to 20,000 Da (Ribeiro, Zimeri, Yildiz, & Kokini, 2003). Polydextrose is available in the form of a viscous solution or amorphous powder due to the high degree of polydispersity, and it is relatively stable in acidic conditions and high temperature. Its glass transition temperature is mainly influenced by the increase in moisture content of the material, which reflects the plasticizing effect of water molecules. Polydextrose is highly soluble in water, but insoluble in glycerol, propylene glycol, and ethanol which was confirmed experimentally in this work (Craig, Anderson, Holden, & Murray, 2008).

Vitrification of the amorphous component of high solid biomaterials brings into play the concept of glass transition temperature (T_g) which is considered as an index of convenience in the control of the rate of physicochemical, enzymatic and biological processes (Roudaut, Simatos, Champion, Contreras-Lopez, & Le Meste, 2004; Gray, Bowen, Farhat, & Hill, 2008; Chaudhary, Panyoyai, Small, Shanks, & Kasapis, 2017). Within the glassy state, i.e. at temperatures below T_g, molecular motion is drastically restricted due to diminishing local hole free volume in the polymeric matrix (Hoare & Kohane, 2008; Panyoyai, Bannikova, Small, & Kasapis, 2015). Formulation of the framework of free volume in the theory of diffusion for concentrated polymer/solvent and polymer/plasticizer systems allows quantification of the molecular transport of the bioactive compound in targeted delivery systems *via* the estimation of the apparent diffusion coefficient (Jadhav, Gaikwad, Nair, & Kadam, 2009; Paramita, Bannikova, & Kasapis, 2015).

A recent investigation on the molecular transport nicotinic acid from bovine and fish gelatin networks, demonstrated the effect of the glass transition temperature, i.e. at conditions of minimum fluctuations in local hole free volume, on the diffusion coefficient of the bioactive compound and the decoupling of its rapid diffusion from the structural relaxation (α-transition) of the polymeric network (Ikasari, Paramita, & Kasapis, 2020). In the present study, we induce distinct three-dimensional structures in the κ-carrageenan/polydextrose system with variable additions of potassium ions to record a range of glass transition temperatures. The measured diffusion coefficients of caffeine are examined in relation to the temperature band of the mechanical and calorimetric glass transition temperatures, which measure distinct distance scales (from micro to macromolecular) in vitrification processes. Thus, the overall objective of this work is to follow the release mechanism of caffeine, as affected by changes in the structural relaxation of κ-carrageenan/polydextrose systems with potassium ion addition and ascertain the role of the thermomechanical glass transition temperature on the picture of molecular motion of the bioactive compound.

2. Materials and methods

2.1. Materials

κ-Carrageenan, extracted from *Euchema cottonii* type III, was purchased from Sigma–Aldrich Co. (Sydney, Australia). As a co-solute, Sta-Lite III polydextrose powder (95% purity with 4% moisture) was supplied by Wilmar BioEthanol Pty. Ltd. (Victoria, Australia). Caffeine [$C_8H_{10}N_4O_2$] used as the bioactive compound was purchased from Sigma–Aldrich Co. in the form of white powder at a ReagentPlus grade. Ethanol (100%) was the release medium in diffusion experimentation and was purchased as an anhydrous colorless liquid from Sigma-Aldrich Co. Potassium chloride was supplied by Sigma–Aldrich a Co. and Milli-Q Type II water was used for ingredient hydration.

2.2. Sample preparation

κ-Carrageenan was changed into the potassium form by eluting Amberlite IR-120 resin with 0.1 M HCl until pH reached 1.0. The resin was then submerged in 2 M KCl solution to convert H^+ to K^+ form and the remaining of the potassium ions were removed by rinsing with water. This is indicated by a clear solution when titrated with $AgNO_3$. The resin was heated to 90 °C and mixed at that temperature with 0.5% (w/w) aqueous κ-carrageenan for 30 min to achieve ion exchange to the potassium form. The resulted solution was then poured into 43 mm diameter when full cellulose-based semi-permeable tubes and dialysed overnight by submerging in Mili-Q water at ambient temperature. This was followed by freeze-drying of the polysaccharide solution. Ionic composition of both commercial and purified κ-carrageenan samples was analysed by us using atomic absorption spectrometry (Varian Inc., Palo Alto, USA). Commercial κ-carrageenan contained 2.32% potassium, 0.07% magnesium, 0.78% sodium and 0.52% calcium, whereas the purified κ-carrageenan exhibited high levels of potassium (7.31%), and low levels of magnesium (0.02%), sodium (0.19%) and calcium (0.21%). Experimental materials were prepared by mixing 2% (w/w) potassium κ-carrageenan, 82% (w/w) polydextrose and 1% (w/w) caffeine. In doing so, κ-carrageenan in the potassium form was dispersed in Milli-Q water, containing 0, 50, 100 or 200 mM KCl, with constant stirring at 90 °C for 10 min followed by addition of caffeine and polydextrose. Thus, four different solutions were prepared to pursue the goals of this study. Finally, solutions were poured in a beaker and placed in a vacuum oven to remove gently excess water. They formed cylindrical gels of 15% (w/w) moisture content with dimensions of 4 cm diameter and 0.5 cm thickness.

2.2. Experimental analysis

2.2.1. Fourier transform infrared spectroscopy (FTIR)

Measurements were conducted on a Spectrum Two GladiATR-Fourier transform infrared spectroscopy instrument (Perkin Elmer, Pike Technologies, Norwalk, US) using a protocol by Panyoyai et al. (2015) with some modifications. Samples of κ-carrageenan, polydextrose, caffeine and their mixtures without and with the addition of 50, 100 and 200 mM KCl were scanned at 600-4000 cm^{-1} with a resolution of 4 cm^{-1} and averaged over 64 scans. Each preparation was recorded three times to yield overlapping interferograms.

2.2.2. Scanning electron microscopy (SEM)

Freeze-dried samples of κ-carrageenan, polydextrose and their mixtures with and without caffeine, 50, 100 and 200 mM KCl were sputtered with iridium coating. They were then analysed using FEI Quanta 200 SEM (Hillsboro, Oregon, USA) under an intense electron beam and high vacuum conditions of 0.6 Torr with a working distance of 10–12 mm following a method by Paramita et al. (2015) with some modifications. Multiple micrograph images of the specimens were taken using an accelerated medium voltage of 30 kV and a spot size of 5. The experimental protocol resulted in high-quality images at a magnification of 3000 ×.

2.2.3. Modulated differential scanning calorimetry (MDSC)

The thermal transitions of single polydextrose and κ-carrageenan/polydextrose matrices with and without the addition of caffeine, 50, 100 and 200 mM KCl were recorded using Q2000 (TA Instruments, New

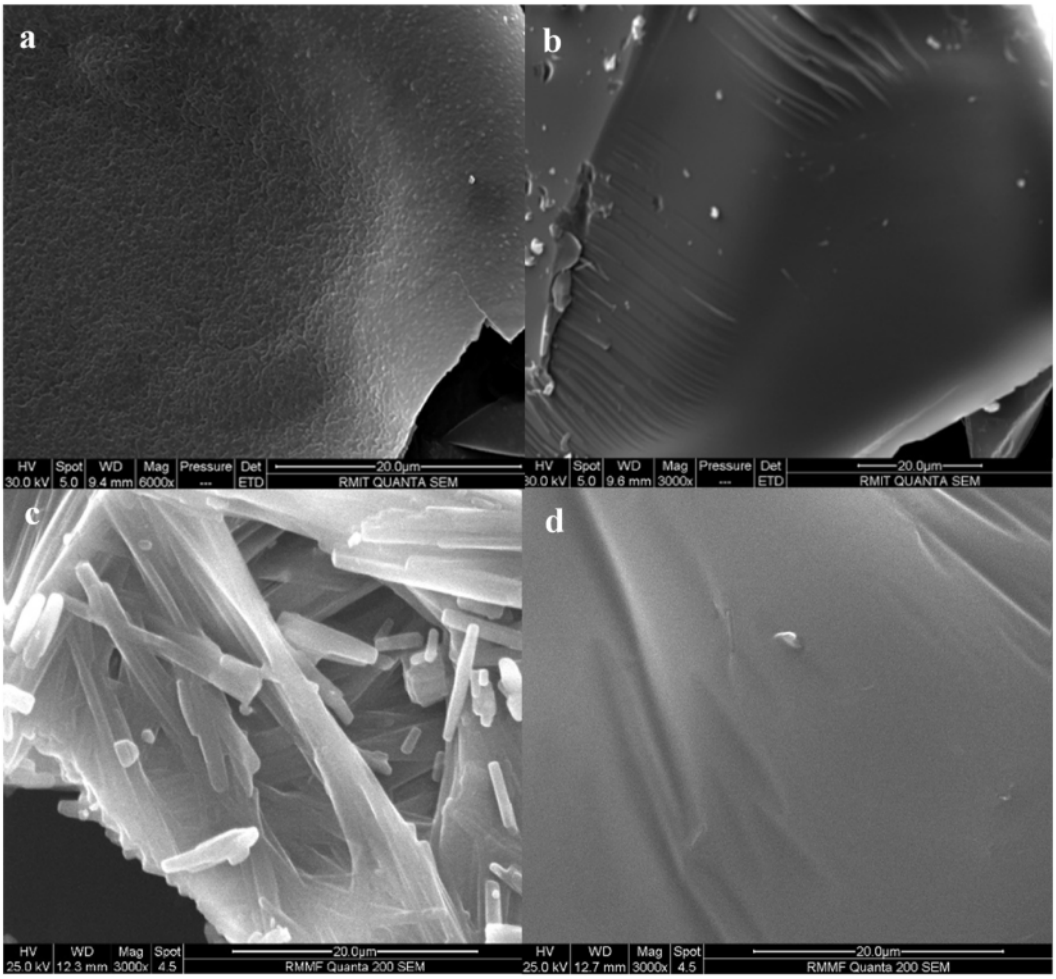

Fig. 2. SEM micrographs for freeze-dried samples of **(a)** 2% κ-car, **(b)** 85% PD, **(c)** Cf, and **(d)** 2% κ-car/82% PD/1% Cf/200 mM KCl.

all our samples are summarised in Table 1. Values of C_1^0 (~10.6), C_2^0 (~51 deg), the fractional free volume at T_g ($f_g \sim 0.040$) and α_f (8.0×10^{-4} deg^{-1}; not shown in Table 1) are consistent with preceding studies on amorphous synthetic and natural polymers (Ferry, 1980; Kasapis & Sablani, 2005; Paramita & Kasapis, 2019), strongly arguing that all relaxation times depend identically on temperature (concept of thermorheological simplicity). The single-point cross-over of the Arrhenius and WLF fits argues for a change in operational dynamics from the free volume theory to the predictions of the reaction rate theory and is considered as the mechanical glass transition temperature (T_{gm}) in Fig. 5a and b. Thus, there are three main observations from the data thus far: i) the T_{gm} predictions of all samples are higher than the corresponding T_{gc} values since rheology emphasizes the macromolecular (network) aspects of the matrix, whereas calorimetry provides information primarily on the mobility of the sugar/co-solute molecules and the relatively small addition of biopolymer in our case is rather a cross-contamination (Kasapis, 2008), ii) increasing addition of potassium counterions elevates the T_{gm} values by creating a more cohesive structure and iii) as mentioned earlier, caffeine incorporation induces intermolecular interactions that further stabilize the polymeric network leading to elevated T_{gm} estimates.

Furthermore, we employed the customary exponential form of the modified Arrhenius equation, i.e. equation (1), to calculate numerical values for the constant activation energy, $E_{a\ matrix}$, and outcomes are reproduced in Table 1. There is a clear progression in the values of $E_{a\ matrix}$ with increasing addition of the counterion, e.g. from 235.4 to 278 kJ/mol at 0 and 200 mM KCl, in the samples without caffeine. And predictions are also higher at corresponding levels of KCl in the presence of caffeine, e.g. from 278.0 to 333.7 kJ/mol at 200 mM KCl without and with the bioactive compound. An earlier study on Brownian dynamics has argued that solute-solute interactions can affect activation-limited reactions (Ganapathy, O'Brien, & Randolph, 1996). Higher values of the activation energy signify the increasing difficulty in the glassy state of the polymer to facilitate rearrangements from one conformation state to another.

3.3. Potassium κ-carrageenan/polydextrose as a delivery vehicle for caffeine

In this section, we have taken advantage of the earlier discussion in the structural characteristics of this polysaccharide/co-solute system to examine its utility as a delivery device for caffeine. The mass transport process involved was examined by monitoring the release of the bioactive compound in the surrounding media (ethanol) and was

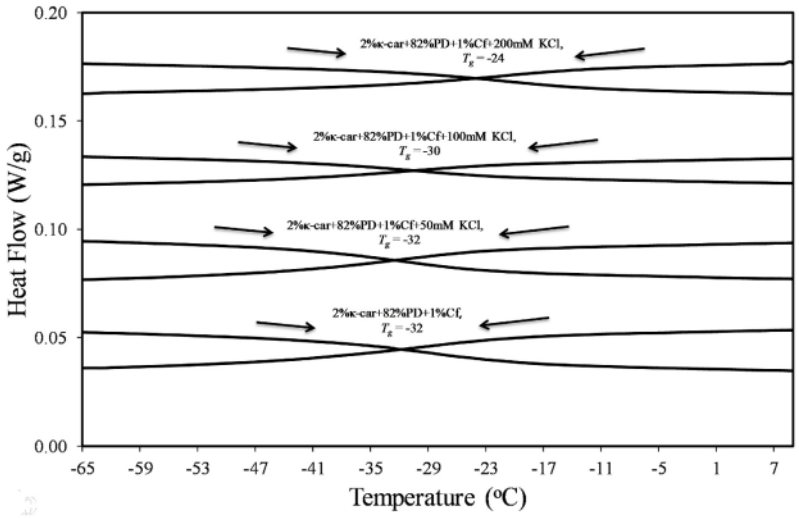

Fig. 3. Modulated DSC thermograms of heating and cooling for 2% κ-car/82% PD/1% Cf, 2% κ-car/82% PD/1% Cf/50 mM KCl, 2% κ-car/82% PD/1% Cf/100 mM KCl, 2% κ-car/82% PD/1% Cf/200 mM KCl arranged successively upwards (scanned at a rate of 1 °C/min).

Table 1
Glass transition parameters and caffeine transport characteristics in κ-carrageenan/polydextrose systems.

System	T_{gc} (°C)	T_{gm}(°C)	T_o (°C)	C_1°	C_2° (deg)	f_g	$E_{a\ matrix}$ (kJ/mol)	$E_{a\ caffeine}$ (kJ/mol)	D_{eff} (m^2/s)	Diffusion exponent, n	Transport mechanism
85% PD	−32	−13	−11	11.1	49	0.039	248.5	–	–	–	–
2% κ-car + 83% PD	−34	−20	−18	10.4	52	0.041	235.4	–	–	–	–
2% κ-car + 83% PD +50 mM KCl	−33	−19	−18	10.6	51	0.040	275.1	–	–	–	–
2% κ-car + 83% PD +100 mM KCl	−31	−17	−14	10.2	53	0.042	276.7	–	–	–	–
2% κ-car + 83% PD +200 mM KCl	−27	−16	−14	10.4	52	0.041	278.0	–	–	–	–
2% κ-car + 82% PD + 1% Cf	−32	−4	−3	10.6	51	0.044	271.2	9.1	4.64×10^{-6}	0.85 ± 0.04	Anomalous
2% κ-car + 82% PD + 1% Cf + 50 mM KCl	−32	0	1	10.6	51	0.042	318.2	14.5	1.34×10^{-6}	0.82 ± 0.02	Anomalous
2% κ-car + 82% PD + 1% Cf + 100 mM KCl	−30	5	6	10.6	51	0.042	319.9	23.0	1.78×10^{-8}	1.03 ± 0.04	Case II
2% κ-car + 82% PD + 1% Cf + 200 mM KCl	−24	10	11	10.6	51	0.041	333.7	24.7	4.05×10^{-9}	0.99 ± 0.03	Case II

Average values with a standard deviation are reported for the diffusion exponent, n, throughout the experimental temperature range (−20 to 30 °C). Values of the effective diffusion coefficient, D_{eff}, are at 5 °C.

quantified using UV–*vis* spectrophotometry at λ_{max} = 273 nm and the Beer-Lambert Law *via* a standard absorbance-concentration fit with a high linear regression coefficient (r^2 = 0.992; data are not shown). Fig. 6a represents a typical profile of caffeine release in the κ-carrageenan/polydextrose matrix at various additions of KCl over 120 min at 30 °C. Increasing times of observation yield higher amounts of caffeine diffusion out of the device, as does the absence of the counterion. Thus, after 120 min of observation, the concentration of released caffeine is 0.54 and 0.18 mg/ml at 0 and 200 mM KCl, respectively.

Fig. 6b illustrates the outcomes of caffeine diffusion as a function of KCl addition within the experimental temperature range of this investigation at 120 min. It appears that the levels of potassium ions underline a rate-limiting step of the entire diffusion sequence achieving high kinetics of release at 30 °C, which is above the mechanical glass transition temperature of the system, i.e. within the glass transition region (Table 1). On the other hand, relatively limited release is observed at −20 °C, which is below T_{gm}, i.e. within the glassy stage of the matrix. The validity of these experimental observations was confirmed using a two-way ANOVA test followed by Tukey's post hoc test, which indicated that the release of caffeine was significantly affected by the KCl additions and the time/temperature settings of this investigation (cutoff for significance is $p < 0.05$).

Next, the caffeine release was followed by an easy-to-apply model (Ritger & Peppas, 1987):

$$\frac{M_t}{M_\infty} = kt^n \tag{4}$$

where, M_t and M_∞ are the caffeine concentrations during experimentation and at completion, k is a characteristic constant of the bioactive compound-polymer system, t is time in seconds, and n is the kinetic diffusion exponent. For the cylindrical disks of this investigation, n values between 0.45 and 0.89 denote an anomalous transport, which becomes a non-Fickian or Case II transport at higher estimates (Siepmann & Siepmann, 2008). Using the gradient in the plot of ln M_t/M_∞ *versus* ln t from equation (4), we obtain for the κ-carrageenan/polydextrose/caffeine matrices at four KCl additions n values within the range of 0.82–1.03 (Table 1). These estimates are at the interface of anomalous and Case II transport, an outcome that

emphasizes the importance of the structural relaxation of the polymer in the quantitative description of caffeine release.

The extended theory of diffusion can be employed to yield the effective diffusion coefficient, D_{eff}, of small molecules from a solid-like delivery vehicle, and this can be achieved for $M_t/M_\infty > 0.6$ in our cylindrical samples with the following model (Siepmann & Siepmann, 2012):

$$\frac{Mt}{M\infty} = 1 - \frac{4}{(2.405)^2} exp\left(-\frac{(2.405)^2 D_{eff} t}{R^2}\right) \quad (5)$$

where, R is the radius of the cylindrical disk. An objective way to compare the temperature dependence of the effective diffusion coefficient in different polymer-based matrices having distinct glass transition temperatures is to use normalized temperature difference variables like $T\text{-}T_{gm}$ (Ehlich & Sillescu, 1990). This approach has been followed in Fig. 7a, which plots D_{eff} *versus* $T\text{-}T_{gm}$ for the samples of 2% (w/w) κ-carrageenan plus 82% (w/w) polydextrose at 0, 50, 100 and 200 mM KCl addition. Diffusion coefficients of caffeine remain relatively constant at temperatures below T_{gm} but exhibit a steeper curvature with increasing molecular mobility in the glass transition region of the high-solid system. The important point to make here is that all materials have the same normalized temperature dependence hence making the mechanical glass transition temperature the overriding consideration for caffeine diffusion in polymers.

Derivation of the diffusion coefficients allows their incorporation in a recently derived mathematical expression that follows their progression relative to the fractional free volume at the glass transition temperature, f_g (Panyoyai & Kasapis, 2016):

$$\log D_T = \log D_{Tg} + \frac{\xi}{2.303}\left[\frac{1}{f_g} - \frac{1}{f}\right] \quad (6)$$

where, diffusion coefficients and fractional free volumes at experimental temperatures are given as D_T and f with D_{Tg} being the diffusion coefficient at T_g. Parameter ξ signifies the critical molecular volume of the jumping unit of a bioactive compound to that of the polymeric matrix. Plotting the logarithmic form of D_T against the reciprocal function of free volume in equation (6) produces a linear relationship with a very acceptable linear regression coefficient ($r^2 = \sim 0.980$) for our samples with four different KCl additions (results are not shown here).

The gradient of the linear relationship allows derivation of ξ values, which are plotted in Fig. 7b as a function of KCl concentration. They can also be interpreted in terms of a coupling parameter that increases with nontrivial interactions between polymeric network and bioactive compound, thus accounting for the extent of coupling of the bioactive compound diffusion to the matrix motion (Ngai & Plazek, 1995). There is a decreasing polynomial progression from 0.41 to 0.28 in the values of the coupling constant with potassium ion variation from 0 to 200 mM KCl in the tertiary systems of this investigation. This should be attributed to the increasing rigidity of κ-carrageenan sequences with binding potassium counterions that reduces the degree of intermolecular associations with the bioactive compound leading to decoupling between its diffusional mobility and the structural relaxation of the polymer.

Next, we plot the viscoelastic response of the polymer, in terms of free volume variation, to increasing experimental temperature and the associated diffusion coefficient of caffeine in Fig. 8(a–d) for the four levels of KCl addition to the matrix of this investigation. Clearly, there is a rapid increase in the values of fractional free volume (from $f_g \sim 0.042$) at temperatures above T_{gm}. Increasing free volume encourages molecular mobility, which is reflected in a low energy requirement for the diffusion of caffeine ($E_{a\ caffeine} < 24.7$ kJ/mol in Table 1),[†] as compared to the activation energies for structural relaxation of the polymeric matrices ($E_{a\ matrix} > 235.4$ kJ/mol). The decrease in dynamic constraints of segmental motion in the polysaccharide/co-solute system is paralleled by a systematic increase in the values of effective diffusion coefficient of caffeine. The gap between the calorimetric and mechanical glass transition temperatures is clearly shown in the four graphical displays. Gratifyingly, there is a high degree of "cooperativity" between characteristics of structural relaxation and diffusion kinetics, which level off once the mechanical glass transition is approached for all preparations of KCl addition. Rheology, of course, is superbly equipped to monitor structural changes around the glass transition temperature, which appear to control diffusant release.

Finally, work on a glassy biomaterial that retains its shape during diffusion (i.e. maintains a constant value of T_g) demonstrated the effect of structural relaxation, *via* the concept of the mechanical glass transition temperature, on the diffusion kinetics of the bioactive compound. There was a quantitative agreement between fractional free volume of the polymer-based matrix and effective diffusion coefficient of caffeine within the mechanical glass transition region. That was demonstrated by modelling with equation (6), which also provided the extent of interaction between constituents in the mixture that retards solute diffusion. Work is directly applicable to added value food or relevant biological systems describing the molecular transport of water-soluble bioactive compounds from a dosage form where the rate of microconstituent diffusion is much higher than that of polymer chain relaxation leading to an Anomalous or Case II process (Table 1). Solvent penetration into the delivery device of a continuous polymeric network, and the subsequent bioactive compound release, will be reflected in a higher free volume following the model of increasing molecular motion established in the temperature analogue of solvent infusion depicted in Fig. 8a–d.

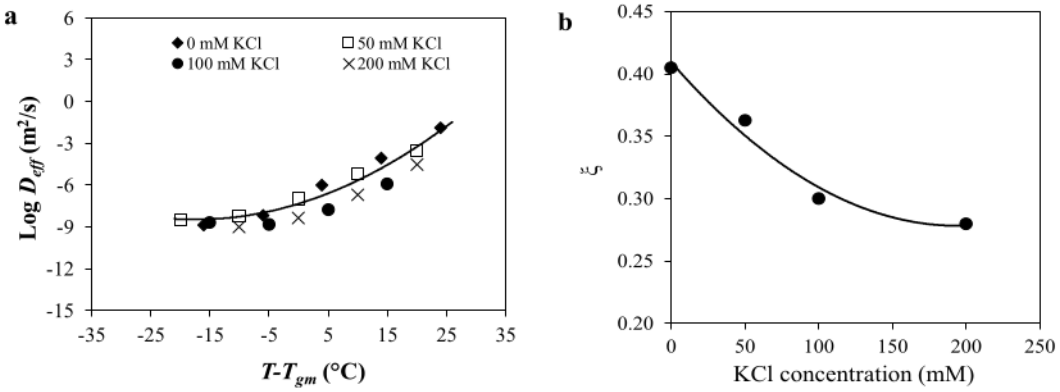

Fig. 7. **(a)** Diffusion coefficients of caffeine in 2% κ-car/82% PD at 0, 50, 100 and 200 mM KCl as function $T\text{-}T_{gm}$, and **(b)** Coupling parameter (ξ) of caffeine release from this κ-car/PD matrix as a function of KCl concentration.

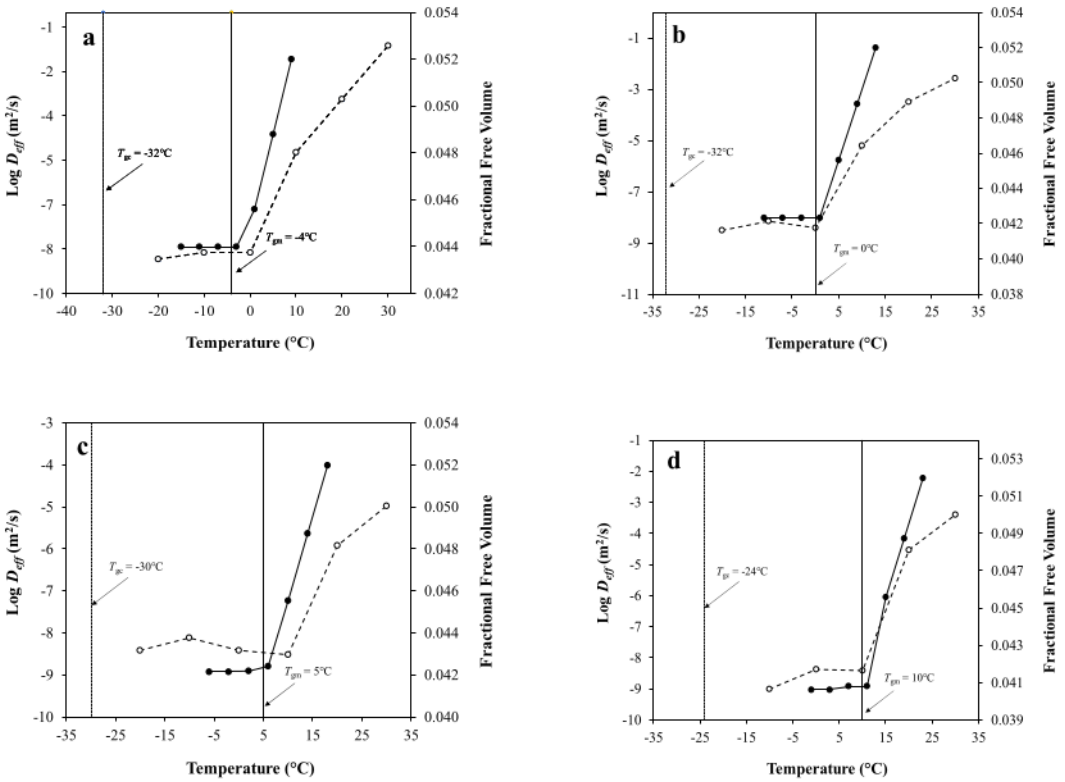

Fig. 8. Effective diffusion coefficient of caffeine (◯, left y-axis) and fractional free volume of 2% κ-car/82% PD/1% Cf (●, right y-axis) at **(a)** 0 **(b)** 50, **c)** 100 and **(d)** 200 mM KCl, with indications of the mechanical and calorimetric glass transition temperatures.

Therefore, the fundamental principle in the driving force of diffusion coefficient and fractional free volume in relation to the mechanical glass transition temperature, as developed from equation (6) for increasing temperature, should be also applicable to solvent infusion, leading in both cases to increasing fluctuations in local hole free volume. This approach can serve as the basis for further explorations in the design of model systems closer to industrial application.

[†]Footnote: We have utilised the relations between caffeine concentration and time (e.g. Fig. 6a) to argue for a zero-order reaction rate, with the gradient being the rate constant, $k = dx/dt$. This allows calculation of the so-called "spectroscopic shift factor": $\log a_T = \log (k_o/k)$, where k_o is the rate constant at the reference temperature, T_o. Thus, $E_{a\ caffeine}$ can be estimated using the modified Arrhenius equation and outcomes are shown in Table 1; further discussion on the spectroscopic shift factor can be found in Paramita and Kasapis (2018).

4. Conclusions

We have designed high-solid biomaterials with vitrification properties over a wide range of temperatures by incorporating a natural polymer, κ-carrageenan, a non-caloric co-solute, polydextrose, and judicious additions of potassium counterions. The aim was to achieve controlled drug release *via* the effective entrapment of caffeine in these materials. Utilisation of the concept of normalized temperature difference variables demonstrated that the diffusion coefficients of caffeine for all systems can be reduced to a common pattern regardless of their physicochemical characteristics. Within the glass transition region of the polysaccharide/co-solute matrices at various levels of added potassium ions, a newly proposed equation for the caffeine diffusion coefficient in relation to the fractional free volume at the glass transition temperature yields the so-called coupling parameter. It was observed that potassium counterion stabilisation of the κ-carrageenan helices increases the decoupling effect between matrix motion and caffeine diffusion. It has been noted earlier in the literature that in this type of systems the mechanical glass transition temperature is distinct from its calorimetric counterpart, with the former being an accurate measure of structural relaxation within the region of α-dispersion. It appears that T_{gm} controls the mass transport of caffeine in the polysaccharide based matrix, an outcome which is congruent with data on the diffusion of nicotinic acid from protein (gelatin) matrices with distinct molecular weight distributions (Ikasari et al., 2020), and bodes well for the design of delivery vehicles with advanced bio-functionality.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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