

Concentration-Dependent Ionic and Macromolecular Reorganization in Sodium Carboxymethyl Cellulose/Curcumin Systems

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Abstract: Sodium carboxymethyl cellulose (NaCMC) is a water-soluble anionic polyelectrolyte whose macromolecular organization is highly sensitive to solvent composition, ionic environment, and interactions with low-molecular-weight compounds. In this study, concentration-dependent physicochemical reorganization of NaCMC/curcumin (CUR) systems was investigated using solvent-controlled conductometry and viscometry. Curcumin was introduced into aqueous NaCMC as a DMSO solution, and an independently measured NaCMC/DMSO system was used to discriminate CUR-associated effects from dilution and mixed-solvent effects. Progressive addition of DMSO alone produced a smooth nonlinear decrease in conductivity, whereas the CUR-containing system exhibited a pronounced discontinuity between 22.5 and 23.0 mL of CUR/DMSO addition, where conductivity decreased from 600.1 to 264.7 $\mu\text{S cm}^{-1}$ (-55.9%), followed by a reversal of the conductivity trend. The absence of an analogous transition in the DMSO control indicates that the discontinuity cannot be explained by solvent dilution alone and is consistent with the onset of a CUR-associated cooperative ionic/supramolecular reorganization within the coupled NaCMC/water/DMSO environment. Viscometric measurements further demonstrated a composition-dependent decrease in the hydrodynamic response of NaCMC upon CUR incorporation, indicating reorganization at the macromolecular level. Importantly, the observed conductivity and viscosity changes are interpreted as multicomponent responses involving solvent reorganization, ion solvation and counterion mobility, polymer hydration, macromolecular rearrangement, and CUR-dependent association rather than as evidence for a single fixed-stoichiometry NaCMC/CUR complex. These results establish a physicochemical framework in which curcumin incorporation induces coupled ionic and macromolecular reorganization of NaCMC and highlight the importance of solvent-matched controls for mechanistic interpretation of polysaccharide-polyphenol systems.

Keywords: Sodium carboxymethyl cellulose; curcumin; polyelectrolyte-polyphenol interactions; molecular association; conductometry; macromolecular reorganization; supramolecular organization.

Introduction

Curcumin (CUR; diferuloylmethane) is a naturally occurring diarylheptanoid polyphenol whose molecular structure combines two substituted aromatic rings with a conjugated β -diketone moiety containing phenolic hydroxyl and methoxy functionalities. This structural organization is responsible not only for its characteristic chromophoric properties but also for its complex acid-base, tautomeric, redox, and intermolecular behavior. Solution-state NMR studies established that curcumin predominantly adopts a keto-enol configuration over a broad range of solvent environments, including aqueous DMSO mixtures, while subsequent LC-MS and time-resolved NMR studies further demonstrated the dynamic and solvent-dependent character of its keto-enol tautomerism [1].

Despite its broad interest as a functional polyphenol, the physicochemical behavior of curcumin severely restricts its direct use in aqueous formulations. Its limited compatibility with water promotes heterogeneous dispersion and association of curcumin molecules, while its chemical state is strongly dependent on solvent composition and pH.[2] Classical kinetic studies demonstrated pronounced pH dependence of curcumin degradation in aqueous media, emphasizing that apparent changes in curcumin concentration or functionality cannot be considered independently of its chemical stability [3]. These limitations have stimulated extensive efforts to incorporate curcumin into macromolecular carriers and structured matrices capable of controlling its molecular environment, dispersion state, stability, and release.

Among polysaccharides investigated for this purpose, carboxymethyl cellulose (CMC) is particularly attractive because it combines the renewable cellulose backbone with water-soluble carboxymethyl substituents. Sodium carboxymethyl cellulose (NaCMC) behaves in aqueous media as an anionic, semiflexible polyelectrolyte rather than as a structurally invariant neutral polymer.[4] Its solution conformation depends on molecular weight, degree of substitution (DS), ionic environment, concentration, and counterion screening. Arinaitwe and Pawlik demonstrated that CMC chains exhibit semiflexible random-coil behavior and that ionic strength exerts a particularly strong influence on their solution conformation [5]. Consequently, incorporation of a low-molecular-weight bioactive compound into a NaCMC solution may affect not only local polymer-solute contacts but also counterion distribution, hydration, chain dimensions, intermolecular association, and ultimately the mesoscopic organization of the polymer-containing phase.

An additional level of complexity arises from the chemical heterogeneity of CMC itself. Average DS describes only the mean number of carboxymethyl substituents per anhydroglucose unit and does not uniquely specify their distribution along the cellulose-derived repeat units.[6] Quantitative multidimensional NMR analysis has demonstrated substitution at the C2, C3, and C6 positions and the coexistence of differently mono-, di-, and trisubstituted anhydroglucose units in NaCMC [7]. Thus, CMC molecular architecture determines the spatial distribution of carboxylate groups, residual hydroxyl functionalities, local charge density, hydration, and chain conformation all of which can influence the accessibility and microenvironment of potential interaction sites for curcumin.

From a molecular perspective, NaCMC and curcumin possess complementary functionalities capable of supporting non-covalent association. Residual hydroxyl, ether, and carboxylate groups of NaCMC can participate in a dynamic hydrogen-bonding and solvation environment, whereas curcumin contains phenolic hydroxyl, methoxy, and keto-enol functionalities together with extended conjugated aromatic regions. Importantly, however, such chemical complementarity does not by itself demonstrate formation of a discrete CMC-curcumin complex. In an aqueous CMC-curcumin formulation, polymer-curcumin contacts compete simultaneously with CMC-water, CMC-CMC, curcumin-solvent, curcumin-curcumin, and counterion-mediated interactions. The resulting state should therefore be regarded as a multicomponent association equilibrium rather than automatically interpreted in terms of a single stoichiometric binding event.

Experimental studies involving CMC-containing curcumin systems support the ability of CMC architecture to modify the physicochemical environment of curcumin, but they also illustrate

the difficulty of assigning such effects to a single molecular mechanism. Li et al. showed that CMC with different DS values affected lysozyme-CMC coacervation and, consequently, curcumin encapsulation, protection, solubility, stability, and antioxidant behavior [8]. Because lysozyme constituted an additional interacting component, however, these results cannot be interpreted as direct evidence for binary CMC-curcumin binding. More recently, Wang et al. demonstrated that addition of CMC to HPMC-based curcumin solid dispersions improved curcumin wettability and solubility and contributed to changes in its solid-state organization. Significantly, the authors attributed the hydrophobic interaction with curcumin to HPMC rather than CMC, indicating that improvement of curcumin physicochemical performance in a CMC-containing formulation does not necessarily imply strong direct hydrophobic CMC-curcumin binding [9].

The importance of CMC molecular parameters is further illustrated by recent multicomponent colloidal systems. In high-internal-phase Pickering emulsions containing peanut protein isolate and CMC, variation of CMC DS (0.7 and 0.9) and molecular weight (90–700 kDa) substantially altered particle structure, interfacial behavior, rheological properties, emulsion stability, and curcumin bioaccessibility [10]. Although such systems are compositionally more complex than binary NaCMC-curcumin mixtures, they provide compelling evidence that CMC molecular architecture can propagate through several structural levels—from macromolecular organization to colloidal properties and ultimately to curcumin performance. CMC-based curcumin hydrogels have likewise demonstrated that modification of the polysaccharide network can regulate curcumin retention and release while supporting biomedical functionality [11].

Collectively, these studies establish the technological relevance of CMC-containing curcumin materials but leave a fundamental physicochemical question insufficiently resolved: how does progressive curcumin incorporation perturb the molecular, ionic, macromolecular, and colloidal organization of NaCMC in solution? Most available studies focus on final formulation performance—encapsulation, solubility, release, bioaccessibility, antioxidant activity, or biological response—whereas comparatively little attention has been paid to the transitions connecting initial molecular association with polymer-chain reorganization and subsequent supramolecular assembly. This distinction is important because an observed change in particle size, viscosity, conductivity, or curcumin solubility cannot, in isolation, establish formation of a unique CMC-curcumin complex.

This problem becomes particularly relevant when curcumin is introduced into aqueous NaCMC from dimethyl sulfoxide (DMSO). DMSO enables preparation of concentrated curcumin solutions, but it is not an inert carrier in a mixed aqueous system. Changing the water/DMSO composition simultaneously modifies solvent polarity, hydrogen-bonding organization, ion solvation, counterion mobility, and potentially the conformation of the polyelectrolyte chain. Curcumin itself is also structurally responsive to its solvent environment; solution-state studies have demonstrated solvent-dependent keto–enol behavior and an important role of solvent-mediated hydrogen bonding in its tautomerization [12]. Consequently, any concentration-dependent transition observed in an aqueous NaCMC/curcumin/DMSO system must be distinguished from the background effects produced by DMSO addition alone.

This distinction provides the central premise of the present study. Rather than assuming *a priori* that NaCMC and curcumin form a discrete complex of fixed stoichiometry, we consider the system as a concentration-dependent, multilevel association landscape in which curcumin-polymer contacts, solvent reorganization, counterion redistribution, polymer-chain conformational changes, and curcumin self-association may occur concurrently. Such a framework predicts that molecular-scale perturbations need not coincide at exactly the same composition with macromolecular or colloidal transitions. Instead, progressive curcumin loading may generate sequential regimes of association, chain reorganization, nanoscale stabilization, and eventually aggregation when the capacity of the polymer environment to stabilize additional curcumin is exceeded.

Accordingly, the present work investigates concentration-dependent organization in the NaCMC/curcumin system by integrating conductometric titration, viscometric/rheological analysis, UV-visible spectroscopy, and dynamic light scattering, with NaCMC-DMSO measurements used as

an essential solvent control. The experimental design is intended to interrogate complementary structural levels: conductivity is used to probe changes in the ionic environment and charge-carrier mobility; viscosity reflects changes in macromolecular organization and hydrodynamic behavior; spectroscopy monitors alterations in the molecular environment of curcumin; and dynamic light scattering characterizes the evolution of colloidal populations. The NaCMC used in the present experimental program has $M_w \approx 250$ kDa and $DS \approx 1.2$, while curcumin is introduced as a DMSO solution, making explicit solvent-background discrimination particularly important.

The objective of this study is therefore to elucidate the concentration-dependent molecular association and hierarchical supramolecular reorganization of NaCMC/curcumin systems and to establish relationships among changes in ionic environment, polymer organization, and colloidal structure. We hypothesize that curcumin incorporation does not produce a single instantaneous “complexation point”, but instead induces a sequence of coupled transitions that can be resolved only by integrating independent physicochemical observables. By distinguishing curcumin-specific effects from DMSO-induced changes and correlating molecular-, macromolecular-, and colloidal-scale responses, this study aims to provide a mechanistic basis for the rational design of CMC-based curcumin delivery and bioactive materials.

Materials and Methods

1. Materials

Sodium carboxymethyl cellulose (NaCMC; Aladdin Chemical Co., Ltd., China) with a weight-average molecular weight (M_w) of approximately 250 kDa and a degree of substitution (DS) of 1.2 was used as the polymer matrix. Curcumin (purity $\geq 98\%$; molecular formula $C_{21}H_{20}O_6$; molar mass 368.38 g mol⁻¹, Macklin Biochemical Co., Ltd., China) was used as the bioactive polyphenolic compound. High-purity dimethyl sulfoxide (DMSO; Sigma-Aldrich) was used as the solvent for curcumin. Distilled water was used for preparation of NaCMC solutions and throughout the experiments. All reagents were used as received without further purification.

2. Preparation of NaCMC and curcumin stock solutions

A 1.0% (w/v) NaCMC stock solution was prepared by gradually dispersing 1.00 g of NaCMC in distilled water and adjusting the final volume to 100 mL. NaCMC was introduced gradually under continuous mechanical stirring to minimize local agglomeration and facilitate uniform hydration of the polymer. The solution was stirred for 3 h at 800-1200 rpm at room temperature until a macroscopically homogeneous solution was obtained.

After dissolution and hydration, the NaCMC solution was sequentially filtered through membrane filters with nominal pore sizes of 1.0 μ m, 0.45 μ m, and 0.22 μ m. This filtration protocol was used to remove undissolved material, dust, and macroscopic/submicron extraneous particles that could interfere with spectroscopic and light-scattering measurements. The same filtration procedure was maintained for samples intended for comparative physicochemical characterization unless otherwise stated.

A 1.0% (w/v) curcumin stock solution was prepared by dissolving 1.00 g of curcumin in high-purity DMSO and adjusting the final volume to 100 mL. The solution was stirred for 1 h at 800-1200 rpm until complete macroscopic dissolution was achieved. Curcumin-containing solutions were protected from direct light during preparation and subsequent handling to minimize photochemical alteration.

3. Preparation of NaCMC/curcumin systems

NaCMC/curcumin systems were prepared by controlled addition of the 1.0% (w/v) CUR/DMSO stock solution to the aqueous 1.0% (w/v) NaCMC solution. For conductometric experiments, 50.0 mL of the NaCMC solution was used as the initial polymer phase. The CUR/DMSO stock solution was subsequently introduced in controlled increments.

For complementary physicochemical characterization, formulations containing different amounts of CUR/DMSO were prepared under otherwise identical conditions. Composition was expressed both as the volume of added CUR/DMSO stock solution (V_{CUR}) and, where appropriate, as the CUR-to-NaCMC mass ratio:

$$R_m = m_{\text{CUR}} / m_{\text{NaCMC}}$$

Because each addition of the curcumin stock simultaneously introduced DMSO and increased the total volume of the system, changes in curcumin concentration, polymer concentration, solvent composition, and dilution were considered jointly during data interpretation. All formulations used for comparative measurements were prepared using the same stock-solution preparation and mixing procedures to minimize experimental variability.

4. Conductometric analysis

a. Conductometric titration of NaCMC with CUR/DMSO

Conductometric measurements were performed using a FiveEasy F30 conductivity meter (Mettler Toledo). The instrument was calibrated before each measurement series according to the manufacturer's recommended procedure using an appropriate conductivity standard. All measurements were performed at 25 ± 1 °C.

A 50.0 mL aliquot of 1.0% (w/v) NaCMC solution was transferred into the measurement vessel. After temperature equilibration and stabilization of the conductivity signal, the initial conductivity (κ_0) was recorded. The 1.0% (w/v) CUR/DMSO stock solution was subsequently added in 0.50 mL increments under continuous mixing. Following each addition, the system was mixed and allowed to equilibrate for 2-3 min before the conductivity value was recorded. Conductivity was expressed in $\mu\text{S cm}^{-1}$. Each measurement series was performed in triplicate ($n = 3$).

b. NaCMC-DMSO solvent control

Because curcumin was introduced as a DMSO solution, a separate solvent-control titration was performed to distinguish curcumin-associated changes from those caused by dilution and modification of the water/DMSO environment. A 50.0 mL aliquot of the same 1.0% (w/v) NaCMC solution was titrated with high-purity DMSO under conditions corresponding to those used for the CUR/DMSO experiment. Conductivity was recorded after equilibration at each addition step.

Thus, two composition-dependent profiles were generated: NaCMC/H₂O + CUR/DMSO and NaCMC/H₂O + DMSO. The latter was treated as the solvent-background response rather than assuming that DMSO behaved as an inert diluent.

c. Normalization and analysis of conductivity data

To facilitate comparison between independent titrations, conductivity values were normalized to the initial conductivity of the NaCMC solution:

$$\kappa_{\text{rel}}(V) = \kappa(V) / \kappa_0,$$

where $\kappa(V)$ is the conductivity after addition of a given titrant volume V and κ_0 is the conductivity before titrant addition.

The deviation of the curcumin-containing system from the corresponding DMSO control was additionally evaluated using:

$$\Delta\kappa(V) = \kappa_{\text{CUR/DMSO}}(V) - \kappa_{\text{DMSO}}(V)$$

This difference was used only as a descriptive measure of deviation from the solvent control and was not interpreted as an isolated or additive "curcumin contribution", because polymer-solute-solvent interactions in mixed aqueous/DMSO media may be non-additive.

Potential changes in the slope of the conductivity-composition relationship were evaluated by segmented (piecewise) regression rather than by visual assignment alone. For a single-breakpoint model:

$$\kappa(V) = \begin{cases} a_1 + b_1 V, & V \leq V_c \\ a_2 + b_2 V, & V > V_c \end{cases},$$

where V_c denotes the estimated critical composition. Where appropriate, derivative analysis ($d\kappa/dV$) was also used to identify regions of maximum conductivity change. A conductivity breakpoint was operationally interpreted as a critical ionic/structural transition region and was not considered, by itself, proof of a fixed stoichiometric NaCMC/CUR complex.

5. Viscometric analysis

The hydrodynamic behavior of the NaCMC/CUR systems was evaluated using a IKA ROTAVISC lo-vi rotational viscometer equipped with a 0.56 mm capillary. Measurements were carried out at 25 ± 1 °C. NaCMC/CUR formulations containing progressively increasing amounts of CUR/DMSO were prepared according to the procedure described above. Each sample was measured three times ($n = 3$), and the mean flow time was used for subsequent calculations.

Relative viscosity (η_r) was determined from the flow characteristics of the investigated and reference solutions, with density correction applied where required. Specific viscosity was calculated as:

$$\eta_{sp} = \eta_r - 1.$$

Changes in viscosity were used as indicators of changes in the hydrodynamic organization of NaCMC chains. A reduction in viscosity was not considered independent proof of a coil-to-globule transition; conformational interpretations were made only in conjunction with the other physicochemical measurements.[13]

Results and Discussion

1. Solvent-controlled conductometric analysis and identification of the critical transition region

Conductometric analysis was used to resolve composition-dependent changes in the ionic environment of the NaCMC/curcumin system (Fig.1,2,3). Because curcumin was introduced as a solution in dimethyl sulfoxide (DMSO), the interpretation was based on paired analysis of the NaCMC/CUR/DMSO titration and an independently measured NaCMC/DMSO solvent control. This control is essential because each addition of the curcumin stock simultaneously increases the curcumin content, DMSO fraction, total solution volume, and therefore the physicochemical environment governing ionic mobility. Accordingly, the conductivity response was interpreted as a coupled solvent–polymer–curcumin phenomenon rather than as a direct readout of a single binding event.

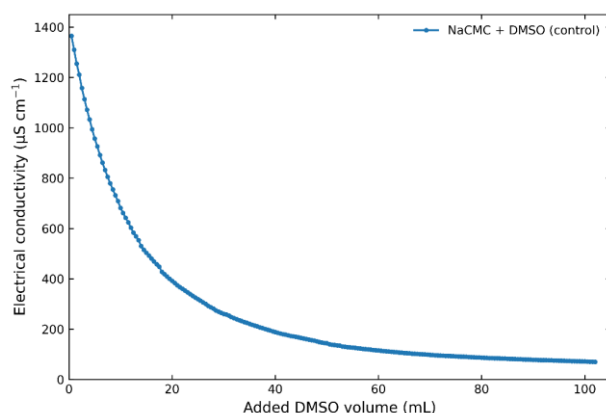


Fig. 1. Effect of progressive DMSO addition on the electrical conductivity of 1.0% (w/v) aqueous NaCMC at 25 ± 1 °C. The NaCMC/DMSO system served as the solvent control for the corresponding CUR/DMSO titration experiments.

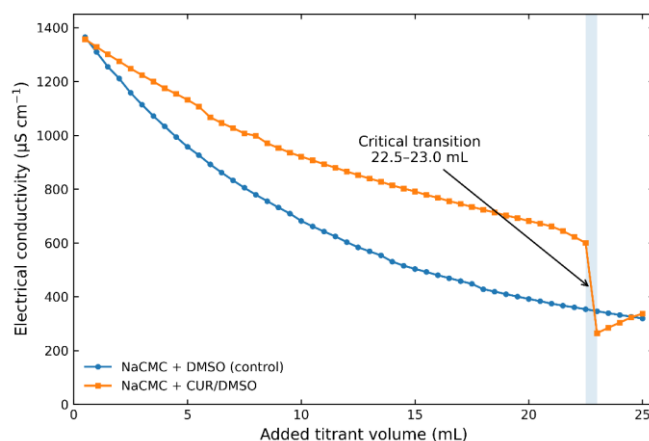


Fig. 2. Comparison of the conductivity profiles of 1.0% (w/v) NaCMC during progressive addition of CUR/DMSO and pure DMSO at 25 ± 1 °C. The shaded interval marks the experimentally observed critical transition region (22.5-23.0 mL) in the curcumin-containing system.

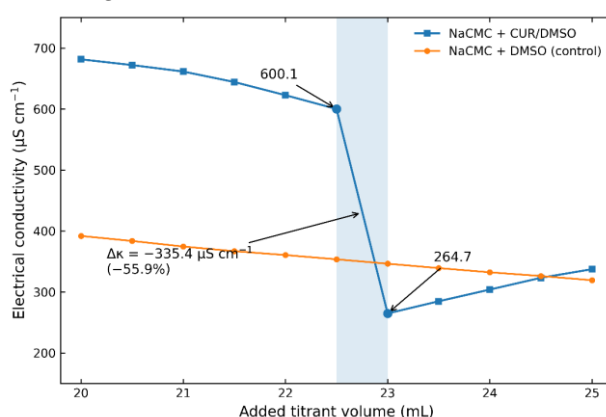


Fig. 3. Enlarged view of the critical conductometric transition region. In the NaCMC/CUR/DMSO system, conductivity decreased from $600.1 \mu\text{S cm}^{-1}$ at 22.5 mL to $264.7 \mu\text{S cm}^{-1}$ at 23.0 mL ($\Delta\kappa = -335.4 \mu\text{S cm}^{-1}$; -55.9%), whereas the NaCMC/DMSO control remained smooth over the corresponding composition range.[14]

The aqueous 1.0% (w/v) NaCMC solution exhibited high initial conductivity, consistent with its polyelectrolyte character and the presence of mobile counterions associated with ionized carboxymethyl groups. In the DMSO-control experiment, progressive addition of pure DMSO produced a pronounced but smooth decrease in conductivity, from approximately $1365 \mu\text{S cm}^{-1}$ at 0.5 mL added DMSO to $70.19 \mu\text{S cm}^{-1}$ at 102 mL (Fig.1). The absence of an abrupt discontinuity over this range demonstrates that solvent addition alone is sufficient to generate a large nonlinear conductivity decrease. This behavior is consistent with simultaneous dilution and modification of ion solvation, solvent viscosity, counterion mobility, and the hydration/conformational state of the NaCMC polyelectrolyte. Therefore, the broad decrease observed during CUR/DMSO addition cannot be assigned exclusively to NaCMC/curcumin association.

The curcumin-containing titration displayed a qualitatively different response (Fig.2-3). Conductivity decreased progressively from $1357 \mu\text{S cm}^{-1}$ at 0.5 mL CUR/DMSO to $681.5 \mu\text{S cm}^{-1}$ at 20.0 mL, followed by a steeper decrease to $600.1 \mu\text{S cm}^{-1}$ at 22.5 mL. A pronounced discontinuity then occurred between 22.5 and 23.0 mL, where conductivity dropped from 600.1 to $264.7 \mu\text{S cm}^{-1}$. This corresponds to an absolute change of $335.4 \mu\text{S cm}^{-1}$, or approximately 55.9% relative to the value measured immediately before the transition. After the minimum, conductivity increased to 284.7 , 303.9 , 323.2 , and $337.3 \mu\text{S cm}^{-1}$ at 23.5, 24.0, 24.5, and 25.0 mL, respectively. Thus, the critical feature is

not merely a minimum in conductivity but an abrupt transition followed by a reversal in the direction of the conductivity response.

Comparison with the DMSO control is decisive. At corresponding titrant volumes, the solvent-control profile changes smoothly and does not reproduce the sharp 22.5-23.0 mL discontinuity. Consequently, the abrupt response cannot be explained by simple dilution alone. Nevertheless, because the DMSO fraction is already substantial in this composition range, the discontinuity should not be interpreted as direct proof of a discrete stoichiometric NaCMC/CUR complex. Instead, it provides evidence that the presence of curcumin introduces an additional cooperative physicochemical process superimposed on the continuously evolving water/DMSO/NaCMC background.

A useful conceptual description of the measured response is:

$$\Delta\kappa_{\text{obs}} = \Delta\kappa_{\text{dilution}} + \Delta\kappa_{\text{solvent/solvation}} + \Delta\kappa_{\text{polymer-state}} + \Delta\kappa_{\text{CUR-dependent}}$$

These terms are not assumed to be quantitatively additive; rather, the expression emphasizes that conductivity is an emergent response of the entire multicomponent system. The CUR-dependent term may include changes in NaCMC hydration, counterion distribution and mobility, polymer-chain organization, curcumin association with the polymer environment, and CUR-CUR self-association. In particular, the conductivity data alone cannot distinguish hydrogen bonding, Na⁺-curcumin ion-dipole interactions, or other specific molecular contacts.

The chemical characteristics of the components nevertheless provide a physically plausible basis for such cooperative reorganization. NaCMC is an anionic, semiflexible polyelectrolyte whose hydrodynamic state is highly sensitive to ionic conditions and solvent-mediated electrostatic screening. Curcumin contains phenolic hydroxyl, methoxy, and β -diketone/keto-enol functionalities capable of participating in hydrogen-bonding and solvent-mediated interactions. At the same time, curcumin contains conjugated aromatic domains and can undergo self-association as its local concentration increases. Native NaCMC does not contain aromatic rings; therefore, π - π interactions, if relevant, should be assigned primarily to CUR/CUR association rather than NaCMC/CUR π - π stacking.

The composition of the medium at the transition further argues against treating the breakpoint as a simple equivalence point. Assuming 50.0 mL of the initial aqueous NaCMC solution and neglecting volume contraction, addition of 22.5-23.0 mL of DMSO-based curcumin stock corresponds to a nominal DMSO fraction of approximately 31-32 vol%. Such a solvent shift is sufficiently large to affect dielectric properties, ion solvation, polymer hydration, and curcumin solvent quality. The experimentally observed discontinuity should therefore be understood as a transition occurring within a coupled NaCMC/water/DMSO/curcumin environment.

To define the transition objectively, the conductivity-composition relationship should be analyzed by segmented regression rather than by visual inspection alone. In this framework, the critical composition (V_c) is the composition at which the slope of the conductivity response changes significantly. Because the experimental series contains an exceptionally sharp change between two adjacent 0.5 mL additions, the present dataset localizes the transition to the narrow interval between 22.5 and 23.0 mL. For publication, V_c should be reported together with its confidence interval from replicate datasets, and the 21-24 mL region should preferably be re-examined using smaller titrant increments (e.g., 0.1-0.2 mL) to refine the breakpoint estimate.

The post-transition increase in conductivity is also mechanistically important. If the decrease before the transition reflected only progressive dilution, conductivity would be expected to continue decreasing. The reversal observed after the abrupt minimum instead indicates that the system enters a new physicochemical regime in which the effective concentration and/or mobility of charge carriers changes differently with further CUR/DMSO addition. Possible contributors include redistribution of counterions, changes in polymer-associated ion mobility, reorganization of NaCMC-rich domains, onset of colloidal association, or changes in the state of curcumin. These alternatives cannot be

discriminated by conductometry alone and must be evaluated against viscometric, spectroscopic, and DLS data.

Taken together, the solvent-controlled conductometric results identify a reproducible candidate critical transition region at approximately 22.5-23.0 mL CUR/DMSO addition. The key evidence is the combination of (i) a smooth nonlinear decrease in the NaCMC/DMSO control, (ii) a sharp curcumin-dependent discontinuity absent from that control, and (iii) reversal of the conductivity trend immediately after the transition. The most defensible interpretation is therefore a curcumin-associated ionic/supramolecular reorganization superimposed on a strong solvent-dependent background. Throughout this work, this region is designated the critical conductometric transition region rather than a stoichiometric complexation point.

2. Viscosity-driven macromolecular reorganization of NaCMC upon curcumin incorporation

Viscometric analysis was used to determine whether the composition-dependent transition identified by conductometry is accompanied by a corresponding change in the macromolecular organization of NaCMC. Whereas conductivity primarily reflects changes in the ionic environment and charge-carrier mobility, viscosity is sensitive to the hydrodynamic state of polymer chains, polymer-solvent interactions, intermolecular association, and changes in effective macromolecular dimensions. The viscosity response therefore provides a complementary probe of the propagation of CUR-associated physicochemical perturbations from the ionic/solvation level to the polymer-chain level.

Progressive incorporation of curcumin resulted in a pronounced and non-uniform decrease in the viscosity of the NaCMC-containing system (Fig. 4). The viscosity decreased from approximately 849 on the reported experimental scale for NaCMC without curcumin (NaCMC:CUR = 10:0) to approximately 705, 599, and 474 at mass ratios of 10:1, 10:2, and 10:3, respectively. At NaCMC:CUR = 10:4, the viscosity decreased further to approximately 369, corresponding to an overall reduction of about 56.5% relative to the initial NaCMC system. Further increases in curcumin content produced only comparatively small changes, with viscosity values of approximately 353 and 337 at NaCMC:CUR ratios of 10:5 and 10:6, respectively. Thus, the viscosity profile is characterized by a pronounced decrease up to the 10:4-10:5 composition range, followed by a substantially weaker composition dependence.

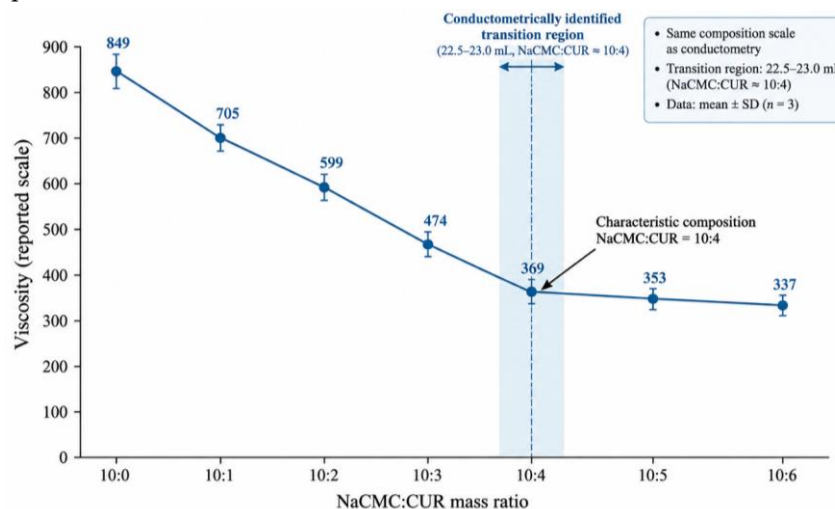


Fig. 4. Effect of progressive CUR/DMSO addition on the viscosity of the NaCMC-containing system at 25 ± 1 °C.

The change in the slope of the viscosity-composition relationship is particularly important when considered together with the conductometric results. Conductometry revealed an abrupt transition between 22.5 and 23.0 mL of added 1.0% (w/v) CUR/DMSO, where conductivity decreased from 600.1 to 264.7 $\mu\text{S cm}^{-1}$, followed by reversal of the conductivity trend. Under the experimental

conditions used for conductometry (50.0 mL of 1.0% (w/v) NaCMC titrated with 1.0% (w/v) CUR/DMSO), this interval corresponds nominally to NaCMC:CUR mass ratios of approximately 10:4.5-10:4.6. Consequently, the characteristic 10:4-10:5 region observed in the viscosity profile lies in close compositional proximity to the independently detected conductometric transition. This correspondence indicates that the pronounced ionic/solvation perturbation and the change in macromolecular hydrodynamic behavior occur within the same broader composition domain rather than representing unrelated phenomena.

Importantly, the viscosity decrease should not be interpreted solely as evidence of direct NaCMC/CUR binding. Increasing CUR/DMSO loading simultaneously changes several physicochemical variables, including NaCMC concentration through dilution, the water/DMSO ratio, solvent quality, ion solvation, Na⁺ counterion mobility, polymer hydration, and the local environment of curcumin. The measured viscosity is therefore an integrated response of the multicomponent NaCMC/water/DMSO/CUR system. Nevertheless, the pronounced change in the concentration dependence near the composition domain identified independently by conductometry suggests that CUR incorporation contributes to a cooperative reorganization of the polymer-containing environment rather than producing only a simple dilution effect.

From a macromolecular perspective, the progressive reduction in viscosity is consistent with a decrease in the effective hydrodynamic contribution of NaCMC chains. Such behavior may arise from reduced chain expansion, modification of polymer-solvent interactions, changes in electrostatic screening and counterion organization, partial intramolecular contraction, and/or rearrangement of intermolecular polymer-associated domains. This interpretation is physically compatible with the polyelectrolyte nature of NaCMC, whose chain dimensions and hydrodynamic behavior are strongly dependent on ionic and solvent conditions. However, viscosity measurements alone do not permit these individual contributions to be quantitatively separated.

The marked attenuation of the viscosity decrease beyond the 10:4-10:5 composition region is also mechanistically significant. Before this region, increasing CUR loading is accompanied by a large change in the hydrodynamic response of the system, whereas further CUR addition produces only a relatively small additional decrease. This behavior suggests that the system approaches a new macromolecular organization regime in which additional curcumin has a substantially weaker effect on the effective hydrodynamic state of NaCMC. The observation is consistent with, but does not by itself prove, progressive saturation of accessible polymer-associated interaction environments or the establishment of a reorganized polymer/solvent/curcumin structure.

The close compositional correspondence between the conductometric and viscometric responses therefore provides stronger mechanistic evidence than either method considered independently. Conductometry identifies a narrow region of pronounced change in the ionic/solvation environment, whereas viscometry demonstrates that the same broader composition domain is associated with a transition in the macromolecular response of NaCMC. Together, these results support a coupled ionic/solvation → macromolecular reorganization mechanism. At the same time, the available evidence does not justify assignment of the transition to a classical coil-to-globule transformation or to formation of a discrete NaCMC/CUR complex of fixed stoichiometry; confirmation of such structural assignments would require independent molecular or scattering evidence.[15]

Conclusions

This study demonstrates that curcumin incorporation induces composition-dependent physicochemical reorganization in aqueous NaCMC systems. Conductometric analysis revealed a pronounced transition at 22.5-23.0 mL CUR/DMSO, where conductivity decreased from 600.1 to 264.7 $\mu\text{S cm}^{-1}$ (-55.9%), whereas the corresponding DMSO control showed no comparable discontinuity. Viscometric analysis showed a substantial decrease in viscosity with increasing CUR content, followed by a markedly weaker response in the NaCMC:CUR $\approx$ 10:4-10:5 composition region. The

close correspondence between the conductometric and viscometric responses supports a coupled ionic/solvation–macromolecular reorganization mechanism. Rather than indicating formation of a discrete fixed-stoichiometry complex, the results identify a characteristic composition domain in which cooperative reorganization of the NaCMC/water/DMSO/CUR system occurs. These findings provide a physicochemical basis for further development and optimization of NaCMC-based curcumin delivery systems

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