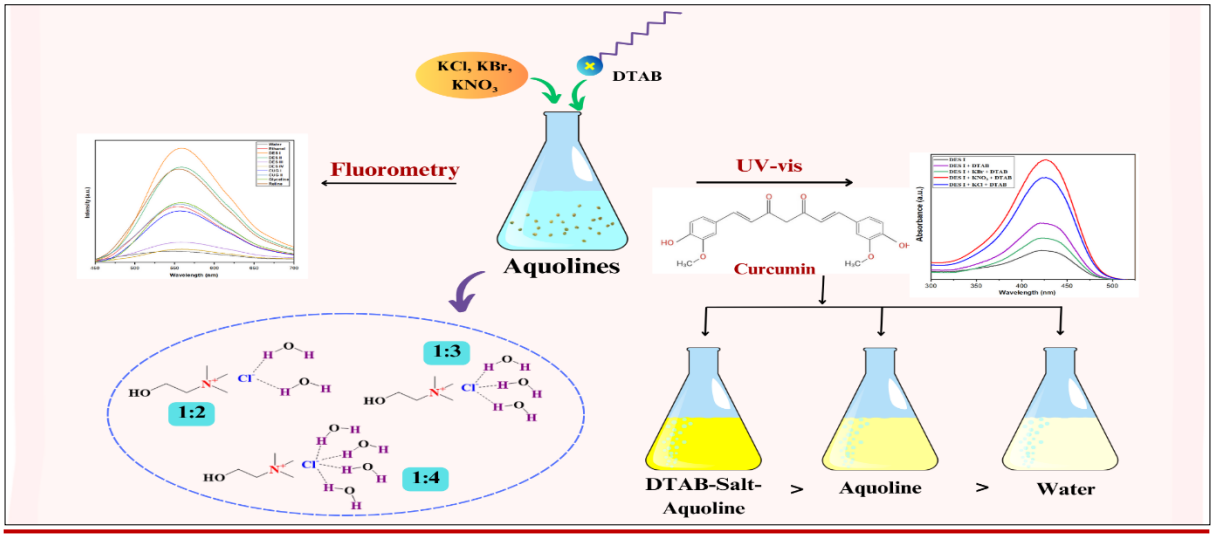
Chapter

6

Solubilization of Curcumin with and without Additives in Deep Eutectic Solvents

Contents

This chapter is mainly focused on the solubilization and photophysical behaviour of curcumin (CCM) in DESs (reline, glyceline, ternary DESs, and aquolines) with and without surfactant and salts. UV-visible and fluorescence spectroscopies are used in this study.



6.1 Introduction

Curcumin (CCM), a natural antioxidant found in turmeric, comprises a significant portion of the yellow-orange pigments of the spices [1]. CCM is a natural antioxidant/anticancer drug (chemically a polyphenol extracted from *Curcuma Longa*) that is also widely used as a key component in several food products due to its numerous therapeutic properties [2–4]. Structurally, it consists of two ferulic acid molecules linked by a methylene bridge at the carbon atoms of the carboxyl groups [5–8]. This lipophilic compound, rich in phenolic groups and conjugated double bonds, exhibits tautomeric forms, with the keto–enol form prevailing in solution due to factors such as solvent characteristics and temperature [9].

CCM possesses multiple biological effects, including anticancer, anti-inflammatory, and anti-HIV characteristics [10]. It is extensively utilized in Ayurvedic and Unani medications. It is employed to mitigate the risk of skin damage caused by exposure to the sun's ultraviolet radiation [9]. Notably, CCM demonstrates its efficacy by inhibiting lipid peroxidation and scavenging various reactive oxygen species, including superoxide anion, singlet oxygen, nitric oxide, and hydroxyl radicals [11]. It possesses health-promoting benefits [12].

The therapeutic use of CCM is hindered by its limited water solubility (~0.02 mg/mL) and bioavailability [13]. A limitation associated with the poor aqueous solubility and stability

of CCM can be addressed by the process of encapsulating within various carriers such as surfactant micelles, nanoparticles, polymeric micelles, cyclodextrins, phospholipids, liposomes, hydrogels, and other similar substances [14–16]. Further, the above media play a non-interacting role during CCM transport. Therefore, designing a drug transport system with biocompatible activities akin to those of the active drug could enlarge the CCM application window [17].

Many research studies on solubilizing drugs, whose findings are currently being utilized in the industry, depend upon non-sustainable or petroleum-derived solvents like methanol or acetone. Acetone is a highly effective solvent, yet it is lacking when it comes to adhering to the 12 principles of green chemistry [18]. It exhibits considerable volatility and is not suitable for intake, so it must be discarded after extraction, leading to waste. Consequently, researchers have investigated other solvents, occasionally in conjunction with microwaves and ultrasound. Ionic liquids (ILs) and deep eutectic solvents (DESs) are commonly employed as environmentally friendly solvents in the pharmaceutical industry due to their significant polarity, lack of reactivity towards the water, low vapor pressure, and exceptional chemical and thermal stability [19–21].

Surfactants, when dissolved in water, can form different structures including micelles and vesicles due to the hydrophobic contact between the alkyl chains of the surfactant molecules [22,23]. Surfactants can also form micelle with different morphologies in DESs and ILs [24–26]. Surfactant aggregates, such as micelles and vesicles, are frequently employed to encapsulate bioactive compounds. This is done to increase their solubility in water, preserve their stability, and boost their bioavailability [27]. The effectiveness of these benefits is greatly influenced by the structure of the surfactant aggregates. Micellar solutions have been used in drug solubilization/ delivery, extraction, reaction media, and enhanced oil recovery among others [28,29]. Most synthesized/natural pharmaceutical compounds show poor solubility in water, which significantly restricts their potential for successful formulation [30,31]. The aqueous solubility of drugs can be enhanced by dissolving them in surfactant micelles [32].

DESs are currently growing in demand and are emerging as potential media for producing organized assemblies [26,33–36]. In the present work, we have checked the solubility of CCM in water and type -III DESs (reline, glyceline, ternary DESs (CUG-I, CUG II), and aquolines (eutectic ratios of used DESs are given in chapter 2)). The prime objective of the study is to investigate the role of the micellar system in enhancing the aqueous solubility

of hydrophobic material (*e.g.,* CCM). This work may open new avenues for obtaining controllable self-assembly and solvent media for water-insoluble drugs, dyes, and insecticides/pesticides. Salt addition in an aqueous surfactant solution is a successful tool for tuning micellization and micellar morphologies [37–39]. This inspired us to exploit the synergy of surfactant-salt-aquoline aggregates towards improving CCM solubility and develop a general strategy for the enhancement of the aqueous solubility of other hydrophobic material. The present work focuses on CCM solubilization data of the DTAB-salt-aquoline system obtained by a UV-vis spectrophotometer. Fluorescence spectroscopy was also used to study the fluorescence behaviour of CCM in various DESs with and without surfactants.

6.2 Experimental section

The materials and methods used are discussed in chapter 2.

6.3 Result and discussion

6.3.1 UV-visible spectral results

The solubility of CCM in different DESs (with and without surfactants/salt) and water, was determined using spectrophotometry. The calibration curve is created by dissolving CCM, which has been weighed previously, in methanol. The absorbance of the solution is then measured at 423 nm as a function of its concentration. The concentration of CCM in the solution was calculated based on the calibration curve shown in **Figure 6.1**, which exhibited a high linear correlation with a coefficient of determination close to 0.998. All the measurements were carried out at 303±0.1 K. The sample preparation method for solubilization of CCM is discussed in chapter 2.

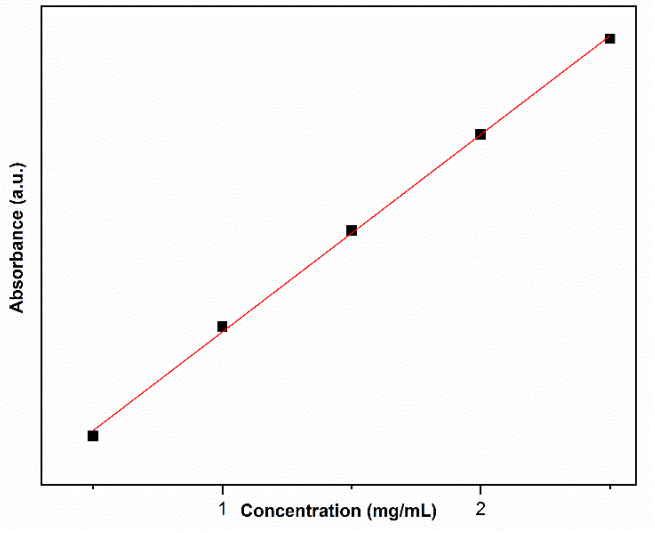


Figure 6.1: Calibration curve of CCM in methanol.

6.3.1.1 Solubilization of curcumin (CCM) in DESs and water

CCM exhibited solubility in both polar and nonpolar organic solvents while showing nearly minimal solubility in water under neutral and acidic pH conditions [40]. The substance exhibited higher solubility in alkaline solutions, probably due to the ionization of its phenolic groups [41]. The absorption spectra of CCM are frequently utilized for observing the interaction of CCM with solvent media and surfactant micelles due to its affinity to the reaction media [42,43]. The UV–vis absorption spectra of CCM in water and DESs (Type III, ternary DESs) are illustrated in **Figure 6.2 (a-b)**. CCM dissolved in water displays a strong absorption of light in the range of wavelengths from 300 to 550 nm. The highest absorption occurs at 423 nm, which corresponds to the absorption of the conjugated diferuloyl structure.

Figure 6.2 (a) explains the effect of different HBDs of DES on the solubility of CCM in reline, glyceline, and ternary DESs. The solubility of CCM in urea and glycerol-based DESs (type III DESs) was considerably higher compared to water-based DES and an aqueous solution **(Table 6.1)**. The data indicates that all of the examined DESs resulted in a considerable enhancement in the solubility of CCM in comparison to water. It is reported that the DES with glycerol as a HBD solubilized more CCM than other DESs with hydroxy sugar-based HBDs (glucose, sorbitol, fructose, etc.) [19]. Out of all DESs that were investigated, the system containing choline chloride and glycerol in 1:2 eutectic proportions (glyceline) had the highest solubility value of 2.20 mg/mL at 303±0.1 K. This finding supports the use of DESs as effective systems for dissolving CCM. Glyceline was also evaluated as a potential method for extracting CCM from natural sources. It proved to be highly effective in this role, primarily due to the safety of natural deep eutectic solvents in the food and pharmaceutical industries. These solvents can be freely administered to individuals, which is not typically the case with organic solvents [19]. It is observed that both urea and glycerol (HBDs) affect the solubility of CCM differently in ternary DESs (CUG I and CUG II). The solubility of CCM follows an order: glyceline > CUG I > reline > CUG II. To explain the influence of water on the solubility of CCM in DESs, the solvation environments for CCM in the DES (aquolines) were analyzed by the utilization of UV spectroscopy. It has been observed that CCM solubility is highest in DES I followed by DES II, DES III, DES IV, and water **(Figure 6.2 (b))**.

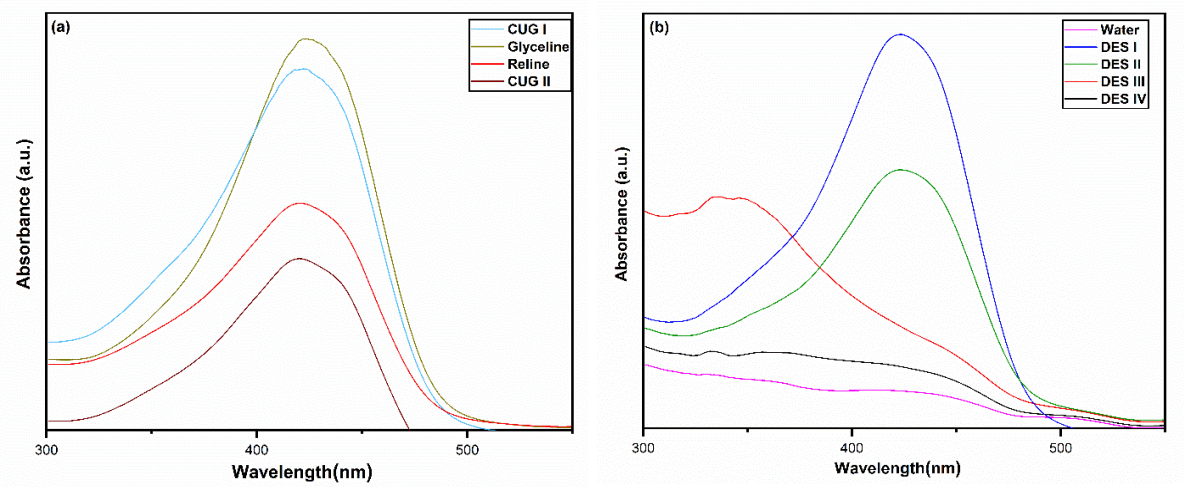


Figure 6.2: Variation of absorbance of CCM with a wavelength in a) Type III DESs; b) water-based DESs and water at 303±0.1 K.

The absorption spectrum in DES I and DES II exhibits a distinct peak at 423 nm whereas, in other aquolines and water, it is moved towards shorter wavelengths compared to DES I and DES II. In a separate study, it is reported that the addition of water alters the cluster of DES and there is an unusual transition from DES to a molecular solution of components in addition to water [44]. As the solubility of CCM is affected by solvation media the observed blue shift for DES III and DES IV is probably due to approaching the transition from aquoline to a molecular solution of ChCl in water. It is observed that as the water content in aquoline increases the solubility of CCM decreases and it approaches towards solubility of CCM in water. **Table 6.1** shows the amount of CCM (in mg/mL), solubilized in various DESs and water.

Table 6.1: Solubility (in mg/mL) of CCM in Type III DESs, aquolines, and water at 303±0.1 K.

System	CCM solubility (mg/mL)
Water	0.06
DES I	0.62
DES II	0.40
DES III	0.16
DES IV	0.10
CUG I	2.06
CUG 2	1.74
Glyceline	2.20
Reline	1.28

6.3.1.2 Solubilization of CCM in aquoline + surfactant system

The solubility of CCM in aquoline in the presence of cationic (DTAB, TTAB, and CTAB) and anionic surfactants (SDS) were investigated using UV–vis spectroscopy and compared with pure aquolines. **Figure 6.3 (a-c)** shows the absorbance spectra of CCM in aquoline with and without surfactants. The solubility of CCM in DESs might be facilitated by interactions like hydrogen bonds, van der Waals forces, ion-dipole, and dipole-dipole interactions between CCM and DESs. The absorptions of CCM can be affected by the polarity of the CCM microenvironment and the association between the surfactant and CCM, leading to shifts in the π-π* and n-π* transition to lower or higher energy levels [45].

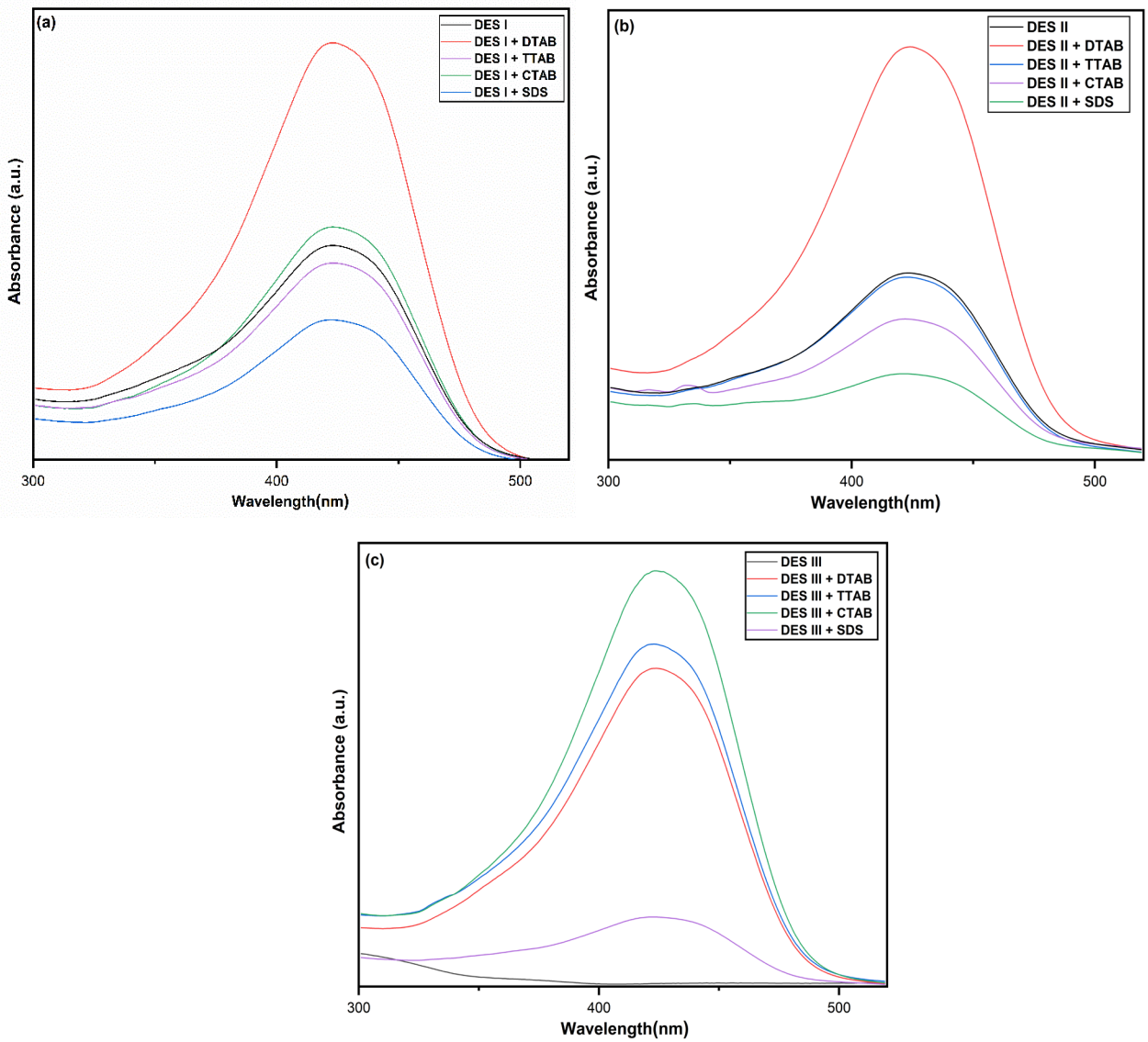


Figure 6.3: Variation of absorbance of CCM with a wavelength in various aquolines (with and without surfactant): a) DES I; b) DES II; c) DES III at 303±0.1 K.

The absorbance spectra show that the influence of surfactant on the solubilization behaviour of CCM in each aquoline is different. It was mentioned in the literature that, DESs exhibit a more complex liquid structure due to the combination of ionic and molecular species, which involves hydrogen bonding and electrostatic interactions [46]. A complex hydrogen bond network was detected among the components of the DES, which may be the reason for the different solubilization behaviour of CCM in aquolines + surfactant systems. The solubility of CCM in water can be improved by adding surfactants [47]. In the case of DES III, solubility in pure aquoline is lower than solubility in an aquoline-surfactant system which may indicate the transition of DES to a molecular solution of ChCl. The amount of CCM (in mg/mL) solubilized in various aquolines + surfactants systems is given in **Table 6.2.** The solubility of CCM in aquoline with a cationic surfactant is higher as compared to aquoline with an anionic surfactant. However, there is no regular trend was observed with increasing chain length of cationic surfactants.

Table 6.2: Solubility (in mg/mL) of CCM in aquoline + surfactant systems at 303±0.1 K.

	Aquolines		
System	**DES I** (mg/mL)	**DES II** (mg/mL)	**DES III** (mg/mL)
CCM	0.62	0.40	0.16
CCM + DTAB	1.20	0.89	1.34
CCM + TTAB	0.56	0.39	1.45
CCM + CTAB	0.67	0.18	1.77
CCM + SDS	0.40	0.30	0.29

6.3.1.3 Solubilization of CCM in DTAB-salt-aquoline system

Figure 6.4 (a-c) shows the variation in absorbance of CCM with a wavelength in aquoline (with and without salt) and aquoline-salt-DTAB systems. The amount of CCM (in mg/mL), solubilized in different solvent DTAB-salt-aquoline systems, has been tabulated in **Table 6.3**. A perusal of data shows that CCM solubility improves in pure aquolines compared to water (~0.006 mg/mL). The presence of DTAB with aquoline shows a gradual increase in the CCM solubility. However, the presence of DTAB with K-salts (KCl, KBr, or KNO_3) and aquoline shows distinct improvement of CCM solubility (in some cases more than 200-fold).

It is also observed that CCM solubility in aquolines is more with KBr as compared to KCl and KNO_3 without DTAB.

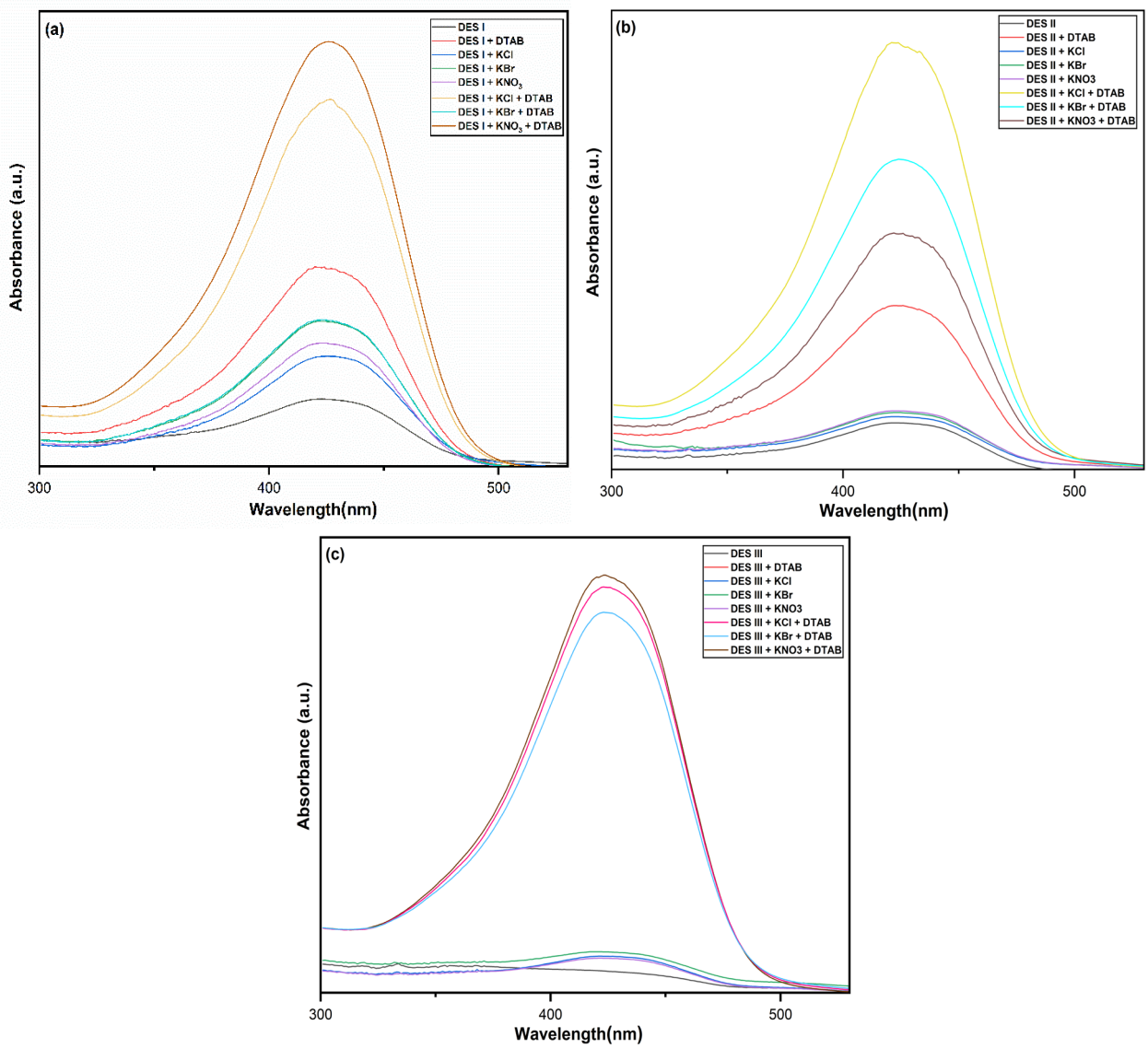


Figure 6.4: Variation of absorbance of CCM with a wavelength in various aquolines with and without surfactant/salt: a) DES I; b) DES II; c) DES III at 303±0.1 K.

When the morphology (chapter 4) is combined with solubility data **(Table 6.3),** it is observed that aggregate size directly influences solubility magnitude. This can be understood in the light of larger hydrophobic volume available with giant aggregates and concomitantly responsible for higher CCM solubilization. Therefore, DTAB-salt-DES systems can be exploited for solubility enhancement.

Table 6.3: Solubility (in mg/mL) of CCM in 10mM DTAB + aquolines with and without salt at 303±0.1 K.

	Aquolines		
System	**DES I** (mg/mL)	**DES II** (mg/mL)	**DES III** (mg/mL)
CCM	0.62	0.40	0.16
CCM + DTAB	1.20	0.89	1.34
CCM + KCl	0.66	0.25	0.17
CCM + KBr	0.87	0.31	0.18
CCM + KNO_3	0.74	0.32	0.15
CCM + KCl + DTAB	2.26	2.35	1.83
CCM + KBr + DTAB	0.88	1.68	1.70
CCM + KNO_3 + DTAB	2.50	1.29	1.85

6.3.2 Fluorescence spectral results

The fluorescence spectra of CCM were analyzed at 303±0.1 K after being excited at its absorption peak in various DESs (with and without surfactants/salt) and water. The data were recorded with fixed excitation at 410 nm, and the slit widths of excitation and emission were also fixed at 5 and 5 nm, respectively. The spectra were recorded from 450 nm to 700 nm.

6.3.2.1 Fluorescence of curcumin (CCM) in DESs and water

The fluorescence emission behaviour of CCM was studied in DESs (type III DESs, ternary DESs) and results were compared with water. The fluorescence intensity and positioning of the most prominent band of CCM were highly influenced by the type of solvent, despite its absorption maxima [48]. Small organic fluorescent compounds with a conjugated structure typically agglomerate at high concentrations through π - π stacking, leading to a change in fluorescence intensity [49]. **Figure 6.5 (a-b)** represents fluorescence spectra of CCM in water and DESs (Type III, ternary DESs). It is observed that CCM shows high fluorescence intensity in reline and glyceline than ternary DESs (CUG I and CUG II) **(Figure 6.5 a)**. This could be attributed to the combination of a polar hydroxyl group and a non-polar alkyl chain in one of the constituents of reline and glyceline (ChCl). This structural feature may play a role in interaction with CCM.

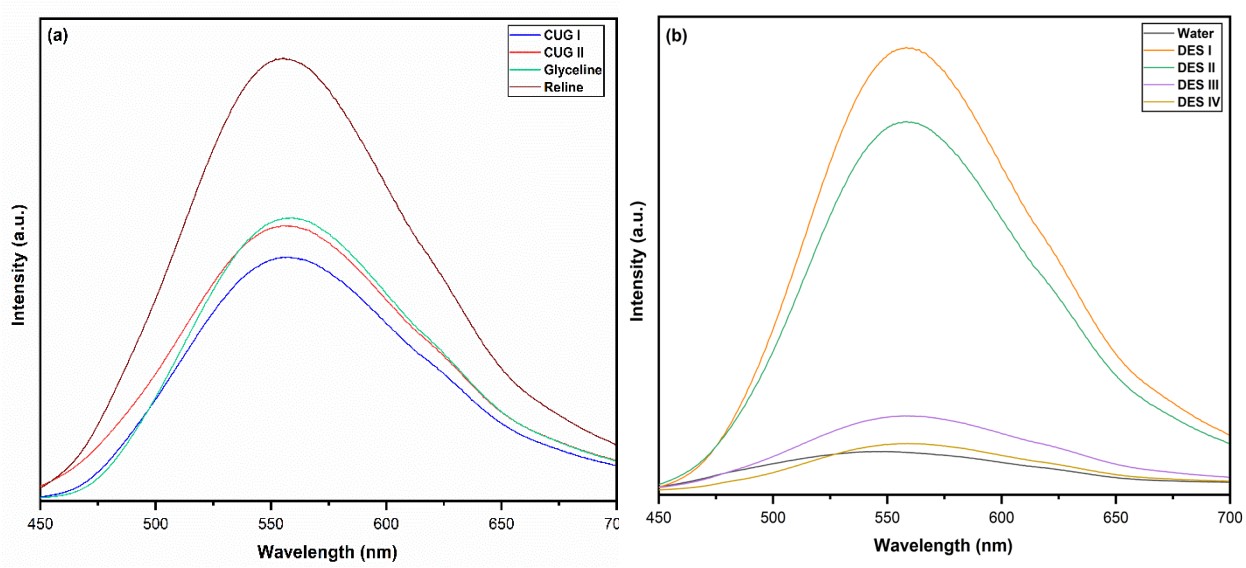


Figure 6.5: Emission spectra of CCM in a) Type III DESs; b) water-based DESs and water at 303±0.1 K.

To gain more understanding of the designer solvent impact, reline and glyceline was altered by incorporating a third component (ternary DESs), and fluorescence data of CCM in it is shown in the same figure. The interactions among reline components decreased gradually as glycerol was introduced. The pH of reline decreases when glycerol is added which may also contribute to the solvation of CCM in the DESs.

Figure 6.5 b shows the emission spectra of CCM in aquolines and water. The order of fluorescence intensity is as follows: DES I > DES II > DES III > DES IV > water. As the water content increases the fluorescence intensity decreases and λ_{max} slightly shifts toward a shorter wavelength (λ_{max}= 558 nm to 540 nm). CCM in an aqueous solution exhibits a very low broad peak at 540 nm.

6.3.2.2 Fluorescence of CCM in aquoline + surfactant system

The fluorescence emission behaviour of CCM was studied in aquoline with cationic (DTAB, TTAB, CTAB) and anionic (SDS) surfactants. Several parameters such as charge, type, chain length, and molecular structure of surfactant have been found to affect the interaction between fluorophores and surfactant assemblies. **Figure 6.6 (a-c)** shows the emission spectra of CCM in aquoline (with and without surfactants). Both cationic and anionic surfactants can be dissolved in aquoline so the micellar solution of surfactants is prepared in aquolines. As CCM contains the β-diketone group which has maximum electron density, it is expected that CCM gives an intense fluorescence peak in aquoline with a cationic surfactant system. This

may be due to both electrostatic and hydrophobic interactions of CCM with surfactants. However, irregularity in trend was observed.

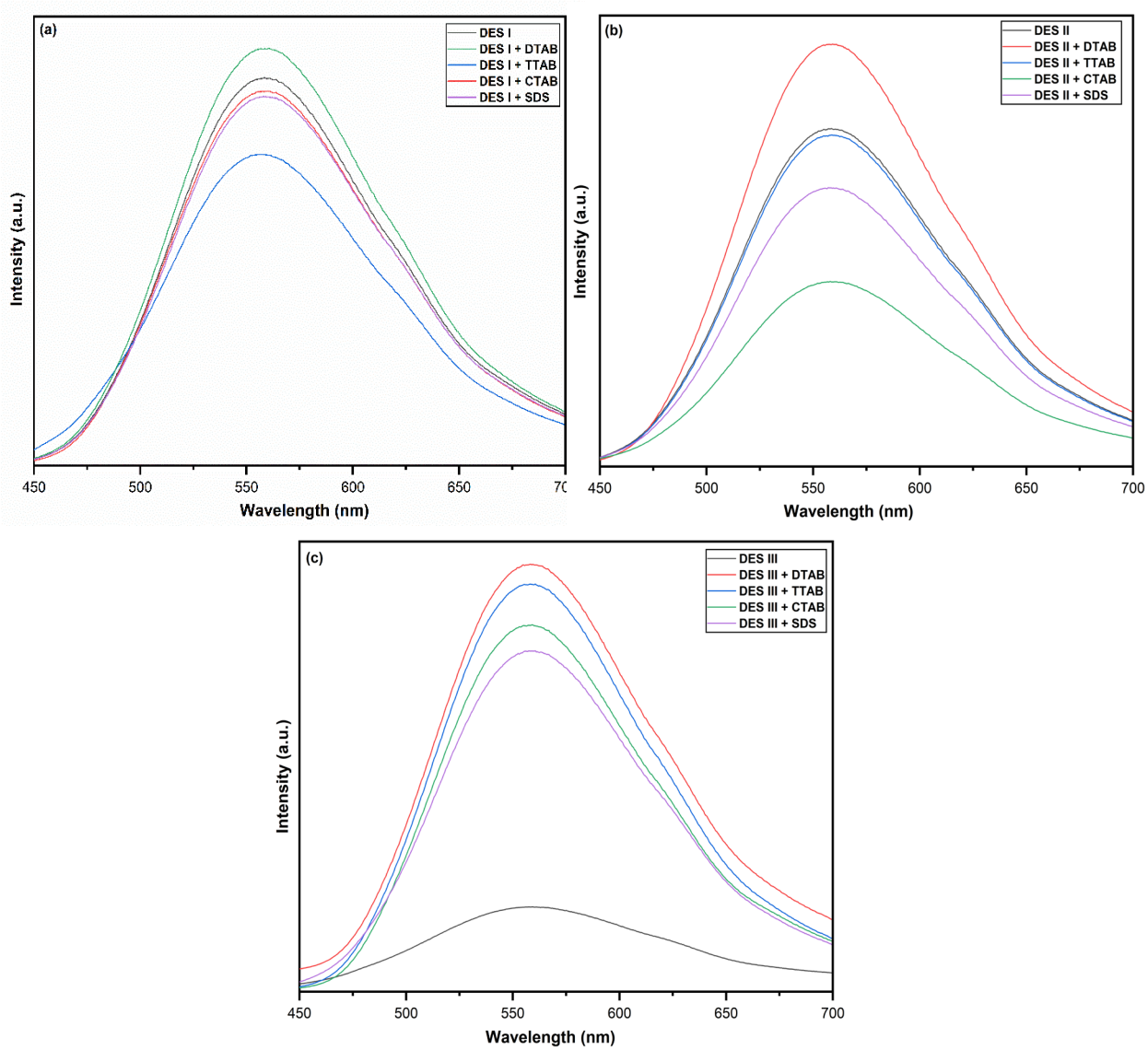


Figure 6.6: Emission spectra of CCM in aquolines + surfactant system a) DES I; b) DES II; c) DES III at 303±0.1 K.

It has been observed that in all aquolines CCM shows a higher intensity with DTAB. In DES II and DES III, the trend of CCM intensity is similar but the observed intensity trend in DES III was different. In DES III, the fluorescence intensity increases with the addition of ionic surfactants. The variation in emission spectra intensity may result from the gradual transfer of CCM molecules from polar surroundings to the hydrophobic portion of the micelles. Fluorescence spectra intensity changes due to alterations in the local environment surrounding the probe molecules caused by factors like polarity and H-bonding ability.

6.3.2.3 Fluorescence of CCM in DTAB-salt-aquoline system

The photophysical properties of CCM in aquolines in the presence of DTAB and K-salt were studied using fluorescence spectroscopy. The effect of the interaction between salt, surfactant, and DES on the emission spectra of CCM is complex and influenced by multiple factors such as concentration, ionic strength, micelle formation, pH, and aggregation state. The addition of salt can alter the ionic strength of the solution, which in turn affects the emission spectra of CCM. High ionic strength can induce aggregation or alter the microenvironment surrounding CCM molecules, leading to changes in fluorescence intensity and emission wavelength.

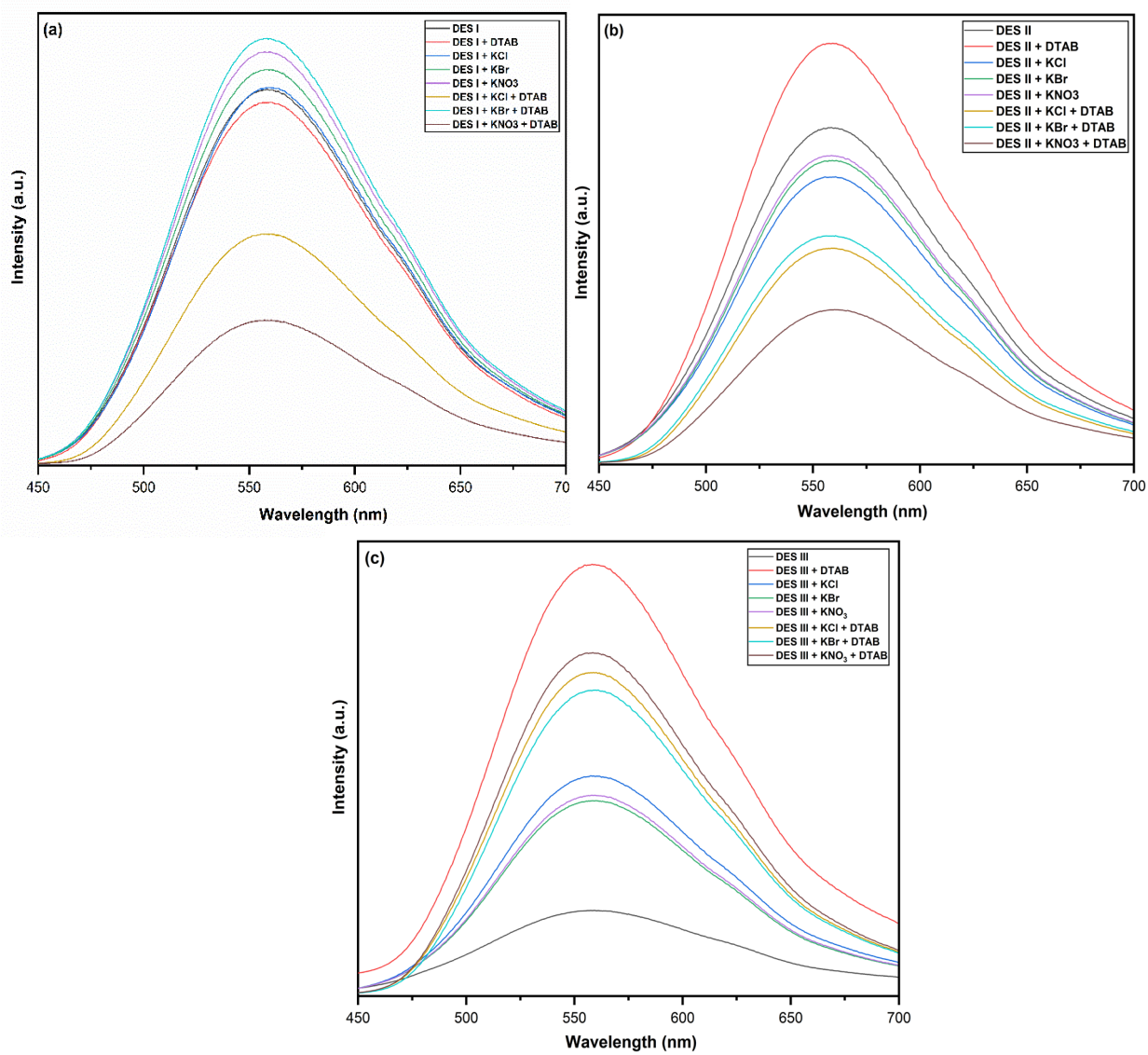


Figure 6.7: Emission spectra of CCM in various aquolines with and without surfactant/salt a) DES I; b) DES II; c) DES III at 303±0.1 K.

Micellar solution of surfactant can encapsulate CCM molecules. This encapsulation can affect the emission spectra by modifying the local environment around CCM, potentially leading to shifts in emission wavelength or changes in fluorescence intensity. Micellar confinement may also reduce the self-quenching of CCM, resulting in enhanced fluorescence emission. **Figure 6.7 (a-c)** shows the emission spectra of CCM in aquoline (with and without DTAB and K-salt). No particular trend was observed in the intensity of CCM (at λ_{max}= 558 nm) in various aquolines (DES I-III) with the same amount of DTAB and K-salts. However, it is observed that in DES III, CCM shows higher fluorescence intensity in aquoline with DTAB and salt as compared to pure aquoline. It has been reported that there are two types of interactions with the DESs, coulombic interactions (due to the positive charge of ChCl) and van der Waals interactions (due to alkyl group) [50,51]. The predominant factor contributing to the stabilization of CCM within micelles appears to be the van der Waals interactions rather than Coulombic forces. The presence of salt does not significantly impact the van der Waals interactions. However, the addition of salt results in a more compact size of the micelles. This may be the reason for irregularity in the trend of fluorescence intensity of CCM in the aquoline-salt-surfactant system.

6.4 Conclusion

The solubilization of CCM in DESs (reline, glyceline, ternary DESs, aquolines) with and without surfactants/salts by UV-visible and fluorescence spectroscopy was studied. CCM solubility shows a distinct improvement in aquolines which distinctly enhances in aquoline-salt-DTAB system. The UV-visible spectral results provided comprehensive insights into the solubilization behaviour of CCM in various solvent systems. The absorption spectra of CCM in water and DESs demonstrated significant differences, with DESs, particularly those containing glycerol as a HBD (glyceline), exhibiting notably enhanced solubility, making it a promising solvent for CCM extraction from natural sources. The addition of surfactants further improved CCM solubility in aquolines, with cationic surfactants proving more effective than anionic ones. The solubility of CCM also increased significantly in aquiline-salt-DES systems, with some cases showing over a 200-fold increase compared to pure aquolines. In terms of fluorescence spectral results, CCM exhibited varying fluorescence intensity and emission spectra depending on the solvent environment, presence of surfactants, and salts. The fluorescence intensity of CCM was higher in reline and glyceline compared to ternary DESs, possibly due to interactions between CCM and DES components. Similarly, CCM fluorescence was influenced by the presence of surfactants, with cationic surfactants generally resulting in

higher fluorescence intensity compared to anionic surfactants. However, irregularities in the trends observed, indicating the complexity of CCM-surfactant interactions. From the solubility data, it is revealed that a synergy regarding CCM solubility exists in the surfactant-salt-DES system. However, more studies are required to generalize this methodology for enhanced CCM solubility.

6.5 References

[1] R. Carolina Alves, R. Perosa Fernandes, B. Fonseca-Santos, F. Damiani Victorelli, and M. Chorilli, Crit Rev Anal Chem **49**, 138 (2019).

[2] M. Deters, H. Knochenwefel, D. Lindhorst, T. Koal, H. H. Meyer, W. Hänsel, K. Resch, and V. Kaever, Pharm Res **25**, 1822 (2008).

[3] M. A. Salem, R. A. El-Shiekh, A. R. Fernie, S. Alseekh, and A. Zayed, Sci Rep **12**, 10288 (2022).

[4] S. Zorofchian Moghadamtousi, H. Abdul Kadir, P. Hassandarvish, H. Tajik, S. Abubakar, and K. Zandi, Biomed Res Int **2014**, 1 (2014).

[5] D. Ke, X. Wang, Q. Yang, Y. Niu, S. Chai, Z. Chen, X. An, and W. Shen, Langmuir **27**, 14112 (2011).

[6] S. Mondal and S. Ghosh, J Photochem Photobiol B **115**, 9 (2012).

[7] Z. Wang, M. H. M. Leung, T. W. Kee, and D. S. English, Langmuir **26**, 5520 (2010).

[8] M. H. M. Leung, H. Colangelo, and T. W. Kee, Langmuir **24**, 5672 (2008).

[9] S. M. Khopde, K. Indira Priyadarsini, D. K. Palit, and T. Mukherjee, Photochem Photobiol **72**, 625 (2007).

[10] B. A. Witika, P. A. Makoni, S. K. Matafwali, L. L. Mweetwa, G. C. Shandele, and R. B. Walker, Molecules **26**, 4244 (2021).

[11] C. F. Chignell, P. Bilskj, K. J. Reszka, A. G. Motten, R. H. Sik, and T. A. Dahl, Photochem Photobiol **59**, 295 (1994).

[12] Z. Chen, Y. Xia, S. Liao, Y. Huang, Y. Li, Y. He, Z. Tong, and B. Li, Food Chem **155**, 81 (2014).

[13] Y.-J. Wang, M.-H. Pan, A.-L. Cheng, L.-I. Lin, Y.-S. Ho, C.-Y. Hsieh, and J.-K. Lin, J Pharm Biomed Anal **15**, 1867 (1997).

[14] K. Gayathri, M. Bhaskaran, C. Selvam, and R. Thilagavathi, J Drug Deliv Sci Technol **82**, 104326 (2023).

[15] B. Boruah, P. M. Saikia, and R. K. Dutta, J Photochem Photobiol A Chem **245**, 18 (2012).

[16] A. Semalty, M. Semalty, M. S. M. Rawat, and F. Franceschi, Fitoterapia **81**, 306 (2010).

[17] Md. R. Chowdhury, R. M. Moshikur, R. Wakabayashi, Y. Tahara, N. Kamiya, M. Moniruzzaman, and M. Goto, Chemical Communications **55**, 7737 (2019).

[18] P. Anastas and N. Eghbali, Chem Soc Rev **39**, 301 (2010).

[19] T. Jeliński, M. Przybyłek, and P. Cysewski, Pharm Res **36**, 116 (2019).

[20] S. M. H. Sangtarashani, M. Rahmaninia, R. Behrooz, and A. Khosravani, J Environ Manage **270**, 110853 (2020).

[21] P. A. Shah, V. Chavda, D. Hirpara, V. S. Sharma, P. S. Shrivastav, and S. Kumar, J Mol Liq **390**, 123171 (2023).

[22] O. Söderman, K. L. Herrington, E. W. Kaler, and D. D. Miller, Langmuir **13**, 5531 (1997).

[23] M. Villeneuve, R. Ootsu, M. Ishiwata, and H. Nakahara, J Phys Chem B **110**, 17830 (2006).

[24] R. S. Atri, A. Sanchez-Fernandez, O. S. Hammond, I. Manasi, J. Doutch, J. P. Tellam, and K. J. Edler, Journal of Physical Chemistry B **124**, 6004 (2020).

[25] T. Arnold, A. J. Jackson, A. Sanchez-Fernandez, D. Magnone, A. E. Terry, and K. J. Edler, Langmuir **31**, 12894 (2015).

[26] A. Sanchez-Fernandez, K. J. Edler, T. Arnold, R. K. Heenan, L. Porcar, N. J. Terrill, A. E. Terry, and A. J. Jackson, Physical Chemistry Chemical Physics **18**, 14063 (2016).

[27] C. J. Drummond and C. Fong, Curr Opin Colloid Interface Sci **4**, 449 (1999).

[28] B. Patel, S. Singh, K. Parikh, V. Chavda, D. Ray, V. K. Aswal, and S. Kumar, J Mol Liq **363**, 119885 (2022).

[29] P. Sar, A. Ghosh, A. Scarso, and B. Saha, Research on Chemical Intermediates **45**, 6021 (2019).

[30] M. Maswal, A. H. Pandith, N. Islam, and A. A. Dar, J Solution Chem **42**, 1374 (2013).

[31] M. E. N. P. Ribeiro, C. L. de Moura, M. G. S. Vieira, N. V. Gramosa, C. Chaibundit, M. C. de Mattos, D. Attwood, S. G. Yeates, S. K. Nixon, and N. M. P. S. Ricardo, Int J Pharm **436**, 631 (2012).

[32] S.-H. Park and H.-K. Choi, Int J Pharm **321**, 35 (2006).

[33] T. Arnold, A. J. Jackson, A. Sanchez-Fernandez, D. Magnone, A. E. Terry, and K. J. Edler, Langmuir **31**, 12894 (2015).

[34] M. Pal, R. Rai, A. Yadav, R. Khanna, G. A. Baker, and S. Pandey, Langmuir **30**, 13191 (2014).

[35] M. Pal, R. K. Singh, and S. Pandey, ChemPhysChem **16**, 2538 (2015).

[36] I. Manasi, R. Schweins, K. Ma, and K. J. Edler, Langmuir (2023).

[37] Kabir-ud-Din, D. Sharma, Z. A. Khan, V. K. Aswal, and S. Kumar, J Colloid Interface Sci **302**, 315 (2006).

[38] S. Kumar, A. Z. Naqvi, and Kabir-ud-Din, Langmuir **16**, 5252 (2000).

[39] S. Manet, Y. Karpichev, D. Bassani, R. Kiagus-Ahmad, and R. Oda, Langmuir **26**, 10645 (2010).

[40] N. K. Bhatia, S. Kishor, N. Katyal, P. Gogoi, P. Narang, and S. Deep, RSC Adv **6**, 103275 (2016).

[41] B. Zheng and D. J. McClements, Molecules **25**, 2791 (2020).

[42] Y. Niu, D. Ke, Q. Yang, X. Wang, Z. Chen, X. An, and W. Shen, Food Chem **135**, 1377 (2012).

[43] R. Adhikary, P. J. Carlson, T. W. Kee, and J. W. Petrich, J Phys Chem B **114**, 2997 (2010).

[44] O. S. Hammond, D. T. Bowron, and K. J. Edler, Angewandte Chemie - International Edition **56**, 9782 (2017).

[45] B. Aboudiab, A. R. Tehrani-Bagha, and D. Patra, Colloids Surf A Physicochem Eng Asp **592**, 124602 (2020).

[46] S. Kaur, M. Kumari, and H. K. Kashyap, J Phys Chem B **124**, 10601 (2020).

[47] Z. Xi, Y. Fei, Y. Wang, Q. Lin, Q. Ke, G. Feng, and L. Xu, J Drug Deliv Sci Technol **83**, 104351 (2023).

[48] M. Sharma, U. Pal, M. Kumari, D. Bagchi, S. Rani, D. Mukherjee, A. Bera, S. K. Pal, T. Saha Dasgupta, and S. Mozumdar, J Photochem Photobiol A Chem **410**, 113164 (2021).

[49] J. Wang, Y. Zhao, C. Dou, H. Sun, P. Xu, K. Ye, J. Zhang, S. Jiang, F. Li, and Y. Wang, J Phys Chem B **111**, 5082 (2007).

[50] M. K. Banjare, R. Kurrey, T. Yadav, S. Sinha, M. L. Satnami, and K. K. Ghosh, J Mol Liq **241**, 622 (2017).

[51] S. Rani, D. Bagchi, U. Pal, M. Kumari, M. Sharma, A. Bera, J. Shabir, S. K. Pal, T. Saha-Dasgupta, and S. Mozumdar, ACS Omega **5**, 25582 (2020).