RESEARCH ARTICLE

Behavior of suspending and wetting agents in aqueous environment

Shashikant C Dhawale, Sudhir G Wadodkar[1], Avinash K Dorle[1]

Govt. College of Pharmacy, Karad, India, [1]Department of Pharmaceutical Sciences, RTM Nagpur University, Nagpur, India

This work describes the changes in viscosity, conductivity, pH, electrical conductivity, dielectric constant, zeta potential, UV, and IR spectra of aqueous solutions/dispersions of sodium carboxy methyl cellulose (CMC), Tween 80, and sodium lauryl sulphate (SLS) during aging at different temperatures. Significant reduction in viscosity ofh sodium CMC occurred during aging studies, while relatively small decrease in viscosity was seen with Tween 80 and SLS. Increment in specific conductivity was seen with aging of excipients. Significant increase of zeta potential was also seen with aging of samples. Concomitant shift in IR spectra of samples was observed with aging at 40°C.

Keywords: *Na CMC, SLS, suspending agents, Tween 80, stability, wetting agents*

INTRODUCTION

Sodium carboxy methyl cellulose (CMC), Tween 80, and sodium lauryl sulphate (SLS) are widely employed excipients in formulation of pharmaceutical suspensions.[1] Sodium CMC is employed in topical and parenteral products as it imparts viscosity.[2] It is also useful as suspending and flocculating agent. It is adsorbed onto drug molecules and forms bridging. It also contributes to smooth flow. Tween 80 and SLS are used as surfactants for wetting properties.[3-5] Although, the suspensions prepared by using these surfactants and polymers are common pharmaceutical formulations, the parameters by which the stability of such formulations may be assessed or predicted are not very clear.[3] Also uncertain is the fact that as to which changes taking place during storage may be considered as symptoms and which are causative factors. The present work is an attempt to get insight into this aspect.

MATERIALS AND METHODS

Materials

Sodium CMC (medium viscosity grade), Tween 80, and SLS were purchased from Loba Chemi, Mumbai. All other chemicals used were of analytical grade.

Method of preparation

1% concentration of sodium CMC, Tween 80, and SLS solutions were prepared in triple distilled deionized water and stored at 4±2°C, 30±2°C, and 40±2°C for a period of 90 days at atmospheric pressure. The solutions of these agents were examined for changes in viscosity, specific conductivity, pH, zeta potential, dielectric constant, UV visible, and IR spectroscopy.

Address for correspondence:
Dr. S C Dhawale, Department of Biopharmaceutics, Govt. College of Pharmacy, Karad, Maharashtra - 415 124, India.
E-mail: shashid15269@rediffmail.com

DOI: 10.4103/0973-8398.49167

Viscosity measurement

Viscosity measurement of aqueous solutions of samples stored at different temperatures was carried out at different intervals by using Brookfield viscometer model DVII (spindle S-18, RMM100). The viscosity measurements were carried out at 25°C.

Specific conductivity measurement

Specific conductivity (mmhos) was determined using Elico CM 180 conductivity meter at 25°C. The conductivity cell, having cell constant of 1.00 was used for the measurement of specific conductance. The conductivity meter was calibrated by using standard solution of 0.01 N KCl.

pH measurement

pH of solutions were recorded by using Systronics digital pH meter.

Zeta potential measurement

Electrokinetic potential[6] was periodically measured by using Zetameter 3.0. (Zeta-Meter Inc, Staunton, USA). The samples diluted with distilled water (1:50) were used for the analysis.

Measurement of dielectric constant

Dielectric constants of the solutions of the suspending and wetting agents were determined using Universal

Dielectrometer, Type OH 301, Redelkis co., Budapest II, Lukacs U.6., Hungary. (0.9 pF cell was used).

Table 1: Effect of ageing on viscosity of suspending and wetting agents

Name	Temp. (°C)	Viscosity in cp			
		Day 1	Day 30	Day 60	Day 90
Sodium CMC	4	51.8	49.0	47.8	48
	30		39.4	28.6	11.63
	40		11.63	7.82	2.40
Tween 80	4	2.10	2.12	2.05	2.06
	30		1.89	1.78	1.73
	40		1.66	1.29	1.05
Sodium lauryl sulphate	4	1.11	1.09	1.08	1.11
	30		1.09	1.10	1.09
	40		1.10	1.08	1.07

Table 2: Effect of ageing on conductivity of suspending and wetting agents

Name	Temp. (°C)	Conductivity in mmhos			
		Day 1	Day 30	Day 60	Day 90
Sodium CMC	4	1.64	1.66	1.66	1.74
	30		1.70	1.78	1.92
	40		1.79	1.86	2.03
Tween 80	4	0.08	0.09	0.12	0.11
	30		0.13	0.13	0.15
	40		0.12	0.14	0.16
Sodium lauryl sulphate	4	1.65	1.65	1.66	1.66
	30		1.69	1.70	1.71
	40		1.70	1.79	1.74

Table 3: Effect of ageing on pH of suspending and wetting agents

Name	Temp. (°C)	Day 1	Day 15	Day 30	Day 60	Day 90
Sodium CMC	4	8.87	8.66	8.51	8.28	8.08
	30		8.71	8.64	8.57	8.46
	40		8.74	8.68	8.52	8.34
Tween 80	4	6.80	6.6	6.14	5.24	3.67
	30		6.48	6.23	5.88	5.52
	40		6.82	6.60	6.47	5.76
Sodium lauryl sulphate	4	8.72	8.65	8.54	8.32	8.18
	30		8.68	8.68	8.51	8.33
	40		8.66	8.5	8.42	8.24

UV-visible and infrared spectroscopy

UV-1601, Shimadzu Japan and Fourier Transform Infra Red Spectrophotometer (FTIR-8101A) Shimadzu, Japan were used for UV-visible and IR spectroscopy, respectively.

RESULTS AND DISCUSSION

Viscosity measurement

Changes in relative viscosity of solutions of sodium CMC during storage over a period of 90 days are recorded in Table 1. Initial sharp reduction in viscosity occurred for the samples stored at 40°C. Relatively small change in viscosity of Tween 80 and SLS samples were seen. The reduction of viscosity may presumably be due to moderate degradation of polymer which may be due to chain cessation or depolymerization as explained by Zatz and co-workers.[7]

Conductivity measurement

Significant increase in specific conductivity of sodium CMC dispersion stored at 40°C was observed [Table 2]. SLS and Tween 80 solutions showed small increment in conductivity. The rise in conductivity could be presumably due to ionization of functional groups.[8-9] This is indicative of decomposition of solute or surfactants to yield some smaller molecules.

pH measurement

A moderate deviation in pH of solutions of these agents was observed [Table 3]. pH of sodium CMC was found to be decreased at 40 and 30°C with ageing. Greater decrease in pH was observed at 4°C. Reduction in pH of the samples of sodium CMC on storage indicates release of acidic groups due to its degradation.

Zeta potential measurement

Table 4 shows changes in ZP of aqueous dispersions of suspending and wetting agents during storage at different temperatures. Significant rise in ZP of sodium CMC samples were seen. This would be interpreted as change in nature of particles. Change in the environment may be expected when particles decomposing to yield small charged molecules or ions. Electrophoretic mobility of suspended particles depends upon the electrical charge on it, (known as zeta potential) as well as on the environment in which the particle is floating.[10]

Table 4: Effect of ageing on zeta potential of suspending and wetting agents

Name	Temp. (°C)	Zeta potential in mv			
		Day 1	Day 30	Day 60	Day 90
Sodium CMC	4	-33.89 ± 4.21	-34.75 ± 2.51	-36.95 ± 3.34	-37.64 ± 4.24
	30		-35.77 ± 5.23	-38.15 ± 2.41	-41.50 ± 3.16
	40		-49.76 ±2.32	-57.14 ± 4.10	-59.19 ± 2.74
Tween 80	4	-32.19 ± 4.21	-34.56 ± 5.16	-34.25 ± 2.61	-36.19 ± 1.15
	30		-33.25 ± 4.25	-36.48 ± 2.48	-38.24 ± 2.61
	40		-34.19 ± 2.46	-38.56 ± 4.67	-42.30 ± 3.75
Sodium lauryl sulphate	4	-23.80 ± 5.21	-25.65 ± 5.21	25.44 ± 2.46	-28.24 ± 3.31
	30		-24.80 ± 4.25	-27.80 ± 3.29	-29.76 ± 2.56
	40		-29.56 ± 3.26	-35.58 ± 3.26	-38.47 ± 4.67

ZP: zeta potential

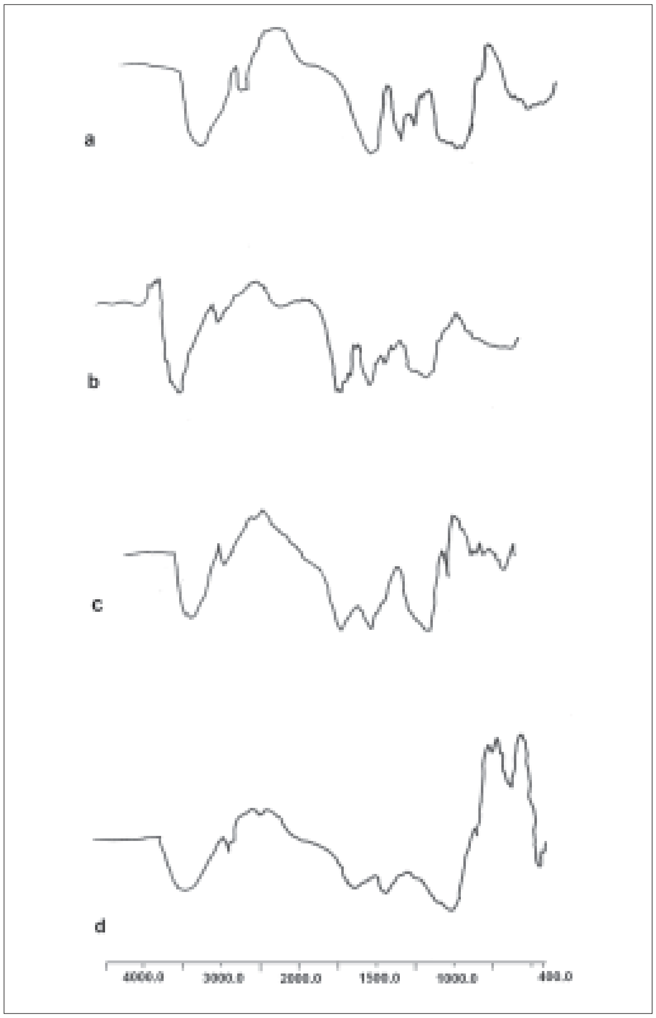

Figure 1: IR spectra of sodiun CMC (a): On day 1 of storage (control), (b) Stored at 30°C for 60 days, (c) Stored at 40°C for 60 days, (d) Stored at 40°C for 90 days

The significant enhancement in zeta potential was observed with suspending agents stored at elevated temperatures. The change in zeta potential at elevated temperature has direct influence on surface properties of particles and hence affects the stability of dispersion. Changes in the environment may be expected when particles decomposing to yield small charged molecules or ions.

Table 5: Dielectric constant of suspending and wetting agents during ageing

Name	Temp. (°C)	Day 1	Day 30	Day 60	Day 90
Sodium CMC	4	40.39	40.39	40.39	40.39
	30		40.89	42.93	42.93
	40		42.93	172	174.72
Tween 80	4	75.93	75.93	75.93	81.4
	30		81.4	83.88	86.56
	40		83.88	86.50	86.56
Sodium lauryl	4	83.5	83.50	83.50	83.5
sulphate	30		83.58	86.56	86.56
	40		83.88	86.56	94.58

Dielectric constant measurement

Significant rise in Dielectric constant (DEC) was observed for sodium CMC stored at 40°C, while no significant change was seen in Tween 80 samples [Table 5]. It may be relevant to assume that change in DEC of a system indicates change in nature of solute. There is a relationship between the DEC of a solvent and solubility of solute.[11] Every solute is soluble in a system of solvent to a maximum degree at one or two specific values of DEC. If reverse is assumed, the change in dielectric constant due to change in nature of solute may be understood. In other words, it may be relevant to assume that change in dielectric constant of a system indicates change in nature of solute.

UV visible IR spectroscopy

Degradation of suspending and wetting agents in aqueous solution was assessed through UV visible spectroscopy [Table 6] and IR spectroscopy. Change of either λ_{max} or absorbance was seen with aging of samples. Concomitant shift in IR spectrum was also observed with aging of samples. The absence of peak at 1327 in sodium CMC samples stored at 40°C for 60 and 90 days indicated the disappearance of hydroxyl group that revealed the formation of ester link. Peak at 721 disappeared in samples stored at 30°C for 60 days [Figure 1] indicated disappearance of C-C stretching which may be due to substitution. Peaks at 846, 951, 1109, 1250, 1358, and 1376 disappeared in samples of Tween 80 stored at 40°C for 60 days. Disappearance of above stated peaks may presumably due to the changes in C=O, -OH groups which may be due to substitution of decrease in alkylation of

Table 6: Effect of ageing on λ_{max} and absorbance of suspending and wetting agents

Name	Temp. (°C)	Day 1	Day 30 λ_{max}	Day 30 Absorbance	Day 60 λ_{max}	Day 60 Absorbance	Day 90 λ_{max}	Day 90 Absorbance
Sodium CMC	4	271.5-0.65	271.5	0.65	271.5	0.55	271.5	0.55
	30		271.5	0.45	271.5	0.40	271.5	0.39
	40		271.5	0.45	279.5	0.064	374.5	0.018
Tween 80	4	234.5-0.62	234.5	0.625	234.5	0.537	234.5	0.237
	30		234.5	0.537	234.5	0.360	254.5	0.331
	40		234.5	0.530	234.5	0.234	227	0.875
Sodium lauryl sulphate	4	270-0.046	270	0.046	270	0.045	270	0.045
	30		270	0.40	270.0	0.34	270	0.018
	40		320.0	0.12	320.0	0.16	320	0.22

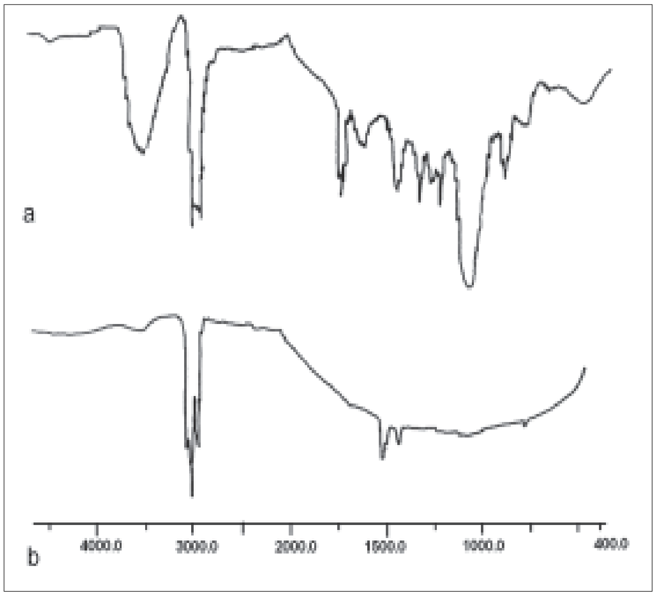

Figure 2: IR spectra of Tween 80 (a): On day 1 of storage (control), (b) Stored at 40°C for 60 days

surfactant [Figure 2]. Additional peak at 1260 for SLS samples stored at 40°C for 90 days indicate the formation of ester link and appearance of peak at 1500-1550 confirms [Figure 3].

CONCLUSION

Ageing of solutions of suspending agents was seen to bring about some characteristic changes. These changes included reduction in viscosity with parallel increase in conductivity and dielectric constant. This occurred in solutions of all the three suspending agents. There is also a moderate change in pH. Conductivity of any solution is a function of electrolytes or ions and change in ionic concentration is known to increase conductivity. The conductivity and dielectric constant often increases with thermal and electrical stress. These changes therefore are indicative of decomposition of solute or surfactants to yield some smaller molecules. This also finds support in the fact that there is concomitant shift in UV and IR spectra. It appears reasonable to suggest that the changes brought about due to decomposition of suspending agents and surfactants contribute to the instability of the suspensions. Therefore, the change in conductivity and dielectric constant, which are due to decomposition of surfactants, may be used as indicative parameters for predicting physical stability of the formulations. It should be interesting to examine as to whether these changes are symptoms of instability or the causative factors contributing to the instability of dispersion systems. The latter appears more likely.

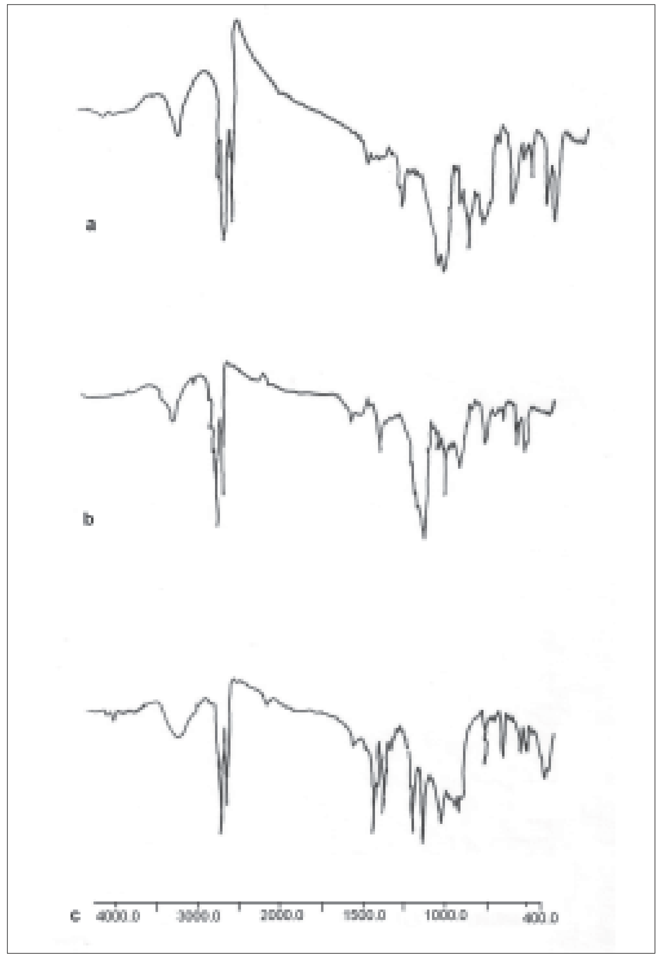

Figure 3: IR spectra of SLS (a): On day 1 of storage (control), (b) Stored at 40°C for 60 days, (c) Stored at 40°C for 90 days

REFERENCES

1. Hussain MA, August BJ, Maynn MB, Wu LS. Injectable suspensions for prolonged release of nalbuphine. Drug Dev Ind Pharm 1991;17:67-76.
2. Aniley W, Paul JW. Handbook of Pharmaceutical excipients. 2nd ed. A Joint publication of Amer Pharm Asso and the Pharm Society of Great Britain; 1994. p. 76-81.
3. Caramella C, Cocchi GA, Catellani P, Colomo U, La Manna A, The effect of some wetting agents on the characteristics of suspensions of sulphamethoxypyridazine and its N'- acetyl derivative. Es Da Boll Chim Farma 1976;115:658.
4. Kuprina NA, Blagovidova YA, Knizhnik AZ. Production and investigation of sulphamethoxine suspension with various stabilizers. Farmatsiya 1997;24:27-30.
5. Muzik M, Turan J, Stachova J. Effect of aerosil and Tween 80 on the stability of a suspension of zinc oxide and talc. Ceska a Slovenska Farmacie 1990;39:1-3.
6. Hunter RJ. Zeta potential in Colloid Science, Academic, New York: 1981.
7. Zatz JL, Berry J, Alderman DA. Pharmaceutical dosage forms, Disperse Systems. Vol. 2. Marcel Dekker Inc.; 1984. p. 75.
8. Zatz JI, Ip BK. Stabilization of oil-in-water emulsions by gums. J Soc Cosmet Chem 1986;37:329-50.
9. Zatz JL, Knapp K. Viscosity of xanthan gum solutions at low shear rates. J Pharm Sci 1984;73:468-71.
10. Calcinari R. Zeta potential and its importance in pharmaceutical technology. Farmaco Ed Prat 1970;25:24-38.
11. Carvalho FD, Nogueira PL, Ramos MR, Cancelo CA. Determination of the dielectric requirement and the solubility parameter of 1,4-benzodiazepines. Anales de la Real Academia de Farmacia (Spain) 1990;56:493-501.

Source of Support: Nil, **Conflict of Interest:** None declared.