Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(7):818-825

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Rheological profiling of a hydrogel drug delivery vehicle

Kannissery Pramod[1]*, Salim Shanavas[2] and Jomon Nadackal Baby[1]

[1]*College of Pharmaceutical Sciences, Govt. Medical College, Thiruvananthapuram, Kerala, India*
[2]*Starch Characterization Laboratory, Division of Crop Utilization, Central Tuber Crops Research Institute, Sreekariyam, Thiruvananthapuram, Kerala, India*

ABSTRACT

Rheology refers to the study of flow and deformation of materials. Rotational and oscillation experiments are most important methods for rheological profiling of polymers. The objective of the present study was to unveil the rheological profile of Carbopol 940 hydrogel, at a concentration of 1%w/w, by subjecting to flow, frequency sweep, creep recovery and thixotropy measurements. From the flow curve measurements it was observed that shear rate has influence on viscosity and shear stress. Carbopol hydrogel behaved as a viscoplastic or yield stress fluid. Higher values for loss modulus than storage modulus from frequency sweep experiments indicated that elastic component is less is prevailing in the hydrogel than the elastic component. Complex viscosity was found to decrease on increasing frequency and thus a pseudoplastic behaviour of hydrogel was confirmed. From the creep recovery plot it was inferred that the hydrogel sample behaves as viscous material at the applied stress. The hydrogel behaved as an ideal viscous material. High structure recovery ratio and hysteresis area obtained demonstrated a good thixotropic property for the hydrogel. Future studies with varying test parameters and conditions would be useful in further elucidating the mechanistic properties of Carbopol hydrogel under stress.

Keywords: Rheology, Flow curve, Frequency sweep, Creep recovery, Thixotropy

---

INTRODUCTION

Rheology refers to the study of flow and deformation of materials under the influence of external stress. Rotational and oscillation experiments are most important methods for rheological profiling of polymers. Rheology modifiers are very beneficial in drug delivery applications and are extensively used. They can control drug release, resist stress caused by body or skin movements and adopt shape of application area [1]. Carbomers are polymers and consists of repeated units of acrylic acid and Carbopol is a branded carbomer. Carbopol 940 is a cross-linked polyacrylate polymer and finds its major application in transdermal and topical drug delivery systems. Carbopol 940 polymers have been well reported at a concentration of 1% w/w in hydrogel based drug delivery systems [2, 3]. Extensive rheological characterization is needed for identification of performance guaranteed products and also to tailor drug delivery systems with desired rheological characteristics. Towards these goals, in the present study, efforts were taken in unveiling the rheological profile of Carbopol 940 hydrogel by subjecting to flow, frequency sweep, creep recovery and thixotropy measurements.

EXPERIMENTAL SECTION

Materials
Carbopol 940 was a gift sample from Noveon Corporation, Cleveland, OH, USA. HPLC-grade water (Merck Mumbai, India) was used for the study.

Preparation of Carbopol hydrogel
Carbopol hydrogel was prepared by dispersing 1% w/w Carbopol 940 in water and subsequently neutralizing the Carbopol dispersion using triethanolamine. In order to minimize entrapment of air bubbles in the gel, the Carbopol dispersion was allowed to stand before addition of triethanolamine. During neutralization, the sample was gently stirred to avoid inclusion of air bubbles. The hydrogel sample was stored for 120 h at room temperature for equilibration before rheological studies [1].

Rheological characterization
Anton Paar Physica MCR 51 rheometer(Anton Paar, Graz, Austria) was used for the rheological profiling of hydrogel. RheoPlus software (Anton Paar, Graz, Austria) was employed for instrument handling and data analysis. All the experiments were carried out at a set temperature of 25ºC unless otherwise mentioned. The parallel plate system employed for the rheological studies was having a diameter of 19.957 mm and the gap was 1 mm [4].

Flow curve
The flow curve was obtained for hydrogel sample by applying a shear rate of 0.1 to 100 s^{-1}. Shear stress and viscosity were measured with the change in shear rate. The yield stress value of the hydrogel from its flow curve was determined using RheoPlus software.

Frequency sweep
Frequency sweep test was carried out on the hydrogel using a parallel plate system. The linear viscoelastic region of the sample was determined by strain sweep test prior to conducting the frequency sweep test. Measurements were conducted at a constant temperature of 30ºC in a frequency range of 0.1-10 Hz and 1% strain. The gel was covered with a thin layer of silicon oil to serve the purpose of avoiding evaporation of water during frequency sweep test. Storage modulus, loss modulus, complex modulus and complex viscosity were recorded.

Creep recovery
The test involved application of constant stress to the hydrogel sample and measurement of the corresponding strain is measured as a function of time [5]. In a shear creep recovery test the ability of a sample to return to its original consistency when the applied stress is evaluated. This ability is usually expressed in terms of total recoverable deformation (γ_R). A two step method was employed in creep recovery measurements. In the first step, a constant shear stress of 100 Pa was applied for 300 s. In the second step, the shear stress was completely removed and then the strain was further measured for 600 s. During this stage the net shear stress available on the sample was 0 Pa. The creep recovery data was also expressed as a creep compliance function. Here the slope of the creep curve gives the ratio of stress to viscosity of the sample. Thus it was possible to determine the viscosity of the sample at the applied stress from the creep compliance data.

Thixotropy
The study was carried out in 3 steps. In the first step, a constant shear rate of 1 s^{-1} was applied for 50 s. In the second step, the shear rate was changed to 100 s^{-1} for 50 s. In the third step, the shear rate was brought down to 1 s^{-1} for 300 s. The purpose of first step was to attain a constant viscosity by applying a lowest possible shear. In the second step the high shear rate applied for 50 s causes a breakdown of internal structure of the hydrogel. The third step of immediate reduction of shear rate to the possible lowest value provides an opportunity for rebuilding or recovery of the internal structure of the hydrogel.

RESULTS AND DISCUSSION

Carbopol hydrogel was prepared and extensively characterized for rheological behaviour.

Rheological characterization of Carbopol gel

Flow curve

From the flow curve measurements the viscosity and shear stress properties of Carbopol gel were studied. Shear rate was found to have influence on viscosity (Fig.1) and shear stress (Fig. 2). A negative slope in Fig. 1 indicated a destruction of internal structure by overcoming the internal forces. Thus a shear thinning process was observed. The slope of the plot can be utilized to measure the microstructural attractive forces present in Carbopol hydrogel. No plateau phase was observed in the plot. First Newtonian plateau which is a measure of the volume fraction of the structure was not visible for the gel in the applied shear rate regime. First Newtonian plateau is expected to be observed at low shear rates. The first Newtonian plateau may be missed out in this study due to the fact that it might be observed for Carbopol hydrogel below a shear rate value of 0.1 s^{-1}. Extrapolation of the data to zero-shear value is also possible from the data. Thus we could correlate the flow property with molecular weight of the polymer used. Further it could be applied as a parameter to monitor batch-to-batch variations in hydrogel manufacturing. Absence of a second Newtonian plateau indicated absence of a complete loss of internal forces. Thus it could be assumed that the gel still retains its internal structure in the applied shear rate regime.

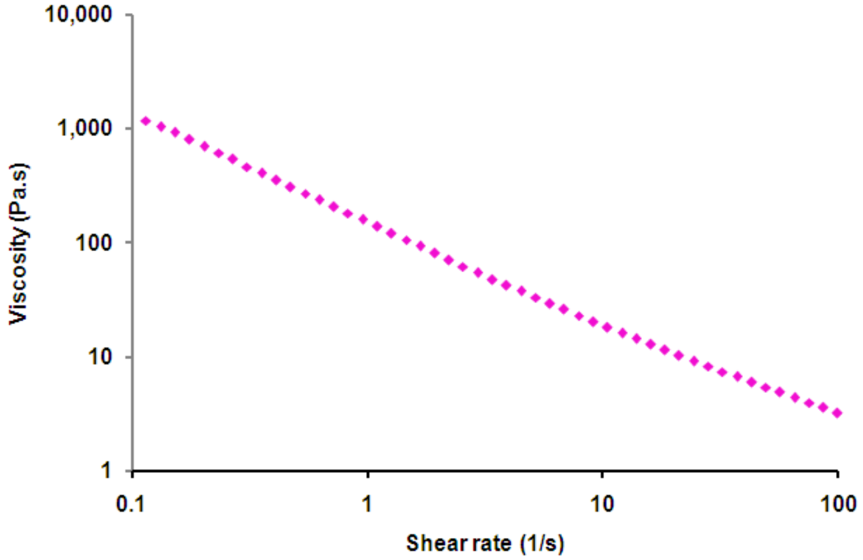

Figure 1: Viscosity versus shear rate plot for Carbopol hydrogel

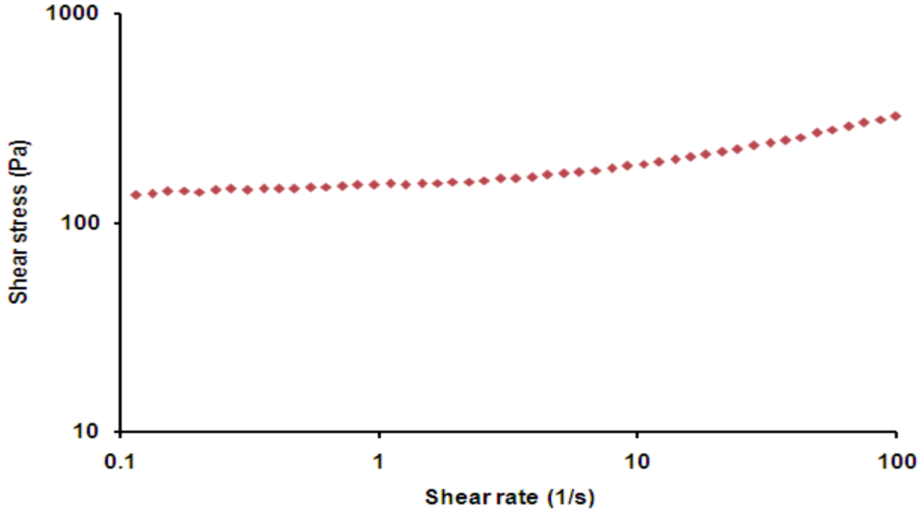

Figure 2: Shear stress versus shear rate plot for Carbopol hydrogel

A plot of shear stress versus shear rate is shown in Fig 2. From the plot it could be observed that Carbopol hydrogel behaves as a viscoplastic or yield stress fluid. It has been reported that Carbopol polymer chains undergo alignment in the direction of flow [1,6,7] and this could be the reason for dependence of shear stress on shear rate. But a notable dependence was observed only at higher shear rate values.

Frequency sweep

The viscoelastic nature of the gel can be studied by frequency sweep tests. The presence of entanglements in polymers may provide rigidity or elasticity for their gel. It is established that more the elasticity higher is the storage modulus (G') for that gel. Storage modulus can be considered as the energy stored per unit volume. In contrast, loss modulus is used as a parameter for expressing the extent of viscous component of gels [8].

Fig. 3a shows the plots of G', G" and complex viscosity of the gel against frequency respectively. It was observed that the storage modulus is less than loss modulus for the hydrogel. This result was indicative of the fact that elastic component is less is prevailing in the hydrogel than the elastic component. Complex viscosity was found to decrease on increasing frequency values (Fig 3b) and thus it could be inferred that Carbopol hydrogel exhibits pseudoplastic behaviour [9].

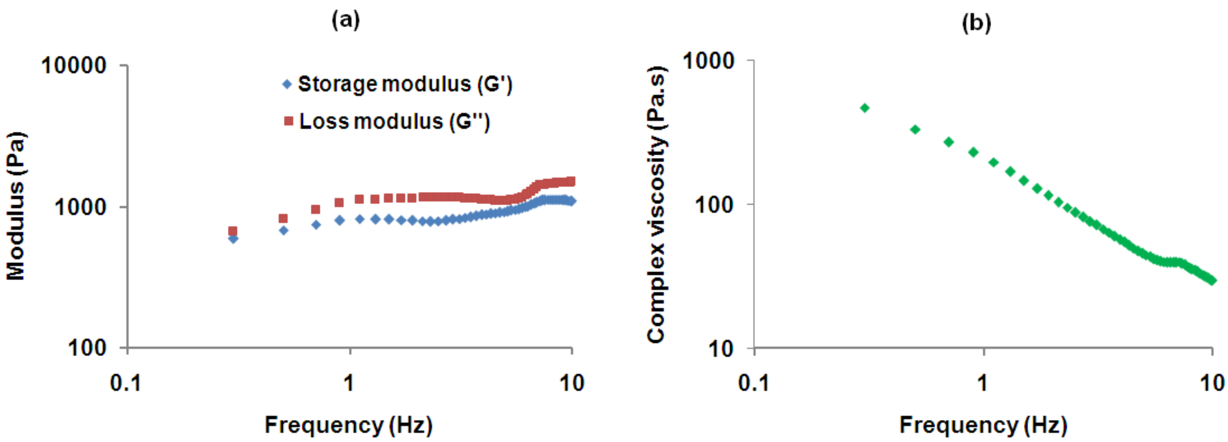

Figure 3: Frequency sweep plots (mechanical spectra) for Carbopol hydrogel

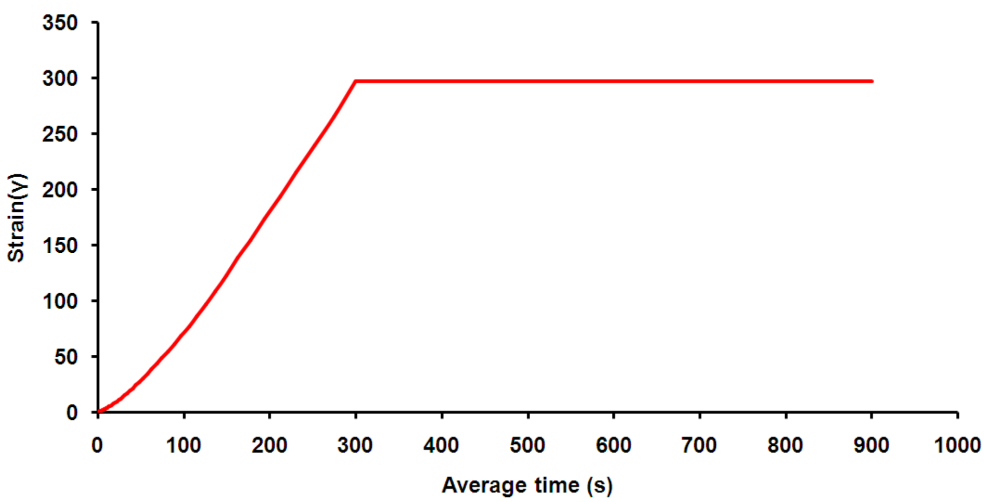

Figure 4: Strain versus average time plot for creep recovery studies

Creep recovery

In the creep test, the hydrogel was subjected to a constant shear stress and measurement of time dependent strain was carried out. The elasticity of the gel sample can be understood by measuring the total recoverable deformation (γ_R). From the creep recovery plot (Fig. 4) it can be inferred that the hydrogel sample behaves as viscous material at the applied stress.

Fig. 5 shows the typical creep and creep recovery plots of ideal elastic (Fig. 5a), ideal viscous (Fig. 5b) and real viscoelastic materials (Fig. 5c). In ideal elastic materials there is a 100% recovery. In the case of ideal viscous materials there will be no recovery and starts to flow. In the case of viscoelastic materials there is an elastic component (γ_E) and a viscous component (γ_V). In all cases permanent deformation of viscous component occurs in viscoelastic materials while the elastic component recovers after a lag time. In the present case with Carbopol hydrogel, the value of γ_R was zero as non-recoverable deformation (γ_{NR}) alone was observed for the sample. Thus from this data it can be assumed that hydrogel sample behaves as viscous sample at the applied stress. This might have happened due to the fact that viscous forces are outweighing the elastic forces in the gel. The recoverable deformation corresponds to elasticity and non-recoverable deformation corresponds to viscosity of hydrogel. The results observed supported data from frequency sweep studies where storage modulus was lower than loss modulus.

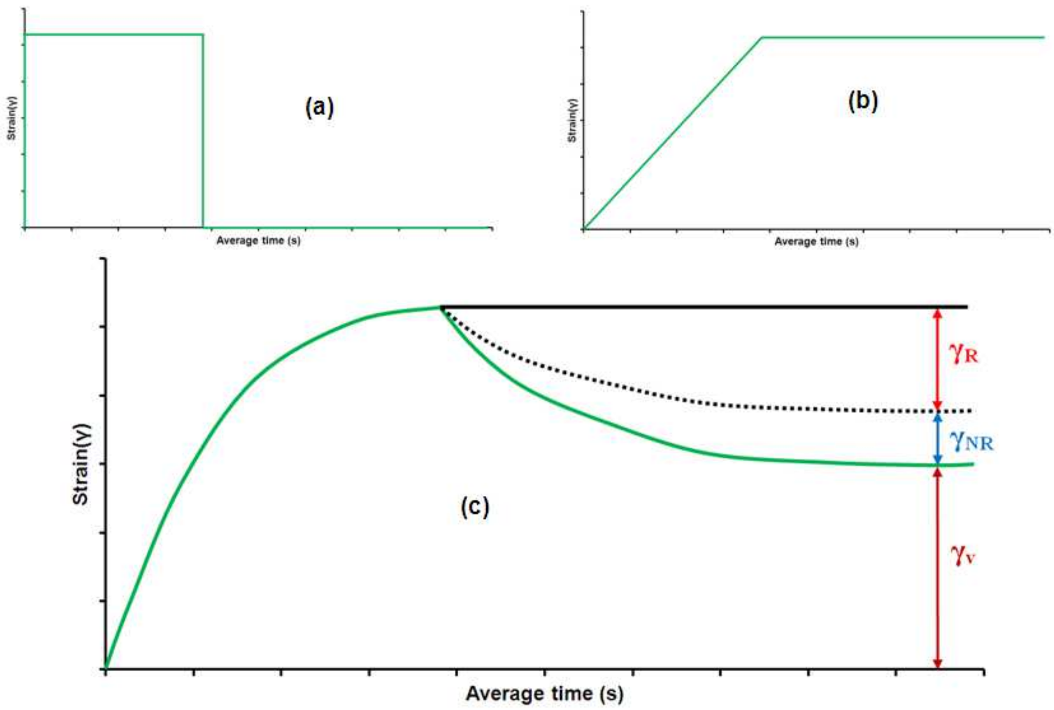

Figure 5: Creep and creep recovery plots (a) ideal elastic (b) ideal viscous (c) real viscoelastic

Fig. 6 shows the plot of creep compliance for the gel against average time. A higher creep compliance value corresponds to a decreased elasticity. The viscosity of the Carbopol gel (at an applied shear stress of 100 Pa) was determined to be 109.20 Pa.s from the slope of the plot.

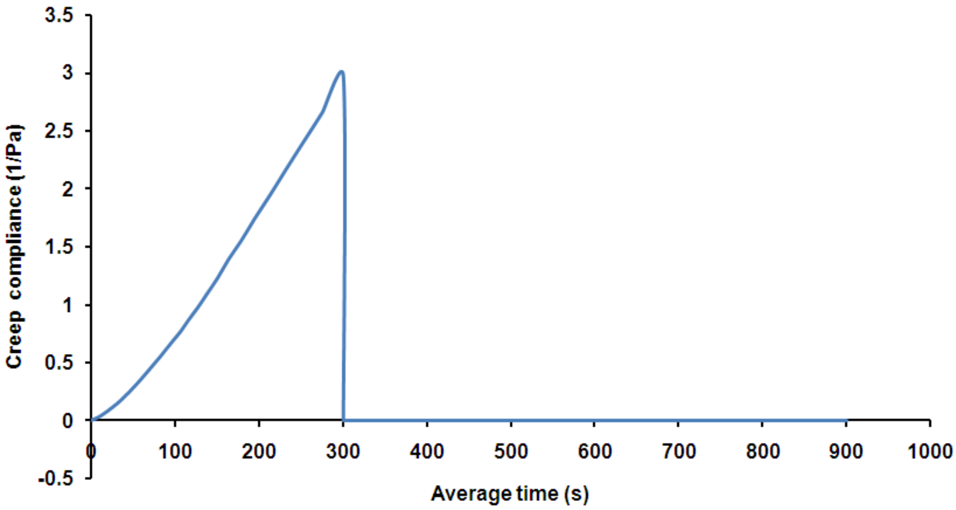

Figure 6: Creep compliance versus time plot

Thixotropy

When triethanolamine is added to an aqueous dispersion of Carbopol, uncoiling of polymer molecules occur. This results in molecular extensions and thus polymer swelling. The rigidity of the gel structure obtained for Carbopol gels are attributed to the electrostatic repulsion of the carboxyl ($-COO^-$) groups present on the extended chains [6]. The rigidity of the gels formed could get affected as a result of internal structural breakdown when subjected to high shear. Fig. 7 shows the thixotropy plot for the Carbopol gel. Thixotropic gels undergo a slow viscosity build after removal of an applied shear. Thus thixotropy studies can be utilized for the understanding of structural rebuilding of gels.

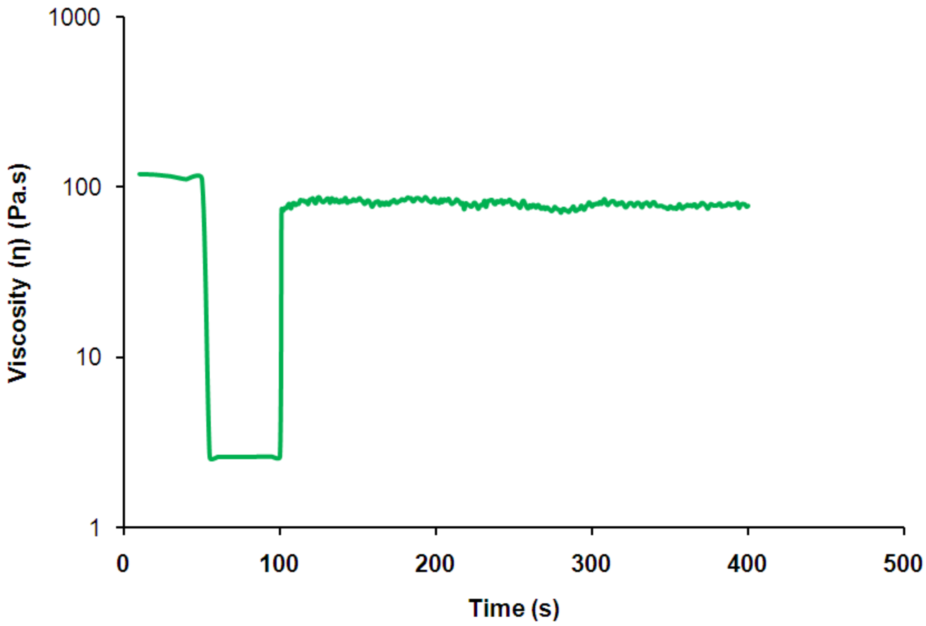

Figure 7: Thixotropy plot for Carbopol hydrogel

Fig. 8 provides an illustration of possible mechanistic explanation for the thixotropic response of the Carbopol hydrogel. In the illustration Carbopol polymer molecules are pictorially represented by short curvy lines in red colour. The structural changes can be predicted from the thixotropy plot obtained for the Carbopol hydrogel. In this study the first step involves applying a constant shear rate of 1 s^{-1} for 50 s. From the plot (Fig. 7) it can be understood that the applied shear was not sufficient to produce a structural breakdown of Carbopol gel (Fig. 8a). The sample rigidity or elasticity is sufficient to resist this change. But on subsequent changing of the shear rate to 100 s^{-1} for 50 s produced drastic change in the thixotropy curve. The applied shear prevailed over the forces imparting rigidity to Carbopol gel and thus a drastic decrease in gel viscosity was noted (Fig. 8b). During the third step of reduction of shear to 1 s^{-1} for 300 s, a perfectly thixotropic material is expected to return to the viscosity value. From the plot it can be assumed that Carbopol gel exhibits sufficient thixotropic property as its viscosity return to more or less original value (Fig. 8c). High structure recovery ratio (70.62% after 60 seconds) and hysteresis area (18189.2 Pa s^{-1}) obtained demonstrated a good thixotropic property for the hydrogel [10-12].

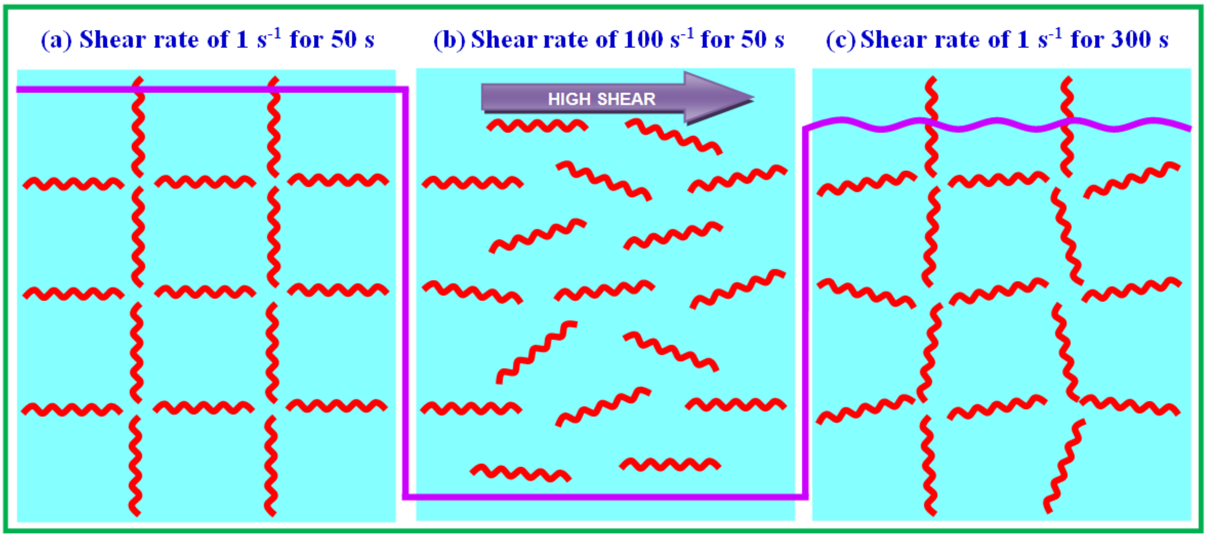

Figure 8: Illustration of possible mechanism of thixotropy in Carbopol hydrogel

CONCLUSION

Detailed rheological profiling of Carbopol 940 hydrogel at a concentration of 1%w/w was carried out. Flow curve measurements were conducted to study the viscosity and shear stress properties of Carbopol hydrogel and it was observed that shear rate has influence on viscosity and shear stress. Carbopol hydrogel behaved as a viscoplastic or yield stress fluid. The data from frequency sweep experiments established psuedoplastic behaviour of Carbopol hydrogel. The storage modulus was less than loss modulus for the hydrogel. Creep recovery studies established the viscous nature of hydrogel at the applied and no viscoelastic property was noted. A notable thixotropic behavior was observed in the Carbopol hydrogel during rheological characterization. The present study unveiling many of the rheological aspects of Carbopol hydrogel. Application of various rheological test methods also helped in identifying different rheological properties. The study results obtained could be employed in developing Carbopol hydrogel drug delivery systems with tailored properties. Future studies with varying test parameters and conditions could further light up the path in rheological profiling of Carbopol hydrogel.

REFERENCES

[1] MT Islam; N Rodríguez-Hornedo; S Ciotti; C Ackermann, *Pharm Res.*, **2004**, 21, 1192-1199.
[2] R Sareen; S Kumar; GD Gupta, *Curr. Drug Deliv.*, **2011**, 8(4), 407-415.
[3] G Misal, G Dixit, V Gulkari. *Indian J. Nat. Prod. Resour.*, **2012**, 3(4), 501-505.
[4] K Pramod; S Shanavas; SH Ansari; J Ali, *Adv. Sci. Lett.*, **2012,** 10, 1-13.
[5] K Baroudi; N Silikas; DC Watts, *Eur. J. Oral. Sci.*, **2007,** 115(6), 517-521.
[6] BW Barry; MC Meyer, *Int. J. Pharm.*, **1979,** 2, 1-25.
[7] BW Barry; MC Meyer, *Int. J. Pharm.*, **1979,** 2, 27-40.
[8] J Kim; J Song; E Lee; S Park, *Colloid. Polym. Sci.*, **2003,** 281, 614–623.
[9] IB Lee; HH Son, CM Um, *Dent. Mater.*, **2003,** 19(4), 298-307.
[10] CH Lee; V Moturi; Y Lee, *J. Control. Release*, **2009,** 136, 88-98.
[11] E Armelin; M Marti; E Rude; J Labanda; J Llorens; C Aleman, *Progr. Org. Coating*, **2006,** 57, 229–235.

[12] K Pramod; S Shanavas; SH Ansari; J Ali, *J. Sol-Gel Sci. Technol.*, **2011,** 61, 161-168.