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Pluronic gels for nasal delivery of Vitamin B_{12}. Part I: Preformulation study

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Abstract

Thermoreversible nasal gels of Vitamin B_{12} using pluronic PF 127 were aimed to improve absorption and patient compliance. In the present research work, effects of Vitamin B_{12} and gel additives, viz. PF concentration, osmolarity, polyethylene glycol (PEG 15000) on thermodynamic properties of phase transitions at gelation (T_1) and gel melting (T_2) is reported. Aqueous PF 127 gels prepared by cold method containing pluronic (20–24%, w/w), vitamin, sorbitol, PEG, and benzalkonium chloride. T_1 decreases and T_2 increases with vitamin and PF concentration. Gelation range narrows with sorbitol and PEG. Suppression of T_2 is significantly higher than T_1 with both the additives. The linearity was observed only for semilogarithmic plot of PF concentration and $1/T_2$ for sorbitol and PEG, which reveals significant interaction of both at gel melting. Enthalpy of both transitions remains unchanged with vitamin indicating no interaction with polymer. Benzalkonium chloride decreased gelation onset temperature. Thermodynamic properties of PF 127 gels are significantly altered with polymer concentration and water-soluble formulation additives.

Keywords: Poloxamer gel; Nasal; Vitamin B_{12}; Additives; Gelation and gel melting

1. Introduction

Transnasal administration of large number of drugs such as, gentamicin, nafarelin acetate, ergotamine tartarate, etc. results in blood levels comparable to intravenous route (Rubinstein, 1983; Chien, 1985; Hussain et al., 1984). However, short nasal residence time of drug formulation result in high interindividual variability in absorption profile. Attempts have been made to improve nasal residence time and bioavailability by designing bioadhesive swelling microspheres, liposomes, and erythrocytes-based bioadhesive systems (Illum et al., 1988; Bjork and Edman, 1988; Iwanaga et al., 2000; Vyas et al., 1993).

Surface active block copolymers of polyoxyethylene-polyoxypropylene (Pluronics) are widely used in medical, pharmaceutical, and cosmetic systems (Schmolka, 1991). Pluronic PF 127 or polaxomer 407 is a ABA type block copolymer containing 70% of polyoxyethylene (PEO) fraction with a molecular weight of 12,500, and a general formula:

$$\mathrm{H\,(O\text{-}CH_2\text{-}CH_2)_a(\,O\text{-}CH\text{-}CH_2)_b\,(O\text{-}CH_2\text{-}CH_2)_a\,OH}$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad \mathrm{CH_3}$$

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Pluronics are available in wide range of molecular weights and their properties depend on the extent of hydrophilic/lipophilic regions. The high solubilizing capacity and non-toxic properties of PF 127 make it suitable for drug delivery. Pluronic PF 127 is more soluble in cold water than hot water. The cold solution process has been attributed to excessive hydrogen bonding between water molecule and ethereal oxygen of the polymer. The concentrated solutions (20–30%) are transformed from low viscosity transparent solutions at 5 °C to solid gels on heating to body temperatures. The temperature-dependent gelling process is micellar in nature, being constructed from cubic orientation of micellar subunits (BASF Wyandotte, 1997). The micellar mode of association has been useful as drug delivery systems (Collectt and Davies, 1984). The reversal thermal gelation exhibited by PF 127 aqueous solutions (20–35%, w/w) has been used as drug delivery system for ophthalmic (Desai and Blanchard, 1998), parenteral (Pec et al., 1992; Katakam et al., 1997a), rectal (Morikawa et al., 1987; Wang and Johnston, 1995), and percutaneous use (Suh et al., 1997). Stratton et al. (1997) has reported the improved stability of proteins and hence their complete recovery of activity in PF gels matrix.

Oral absorption of Vitamin B_{12} involves its complexation with intrinsic factor. The process is complicated and impaired oral absorption cause difficulty in the treatment of pernicious anemia (Monto and Rebuck, 1954; Conely et al., 1951). The development of thermoreversible nasal gels of Vitamin B_{12} using pluronic PF 127 is aimed to improve systemic absorption and ease of administration. Aqueous PF 127 gels show temperature-dependent gelation and gel melting. Number of drugs and formulation additives affect the thermodynamic and rheological properties of the gels. The normal gelation process has been studied extensively (Schmolka, 1972). The rheological and thermal characterization of reverse gelation process has not much investigated. The research work is undertaken to elucidate the effect of pluronic concentration, presence of drug, effect of osmotic agent (sorbitol) and gel point enhancer (PEG 1500) on gelation and gel melting temperature and enthalpy of phase transitions. Effect of concentration of PF and benzalkonium chloride (BKC) on rheological properties of gels is also investigated. Such properties are important in understanding the stability and behavior of pluronic gel as nasal drug delivery systems.

2. Materials and methods

2.1. Materials

Pluronic PF 127 was a gift sample from BASF Corporation, New Jersey. Vitamin B_{12} was kindly supplied by Brihans Labs, Pune, India. PEG 15000 and sorbitol of extra pure grade were purchased from E. Merk, India Ltd. Benzalkonium chloride was procured from Loba Chemicals, Mumbai, India. All other chemicals were of research grade and were used without further purification.

2.2. Preparation of PF 127 gels

Pluronic gels were prepared by cold technique described by Schmolka (1991). A weighed amount of PF 127 (20, 22 and 24%, w/w) was slowly added to 35 ml of water (at 10 °C) in a beaker with continuos magnetic stirring. Aqueous PF 127 mixture was kept overnight at 4 °C and weight was adjusted to 50 g with deionised water. Gels containing 0.52% (w/w) of Vitamin B_{12} and 20, 22, and 24% (w/w) of PF 127 were prepared separately, where 260 mg vitamin was added to water before PF 127. Gels with sorbitol (0.5, 1.0, and 1.5 M) and PEG 15000 (0.6, 1.1, and 1.6%, w/w) were prepared with a slight adaptation of the method. The water-soluble solutes were dissolved prior to PF 127 addition to optimize the mixing. Similarly, weighed quantity of benzalkonium chloride was added to aqueous phase to obtain 0, 0.005, 0.05, 0.1, 0.125, and 0.25% (w/v) of preservative in PF 127 gels containing 20% (w/w) polymer. All gels were stored at cold temperature and evaluated within 48 h.

2.3. Evaluation of gels

2.3.1. Gelation and gel melting

Gelation and gel melting was assessed using a modification of Miller and Donavan (1982) technique. A 2 ml aliquot of gel was transferred to test tubes, immersed in a water bath at 4 °C and sealed with aluminum foil. The temperature of water circulation bath (Haake C25 P) was increased in increments of 1 °C

and left to equilibrate for 5 min at each new setting. The samples were then examined for gelation, which was said to have occurred when the meniscus would no longer move upon tilting through 90°. The gel melting temperature, a critical temperature when the gel starts flowing upon tilting through 90° was recorded.

2.3.2. Enthalpy of gelation and gel melting

The enthalpy of gelation (ΔH°_{gel}) and gel melting (ΔH°_{mel}) for plain PF 127 gels and for gels with various formulation additives were calculated using a methodology described by Eldridge and Ferry (1954) and Pandit and Kisaka (1996). Enthalpy of transition was obtained from the semi-log plot of PF concentration (Lm C) versus reciprocal of transition temperature using following equations:

$$\mathrm{lm}\, C = \frac{\Delta H^{\circ}_{gel}}{RT_1} + \text{constant} \quad (1)$$

$$\mathrm{lm}\, C = \frac{\Delta H^{\circ}_{mel}}{RT_2} + \text{constant} \quad (2)$$

where, ΔH°_{gel} and ΔH°_{mel} are enthalpy of gelation and gel melting, respectively, T_1 and T_2 represent gelation and gel melting temperature, respectively.

2.3.3. Viscosity studies

Viscosity of plain PF 127 gels, and gels containing BKC were measured using the Brookfield's LVDV II+ model. The gel sample (about 10 ml) at low temperature was placed in small sample adapter. The temperature of the sample was raised above 40 °C using circulation bath (Haake C25P model). The sample was allowed to cool and the viscosity at various temperatures was recorded using suitable spindle.

3. Results

3.1. Effect of formulation additives on gelation process

Gel transition temperatures for plain PF 127 gels were observed for the concentration range of 20–24% (w/w) polymer. The decrease in gelation temperature (T_1) and increase in gel melting temperature (T_2) were dependent on the concentration of PF 127. In the preliminary studies the decrease in T_1 was significantly high and at higher concentration of the polymer (40%, w/w) gelation occurred at refrigeration temperatures. The gel melting temperatures were outside the instrumental range (100 °C). The concentration of Vitamin B_{12} was kept at 0.52% (w/w), which is the strength of formulation. The presence of Vitamin B_{12} lowered the gelation temperature, whereas the melting temperature increased. Thus, gelation range broadens with the concentration of the polymer and in presence of Vitamin B_{12} (Fig. 1).

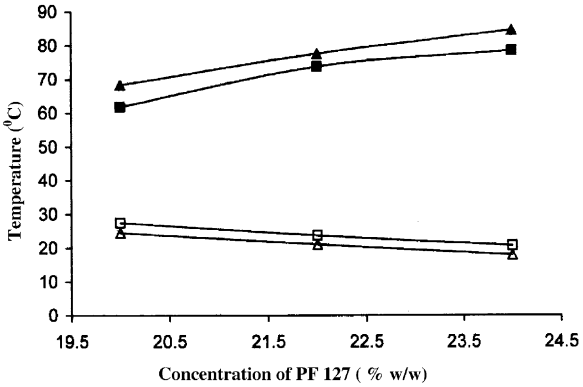

Fig. 1. Effect of concentration of PF 127 and presence of Vitamin B_{12} on T_1 and T_2 (△, T_1 B_{12}; ▲, T_2 B_{12}; □, T_1 plain; ■, T_2 plain).

The effect of sorbitol used as an osmotic agent in nasal gels was studied at three levels, 0.5, 1 and 1.5 M. The gel formation and gel melting temperature decreases with the concentration of sorbitol at constant PF 127 concentration. The same trend in the change in gelation process was observed at all the three concentrations of PF 127. The slope of the transition lines decreases with increase in the sorbitol concentration indicating that the effect of concentration of PF 127 is nullified at the higher concentration of sorbitol. The extent of suppression of T_2 is significantly higher as compared to the suppression of T_1. The effect was very pronounced at 1.5 M sorbitol concentration and the gel melting occurs at a temperature below room temperature. Therefore, gelation range is significantly narrowed (as shown in Fig. 2) and shifts to lower temperatures due to presence of sorbitol.

PEG 15000 is used as gel point enhancer in nasal gels. The effect of concentration of PEG 15000 on the gelation temperature and gel melting temperature

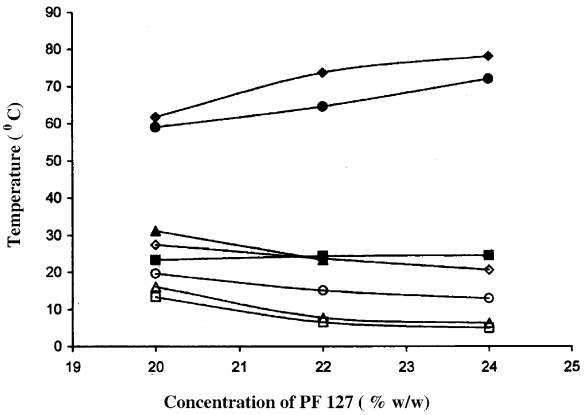

Fig. 2. Gel range of PF 127—effect of sorbitol concentration (□, T_1 1.5 M; ■, T_2 1.5 M; △, T_1 1 M; ▲, T_2 1 M; ○, T_1 0.5 M; ●, T_2 0.5 M; ◇, T_1 plain; ◆, T_2 plain).

of PF 127 solution was investigated in the range of 0–1.6% (w/w). Addition of PEG caused an increase in sol- gel transition temperature, in contrast to the effect of increased PF 127 concentration in plain gels and presence of Vitamin B_{12}. The linear increase in gelation temperature was observed with the PEG 15000 concentration. Similar effect was observed in decrease in gel melting temperature with PEG 15000 concentration. The simultaneous effect of PF and PEG 15000 concentrations on gelation range is shown in Fig. 3. Similar to the effect of sorbitol, PEG also narrows the gel range of PF 127 gels. The effect was observed even at higher concentration of PF 127.

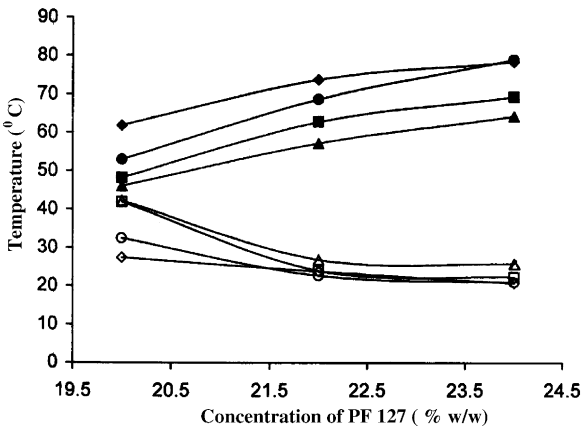

Fig. 3. Gel range of PF 127—effect of PEG 15000 concentration (△, T_1 1.6%; ▲, T_2 1.6%; □, T_1 1.1%; ■, T_2 1.1%; ○, T_1 0.6%; ●, T_2 0.6%; ◇, T_1 plain; ◆, T_2 plain).

Table 1
Effect of various additives on enthalpies of gel melting of PF 127 gels

S. No.	Additive	ΔH°_{mel} (kcal/mol)
1	Plain PF 127	−3.097
2	Vitamin B_{12}	−3.506
3	Sorbitol 0.5 M	−4.049
4	Sorbitol 1.0 M	−1.795
5	Sorbitol 1.5 M	−0.28
6	PEG 0.6%	−2.014
7	PEG 1.1%	−2.311
8	PEG 1.6%	−2.714

3.2. Effect of additives on enthalpy of gelation and gel melting

The enthalpy of both the transitions, at gelation and gel melting, was obtained for plain PF 127 gels (20, 22, and 24%, w/w) and gels containing Vitamin B_{12}, sorbitol and PEG 15000 from the semi-log plot of polymer concentration versus reciprocal of transition temperature. The enthalpy of gelation and gel melting for various gels under investigation are reported in Table 1. The enthalpy change of plain PF 127 gels was in agreement with the previous reported values (Tung, 1994). Though Vitamin B_{12} broadens the gel range, the semi-logarithmic plots of both the transition temperatures in presence of Vitamin B_{12} were parallel to that of the plain PF 127. This implies that enthalpies of both the transitions remain unchanged in presence of Vitamin B_{12}. In presence of sorbitol as well as PEG, a linear relationship was not observed between log of polymer concentration and reciprocal of gelation temperature (Figs. 4 and 5). However, as seen in Figs. 6 and 7, linearity was observed in the semilogarithmic plot of PF 127 concentration and reciprocal of gel melting temperature for sorbitol and PEG 15000 concentration, respectively. The negative value of enthalpy (melting) decreases with sorbitol concentration, while the PEG 15000 shows increase in gel melting enthalpy.

3.3. Effect of concentration of PF 127 and BKC on viscosity of gels

The dilute solutions of PF 127 (up to 10%) do not show any significant change in viscosity and the solutions mostly remain Newtonian in nature. The

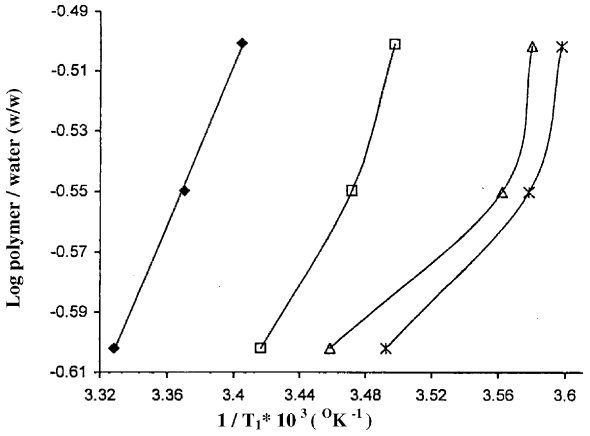

Fig. 4. Enthalpy of gelation—effect of sorbitol concentration (◆, plain; □, 0.5 M; △, 1.0 M; ✳, 1.5 M).

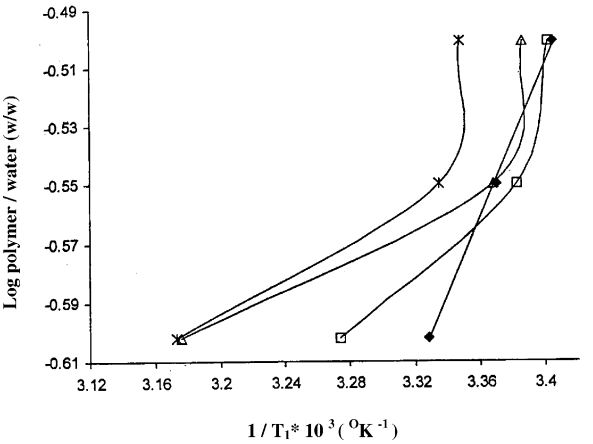

Fig. 6. Enthalpy of gelation—effect of PEG concentration (◆, plain; □, 0.6 M; △, 1.1 M; ✳, 1.6 M).

slight increase in viscosity was observed for 15% (w/w) PF 127 solution at temperatures above 20 °C. However, at concentrations of 20% (w/w) PF and above, sudden increase in viscosity was observed. A temperature–viscosity profile of 20% (w/w) and 25% (w/w) PF 127 gel show a gelation onset temperatures of 19.8 and 13.5 °C; and rate of increase were 5463 and 24537 cP/°C, respectively.

Effect of BKC on viscosity of the gel (20%, w/w, PF 127) was evaluated with respect to temperature under constant shear rate, as the gels were non-Newtonian. The viscosity–temperature relationship is shown in Fig. 8. Although linear relationship was not between viscosity and BKC concentration the viscosity rise of the gel was directly proportional to BKC concentration. The slope of the linear portion of the lines for BKC concentration of 0, 0.050, 0.100, 0.125, and 0.250% (w/v) were found to be 4250.8, 5742.79, 6004.03, 9026.39, and 11449.37 cP/°C, respectively. It was observed that the slope of viscosity–temperature line increases with increase in BKC concentration.

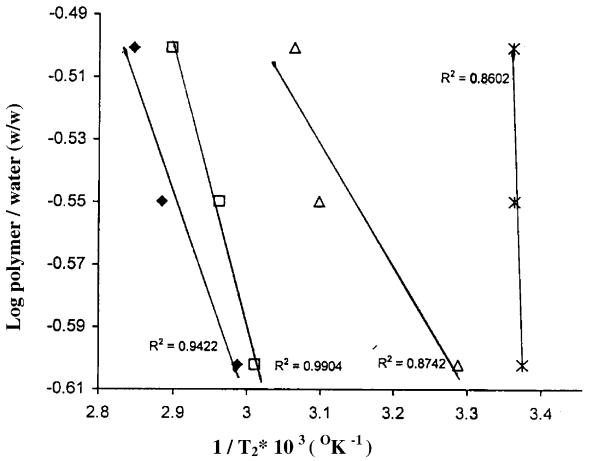

Fig. 5. Enthalpy of gel melting—effect of sorbitol concentration (◆, plain; □, 0.5 M; △, 1.0 M; ✳, 1.5 M).

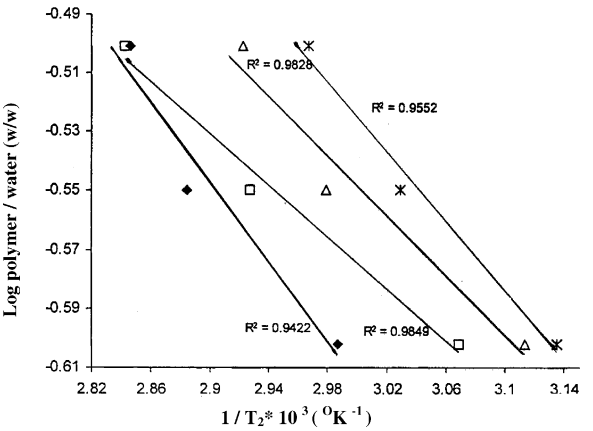

Fig. 7. Enthalpy of gel melting—effect of PEG concentration (◆, plain; □, 0.6 M; △, 1.1 M; ✳, 1.6 M).

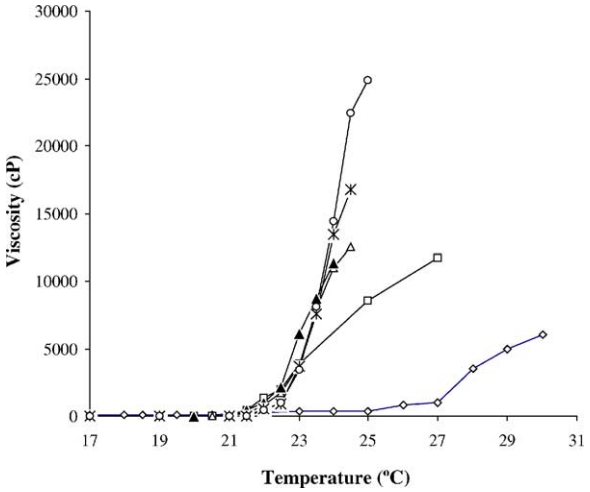

Fig. 8. Effect of BKC on temperature–viscoity relationship of PF (20%, w/w) gel (◇, plain PF gel; □, BKC 0.005% PF gel; △, BKC 0.05% PF gel; ▲, BKC 0.1% PF gel; ✳, BKC 0.125% PF gel; ○, BKC 0.25% PF gel).

4. Discussion

Concentrated aqueous solutions of PF 127 (above 20%, w/w) exhibit reverse thermal gelation (Brown and Schillen, 1991). As the temperature increases, micellar entanglement is promoted, leading to gel formation and an overall increase in bulk viscosity. Researchers have investigated the gelation of PF 127 as a result of body-centered cubic packing of spherical micelles (Mortensen and Talman, 1995). Temperature plays an important role in the micelle formation of PF 127 through the temperature-dependent hydration of the ethylene oxide units. Water is good solvent for PEO as well as PPO chains of polymer at low temperatures. However, at higher temperature the solubility of PPO is reduced and micelle formation occurs.

Ultrasonic velocity and light scattering studies of aqueous solutions of PF 127 clearly indicated micellar mode of association (10–40 °C). A pronounced decrease in critical micellar concentration accompanied the micellar association (Rassing and Attwood, 1983). Aggregates were asymmetric at low temperature but spherical above 25 °C. Temperature-dependent changes in micellar properties have been related to the reversible thermal gelation of PF 127. The microviscosity of PF 127 gels studied using fluorescent probe molecules like pyrine and 8-anilino-1-napthalene sulphonic acids, decrease with increasing temperature (Rassing et al., 1984). The ^{13}C NMR studies reveals that, increased temperatures produced conformational changes in the methyl group of the polyoxypropylene within the hydrophobic micellar region and also in the motion of the hydrophilic end chains. The subsequent dehydration and increased end chain friction causes the gel formation. The small angle neutron scattering studies by Prudhomme et al. (1996) has shown the absence of higher order diffraction peaks at low concentration of PF 127 and temperature. In the gelation range presence of higher order diffraction peaks confirms the superamicellar structure (Prasad et al., 1979). According to the thermodynamic model, there exists a local higher order of water molecules around the hydrophobic unit of the polymer in solution. As gelation occurs, the interaction between the hydrophobe unit of polymer molecules, squeezes out these ordered water molecules into the bulk solution of lower order. This results in an overall disorder or increased entropy, which is the driving force for hydrophobic association. Furthermore, hydrophobic interactions are characterized by endothermic heat changes, which is the case in the gelation of pluronic solutions (Vadnere et al., 1984).

These fundamental physico-chemical approaches of understanding the nature of the gelation process exhibited by the block copolymers can be used to illustrate and explain the results presented. The decrease in the gelation temperature with increase in PF 127 concentration may be attributed to the higher number and volume occupied by micelles at lower temperatures. As the concentration of PF 127 increases, the gel structure becomes more closely packed with the arrangement in a lattice pattern. In turn, the disruption of the lattice melting of gel occurs at higher temperatures. This is also indicated by the negative value of enthalpy of gel melting. This study has shown that Vitamin B_{12} in the concentration of 0.52% (w/w) has significantly reduced the gelation temperature at all concentrations of PF 127. This may be attributed to high water solubility of the vitamin. Gelation of pluronic PF 127 is predominantly dependent on aqueous solubility of the polymer. Water is a good solvent for PEO chains of pluronic PF 127. The presence of vitamin predominantly decreased the critical micellar concentration, and is accompanied by increased micellar aggregation (Rassing and Attwood, 1983). Ultimately, it resembles

the concentration effect of polymer in aqueous system. Thus, the gel formation occurs at low temperatures compared to plain gels. This pluronic PF 127 gel strengthening effect of vitamin is evident as the gel melting temperatures are increased subsequently. The enthalpy of gelation process will depend on the type and extent of interaction favored. Vitamin B_{12} does not alter the enthalpy of gelation and hence shows no interaction with the polymer chains. In contrast to the effect of salts, Vitamin B_{12} has shown to increase significantly the gel melting temperature, T_2. The entanglement of the large size molecule in the outer PEO chains favoring hydration may be the factor responsible for increase in T_2. At gel melting Vitamin B_{12} favors hydration of PEO chains of the polymer and increases T_2. Similar effect have been obtained by Youg et al. (2001) in the study of effect of sodium chloride on PF 127 gels. Sodium chloride has significantly decreased the gelation temperature, while diclofenac sodium has shown the opposite effect.

Sorbitol decreases the gelation temperature of PF 127 gel at each concentration. The decrease in gel point may be attributed to the favoring of association between the polymer molecules due to participation of sorbitol in hydrogen bonding with the etheral oxygen of the polymer. Similarly, sorbitol has exhibited the property to decrease gel melting temperature T_2, which is attributed to the desolvation of PEO chains of the polymer by sorbitol. The enthalpy of gelation decreases with increase in sorbitol concentration. As concentration of sorbitol increases, the difference in the gel melting temperature reduces and the enthalpy increases. Gels containing 1.5 M of sorbitol show that gel melting is independent of polymer concentration. Thus, sorbitol squeezes out water and favors polymer association by H-bonding. Polymer association decreases T_1. The participation of sorbitol in desolvation of PEO causes suppression of T_2.

The plots of polymer concentration versus $1/T_1$ obtained at various concentrations of sorbitol and PEG have shown deviation from linearity and concavity was observed at lower polymer concentration. Similar deviation was observed by Eldridge and Ferry in $\log C$ versus $1/T$ plot of low molecular weight gelling gelatin, which was attributed to formation of cross-links having lower heats of reaction instead of or in addition to more stable ones. Similarly, though gelation of pluronic occurs due to hydrophobic interactions, in the presence of sorbitol or PEG, low energy bonding such as hydrogen bonds are formed which cause concavity in the curve. The concavity increases with increase in concentration of H-bonding additive, which is in direct proportion to the extent of hydrogen bonding as compared to relatively high-energy hydrophobic interactions. As the polymer concentration increases, the proportion of low energy bond reduces as compared to hydrophobic interactions and therefore slopes of the line increases again. Thus, in nutshell, the dominant effect of hydrogen bonding at low polymer concentration is responsible for the concavity in the gelation curve.

Addition of water-soluble polymer PEG produces increase in the gel–sol transition temperature of PF 127 depending on the concentration of PEG. The phenomenon may be mediated through the modification of the process of micellar association of the PF 127 molecules. In addition the PEG molecules may form mixed micelles with PF 127. Addition of PEG causes an increase in sol-gel transition temperature of PF 127 solutions. The hydrophilic end chains of PF 127 comprises the same PEO chains that are present in PEG. It is suggested that the esters bind to these chains, promoting dehydration and causing an increase in entanglement of adjacent micelles. In the presence of PEG, association of pluronic molecules is hindered and a mixed micellar system with different physico-chemical properties is formed. The trend observed is identical to the effect of water-soluble solutes on gelation of PF 127 by Gilbert et al. (1987).

Prudhomme et al. (1996) have reported that PF 127 concentrated solutions exist as spherical micelles packed on to simple cubic lattice to form gel. In low micellar region, micelles are well separated to be an isotropic Newtonian fluid, where effective volume fraction of the micelle is low. Temperature affects the micelle formation through hydration of ethylene oxide units. At very high temperatures, ethylene oxide units dehydrate, effective volume fraction decreases to give Newtonian fluids. The 10–12.5% (w/w) polymer solutions were Newtonian over the temperature range from 10 to 75 °C suggesting absence of large structure in higher polymer concentration. The fluids are non-Newtonian over an intermediate range of temperatures and the temperature window becomes wider at higher polymer concentration. For a 15% (w/w) PF 127 solution the shear thinning occurs

between 35 and 45 °C. The liquid shows a very slight decrease in the low temperature region which was attributed to the dehydration of PPO blocks of the unimers with rise in temperature. The unimers start to form spherical micelles causing increase in intrinsic viscosity as a result of extremely high solvation in the miceller shell. At temperatures above 30 °C, almost all polymer exist in the micellar form and dehydration of the miceller shell decreases, intrinsic viscosity of the micelle becomes dominating factor in the higher temperature region. At higher polymer concentration the transition between Newtonian and non-Newtonian behavior is abrupt. A 1 °C temperature increase causes 10% increase in the miceller concentration and 3.3% decrease in the intermiceller distance as well as two-fold increase in viscosity.

BKC is the commonly used preservative in the nasal formulation. The increase in viscosity of aqueous PF gels was observed proportional to BKC strength. The temperature viscosity data followed $\eta = kt^n$ relationship. The inflection point observed in the viscosity temperature curve indicates the onset of close packing of the micelle. Presence of BKC significantly reduced the gelation onset temperature from 27.94 to 22.2 °C. BKC a quaternary ammonium compound is a mixture of alkyls with chain length between C8 to C18 and exhibit weak surface tension lowering property (Kibbe, 2000; Lien and Perrin, 1976). The lowering of gelation onset temperature due to BKC may be attributed to the hydrophobic interactions between alkyl chains of BKC and PPO chains of pluronic. This may squeeze out water causing increase in viscosity at lower temperatures. It is also responsible for reduced solubility of PPO of polymer and in turns the temperature at which micelle formation and aggregation occurs.

At constant concentration, abrupt changes in viscosities were observed due to sudden rise in miceller concentration. The CMC values for PF 127 reported on the basis of thermodynamic data are 5.6, 4.3, and 2.8% (w/w) at 19.1, 19.9, and 21.1 °C, respectively (Miller and Drabik, 1984). In a 20% PF 127 gel, the miceller concentration are 14.6, 15.9, and 17.4% (w/w), respectively, at 19.1, 19.9, and 21.1 °C. The 20% samples were reported to behave as Newtonian fluid at 15% and gel at 17% miceller concentration. This indicates the abruptness of transformations in the viscosities of the polymer solution. The controlled drug delivery applications of PF 127 solutions would aim to utilize the copolymers solubilizing capacity.

5. Conclusion

The results of this study reveal that addition of drug alone or the formulation additives results in alteration of gelation properties. The thermodynamic properties of pluronic PF 127 gels are dependent on the concentration of the polymer and water-soluble additives. The gelation range broadens with polymer concentration and in presence of vitamin. Sorbitol and PEG 15000 narrows the gel range. The effect was significant in the case of sorbitol. The enthalpy change was significant in gels containing sorbitol and PEG, indicating interaction with the polymer during the phase transitions. The aqueous gels become non-Newtonian with higher concentration of polymer. The hydrophobic interaction of BKC with pluronic produces higher gel viscosity. Addition of PEG 15000 affords the advantage of desired gelation characteristics for increased drug loading and use of desired formulation additives.

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