J. Cosmet. Sci., 53, 199–208 (July/August 2002)

Development and characterization of rosin-based polymer and its application as a cream base

V. T. DHANORKAR, R. S. GAWANDE, B. B. GOGTE, and A. K. DORLE, *Department of Pharmaceutical Sciences, University Campus (V.T.D., R.S.G., A.K.D.), and Laxminarayan Institute of Technology (V.T.D., B.B.G.), Nagpur University, Nagpur 440 010 (MS), India.*

Accepted for publication January 31, 2002.

Synopsis

The literature contains many references to the wide range of uses of rosin-based polymers, but little has appeared in the area of rosin-based polymers used as cream bases. Various rosin polymers based on glycerol, sorbitol, and pentaerythritol were prepared and screened for efficacy as cream bases. Among these polymers, polymer 2 (glycerol-based) is reported in the present study as it produced creams with a better stability and release profile as compared to other creams. The creams were formulated employing polymer 2 (P2) and Tween 60 as surfactants. The stability of the prepared creams, as well as the diclofenac diethylammonium release pattern, was investigated using particle size analysis, conductivity, relative dielectric constant, spreadability, and irritation potential measurement, and was compared with that of creams containing Tween 60 (RT) prepared in the laboratory. The release of the drug, diclofenac diethylammonium, was measured after eight hours and compared with a standard cream (RT) and a marketed cream (RM).

INTRODUCTION

Rosin and its derivatives are widely used in paints (1), primers (2), cosmetics (3), microencapsulating materials (4), and pharmaceutical coating materials (5). Rosin and its derivatives are also used as binding agents in tablet formulation (6). Rosin is a solid resinous material obtained naturally from various varieties of pine tree (7,8). The principle commercial sources of rosin are *Pinus soxburghi, Pinus longifolium, Pinus palustrius,* and *Pinus toeda.* Rosin is composed of approximately 90% rosin acids and 10% non-acidic materials. Rosin acids are monocarboxylic acids having the typical molecular formula ($C_{20}H_{30}O_2$. There are two types: the abietic acid type (9) and the primaric acid type (10).

Rosin is reported to have emulsifying properties (11). The use of rosin-based esters was previously reported in cream bases (12). Based on these data and work carried out in our

Address all correspondence to V. T. Dhanorkar.

laboratory, we were prepared to detect the utility of rosin-based polymers as a cream base. The rosin-based polymers were prepared by the esterification of rosin with glycerol and pentaerythritol at 220–240°C in the presence of sodium sulphide and sodium bisulphate as catalysts. The primary aim of the present work is to evaluate polymer 2 as a cream base. The cream-containing polymer 2 (R2) was also studied for its stability and the release profile of diclofenac diethylammonium. The prepared cream was compared with a standard cream containing Tween 60 (RT) and a marketed preparation (RM).

EXPERIMENTAL

MATERIALS

The procured materials along with their sources are as follows: rosin N grade (Tayebai Ebrahimji Pettodwala, Mumbai), glycerol (Qualigen), sorbitol (Qualigen), Tween 60 (S.D. Fine), maleic anhydride (Qualigen), pthaleic anhydride (Qualigen), castor oil (P.J. Chemicals, Nagpur), glycerin (Qualigen), isopropyl myristate (Qualigen), cetyl alcohol (S.D. Fine), stearyl alcohol (S. D. Fine), propylene glycol (Qualigen), and diclofenac diethylammonium (Crossland Laboratories Ltd., Pune). Distilled water was used when collected fresh. The polymers based on rosin were prepared in the Laboratory of Pharmaceutical Sciences, Nagpur University, Nagpur.

PREPARATION AND DETERMINATION OF THE PHYSICOCHEMICAL PROPERTIES OF ROSIN-BASED POLYMERS

Preparation of rosin-based polymers. The reaction of polymer synthesis was conducted in a four-neck two-liter glass reactor. This reactor was fitted with a condenser, stirrer, and temperature control arrangement. The reaction temperature was maintained within ±2°C with the help of an accurate thermometer. As a first step, rosin, part of the maleic anhydride, castor oil, and sodium sulphide and sodium bisulphate (catalysts) were added to the reactor and the temperature was slowly raised to 160°C. The reaction was maintained at this temperature for one hour. After this, the temperature was lowered to 120°C and glycerol and sorbitol were added slowly after about 15 minutes. The cooling was continued for three to four hours at 210–250°C. At the end of this period, the calculated solvent, part of the maleic anhydride, and pthaleic anhydride were slowly added after about 15 minutes. Further cooling was done at a lower temperature for three to four hours until the desired acid value was reached. Finally, xylene was stripped off totally by heating at a slightly higher temperature (150°C) using a vacuum. The sample was finally strained through a fine mesh and stored carefully. During the process, the acid value of the product was determined intermittently as reported previously (13).

Determination of physicochemical properties of rosin-based polymer. The acid value is the number that expresses in milligrams the amount of KOH necessary to neutralize the free acids present in one gram of the substance. The acid value of the polymers was determined by using the test described in the Indian Pharmacopoeia (*Pharmacopoeia of India, 1996*). The maximum acid value for rosin-based polymer should not exceed more than 10.

Two grams of rosin-based polymer was dissolved in 50 ml of a mixture of equal volumes of ethanol (95%) and ether previously neutralized with 0.1 M KOH to phenolphthalein

solution. One milliliter of phenolphthalein was added to the above mixture and titrated with 0.1 M KOH until the solution remained faintly pink after shaking for 30 seconds.

The average of three readings was reported. The acid value = 5.61 N/W, where N is the number of milliliters of 0.1 molar KOH required, and W is the weight of the substance in grams.

The specific gravity was determined using a simple displacement method using a gravity bottle as described in the *Pharmacopoeia of India, 1996.*

The saponification value is the number of milligrams of KOH required to neutralize the free acid and to saponify the ester present in one gram of sample. It is determined as per the procedure described in the *Pharmacopoeia of India, 1996.*

Four grams of rosin-based polymer was introduced into a 200-ml borosilicate glass fitted with a reflux condenser. To it 25 ml of ethanolic KOH was added along with a little pumice powder, and it was refluxed on a water bath for 30 minutes. One milliliter of phenolphthalein was added to it and titrated with 0.5 ml of HCL (a). The experiment was repeated omitting the rosin-based polymer (b). The saponification value = 28.05 (b – a)/w, where w is the weight of the substance taken.

The HLB of the prepared rosin-based polymers for the present experiment was determined by following a formula described by Griffin: HLB = 20 (1 – S/A), where S is the saponification number and A is the acid number of the acid.

The viscosity of the prepared polymers was determined by using a Brookfield synchrolectic viscometer, model RVT. The sample was taken in suitable size glass bottles, and the spindle was inserted in it up to the mark. Spindle number 1 was used in all the cases. The dial reading thus obtained was multiplied by the factor given in the chart supplied by the manufacturer. The composition of the polymers used to prepare the creams and their physicochemical properties are given in Tables I and II, respectively.

PREPARATION OF THE CREAMS

The ingredients used to prepare cream bases are listed in Table III. The cream bases were formulated using a regular fusion method: The surfactants (Tween 80/rosin-based) were added to water to which diclofenac diethylammonium was dissolved with constant stirring at 70°C in a glass beaker. Cetyl alcohol and stearyl alcohol were melted by heating at 70°C. The mixture of propylene glycol, isopropyl myristate, and glycerol was preheated to 70°C and added to the melted cetyl alcohol and stearyl alcohol. To this

Table I
Composition of Polymer 2

Composition	Weight in grams
Rosin	50
Castor oil	35
Glycerol	2.2
Sorbitol	14.7
Maleic anhydride	6
Pthaleic anhydride	2
Pentaerythritol	—

Table II
Physicochemical Properties of Polymer 2

Polymer number	Acid value	Sap value	HLB	Viscosity*	Weight per ml* (1% solution)	Refractive index* (1% solution)
Polymer 2	0.093	108.42	9.92	45000	1.2549	1.3335

* Readings taken at 37°C.

Table III
Formulation of Cream Bases

Ingredients	R2	RT
Cetyl alcohol	5%	5%
Stearyl alcohol	5%	5%
Propylene glycol	5%	5%
Isopropyl myristate	8%	8%
Glycerin	5%	5%
Polymer 2	2.5%	—
Tween 60	—	2.5%
Diclofenac diethylammonium	1.16	1.16
Distilled water	Up to 100 ml	Up to 100 ml

melted material the aqueous phase containing diclofenac diethylammonium and surfactant was added with continuous stirring at 70°C. The mixing was continued for five minutes with the help of a stirrer. The creams were then distributed to glass bottles and stored at various temperatures for stability studies. The evaluation data of the creams is presented in Table IV.

SPREADABILITY

The spreadability of the creams was evaluated by spreading a sufficient quantity of the cream on the hand.

PREPARATION OF THE SKIN MEMBRANE

Full-thickness abdominal skin was obtained from freshly sacrificed albino rats (Wistar strain; male; weight 200–250 g). It was washed thoroughly with distilled water to

Table IV
Evaluation Data of Prepared Creams

Formulation	Percent drug content	Viscosity	pH	Homogeneity
R2	97.5	6400	6.4	*
RT	96	5600	6.3	*
RM	98	6200	6.2	*

* Indicates good homogeneity.

remove any subcutaneous matter and fatty tissues. It was then immersed in phosphate-buffered saline (pH 7.4) at 37°C for 30 minutes for equilibration before use in release studies.

EVALUATION OF DRUG RELEASE

A Keshary Chien diffusion cell was used for this part of the study (14). Phosphate-buffered saline (10 ml), used as a receptor medium, was placed in the lower part of the diffusion cell. It was placed on a magnetic stirrer with a small magnetic needle placed inside for uniform distribution of the diffusant. The temperature of the cell was maintained at 37°C ± 5°C, by a thermostatically controlled water bath. Isolated rat skin was carefully placed over a 1-cm^2 orifice of the receptor chamber, and precisely weighed formulations were applied to the epidermal side of the mounted skin. Samples (1 ml) were removed from the receptor compartment at regular intervals of one hour, and an equal volume of fresh phosphate-buffered saline was added. Samples were assayed by the colorimetric method of analysis after subsequent dilution. The study was performed for eight hours, and percent release was calculated.

STABILITY STUDIES

The prepared creams were stored at three different temperatures: room temperature, 40°C, and 55°C, for 50 days using a controlled-temperature oven (Thermonic Labs. Pvt. Ltd.). The parameters of stability assessment were drug content, pH, particle size, conductivity, relative dielectric constant, and viscosity.

Drug content. The drug content of the creams were determined by dissolving one gram of the cream in water and estimating the drug by using a UV spectrophotometer (Shimatzu-1602) at 254 nanometers, for diclofenac diethylammonium. The standard graph was prepared by dissolving 50 mg of diclofenac diethylammonium in water. Five milliliters of this solution was then diluted to 100 ml, and absorbance of this solution was measured at 254 nanometers. The standard graph was plotted using various dilutions, and the drug content in the creams was calculated from the absorbance of the solutions of prepared creams.

Determination of pH. The pH of 1 g% of the suspension of cream was determined using a pH meter (Hanna Instruments).

Particle size determination. The particle size of the prepared creams was determined using a Leitz-Larolux-S-microscope. Three hundred globules were counted using an eyepiece micrometer attached to a 10X eyepiece and with a high power objective of 45X. The eyepiece micrometer was calibrated using a stage micrometer. The average size of a globule in terms of eyepiece micrometer was multiplied by a magnification factor to obtain actual globule size in microns.

Conductivity and relative dielectric constant measurement. The conductivity was determined using a digital conductometer (Elico Pvt. Ltd.; model CM-180). The relative dielectric constant was determined using a Universal dielectrometer (Type: OH-301, no. 457). The measurement of the relative dielectric constant was carried out by reading the capacitance of a condenser containing the solution of the polymer between the plates. A probe capacitance cell, which could be attached to the dielectrometer through a coaxial

plug, was used to measure the pF value (capacitance). About 30 ml of polymeric solution was taken into a suitably sized cylinder, and the head of the probe cell was dipped into the solution. Care was exercised to take all the readings at the same temperature and at the same height. All measurements were done at a fixed frequency of 3 mc/S. The conductivity measuring cell lends itself to relative measurement of pF value for comparison. The recorded pF values were used as such without further reduction and were thus designated relative dielectric constants (relative DEC). The relative DEC for water was found to be 54, whereas the value of DEC is 80. The creams were allowed to equilibrate to room temperature before the readings were taken.

Viscosity measurement. The viscosity study was done by a Brookfield synchro-lectic viscometer, using the method as specified by the manufacturer.

RESULTS AND DISCUSSION

It was observed that the creams show good spreadability and homogeneity.

EVALUATION OF DRUG RELEASE

Figure 1 shows the percent release of diclofenac diethylammonium from various creams in the receptor medium across the rat skin. Cream containing polymer 2 showed better release of the drug for the first two hours than did the marketed cream. The overall release was greater for the marketed preparation after two hours. The cream containing Tween 60, however, showed a poor release pattern as compared to the marketed preparation and creams containing polymer 2. The cream containing polymer 2 showed the

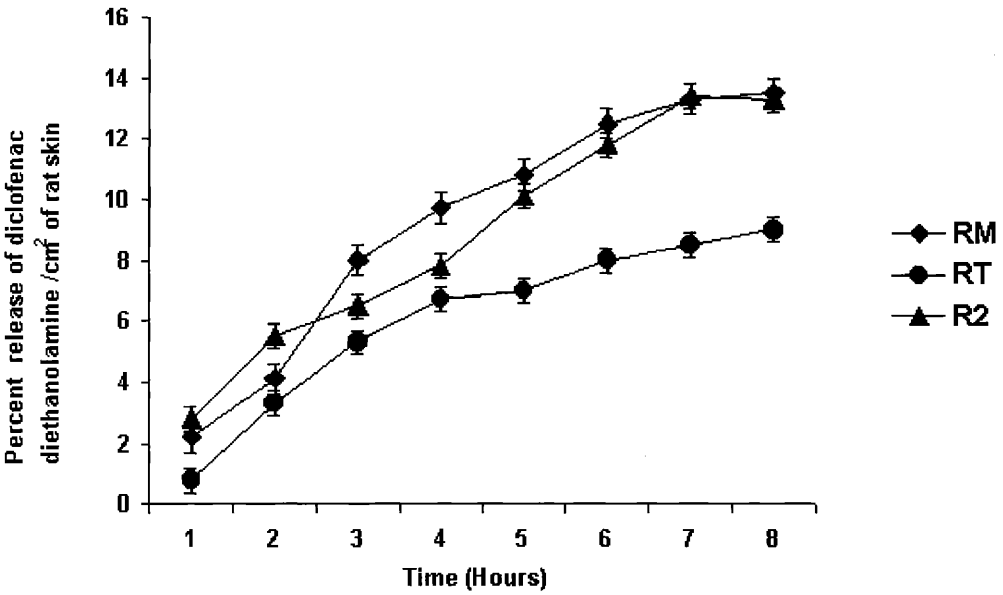

Figure 1. Comparison of *in vitro* release profile of diclofenac diethylammonium from various cream bases with marketed preparation using Keshary Chien diffusion cell. RM: marketed cream. RT: cream with Tween 60. R2: cream with polymer 2.

release of drugs from 2.8 to 13.3 percent over the period of eight hours. The marketed preparation showed release of the drug from 2.2 to 13.6 percent. Thus the amount of drug released at the end of eight hours was similar for the marketed preparation and the cream containing polymer 2. This is also evident from a Student's t-test, which revealed that there is no statistically significant difference ($p < 0.01$) in the overall release of the creams containing polymer 2 and that of the marketed cream.

STABILITY STUDIES

Drug content. The creams containing polymer 2 showed an initial drug content of 97.5 percent. After storage at 40°C and 50°C for 50 days, the drug content decreased to 97.2 percent and 97.0 percent, respectively. The creams containing Tween 60 showed an initial drug content of 97.7 percent. After storage at 40°C and 50°C for 50 days, the drug content decreased to 97.5 percent and 97.0 percent, respectively. The marketed preparation showed an initial drug content of 97.8 percent. After storage at 40°C and 50°C for 50 days, the drug content decreased to 97.5 percent and 97.3 percent, respectively. This indicates that the stability of the active ingredient in creams is reasonably satisfactory.

pH. The pH of the creams ranged from 6.0 to 7.0, which is the normal pH range of skin.

Particle size. The changes in particle size of the creams during storage are presented in Figure 2. The particle size data is in good agreement with all the other parameters tested for the stability of the creams. As shown in the figure, the particle size increased more in the case of creams containing Tween 60 and stored at 40°C and 55°C. The slight

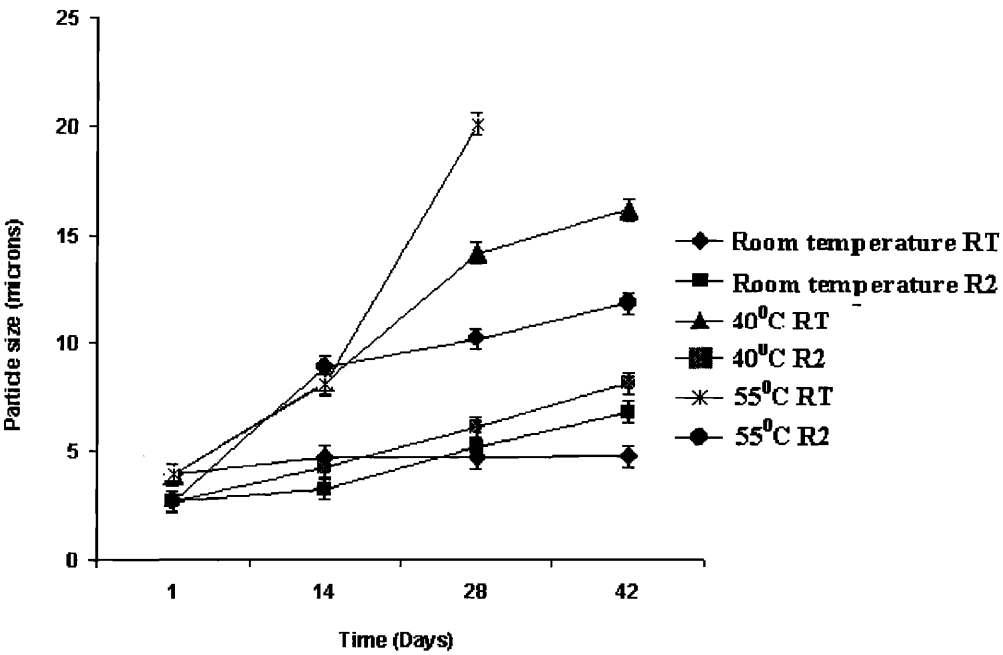

Figure 2. The changes in particle size of the prepared creams during aging. RT: cream with Tween 60. R2: cream with polymer 2.

change in the particle size in creams containing polymer 2 upon storage at various temperature ranges again gives evidence of good stability of this cream as compared to cream prepared with Tween 60.

Conductivity and relative dielectric constant. The conductivity behavior of all the creams is shown in Figure 3. The formulations containing polymer 2 showed an increase in conductivity upon exposure to higher temperature. This may be due to the anionic nature of the polymer 2 itself, which shows an enhanced conductivity at higher temperatures.

The changes in relative dielectric constant of the various creams are shown in Figure 4. The creams containing polymer 2 showed a slight change in relative dielectric constant upon storage at higher temperature as compared to the Tween 60-based creams. The creams containing Tween 60 showed a drastic rise in the dielectric constant with respect to temperature and showed signs of breaking after 28 days, which is in good agreement with conductivity observations.

Viscosity. The result of changes in the viscosity of creams on exposure to various temperatures is presented in Figure 5. The viscosity of the creams ranged from 5600 to 6400 centipoises. The viscosity was found to decrease with the rise in storage temperature for all the creams tested. The viscosity of the cream prepared with polymer 2 was comparatively less affected than the standard cream at all the temperatures. The fact that near constant viscosity could be achieved in a cream containing polymer 2 at various temperatures demonstrated that it maintains viscosity at elevated temperatures during long-term storage. The formulation containing Tween 60 showed signs of breaking after 28 days of storage at 55°C. The viscosity of these creams could not be determined because of this.

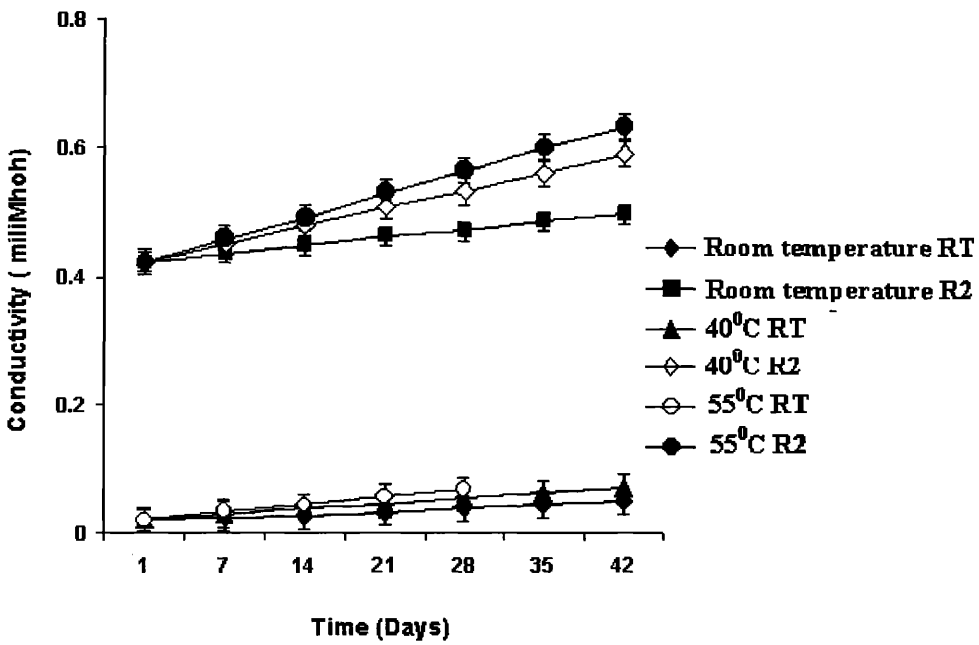

Figure 3. The changes in conductivity of the prepared creams during aging. RT: cream with Tween 60. R2: cream with polymer 2.

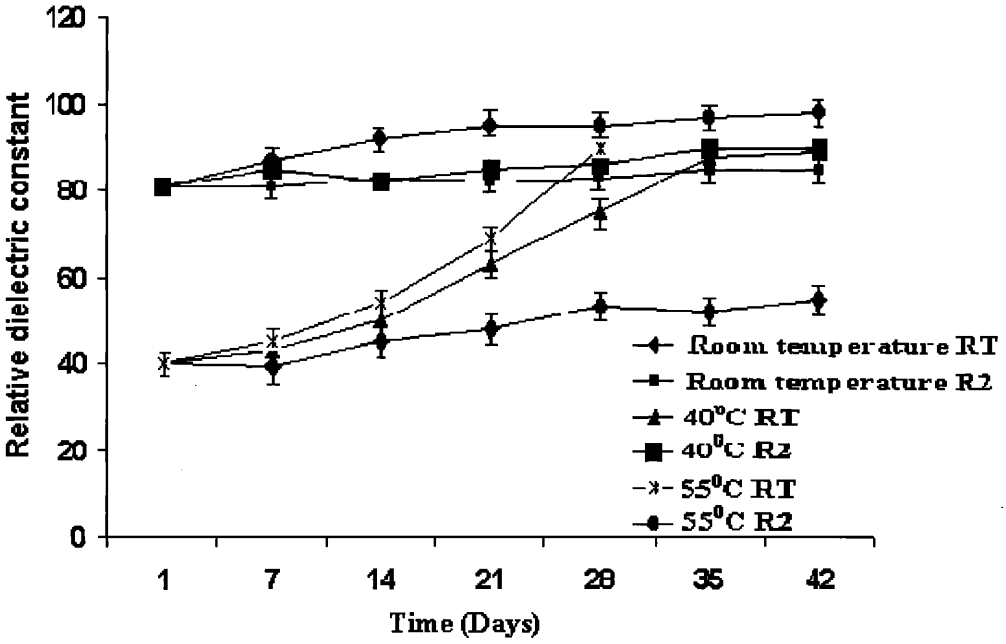

Figure 4. The changes in the relative dielectric constant of the prepared creams during aging. RT: cream with Tween 60. R2: cream with polymer 2.

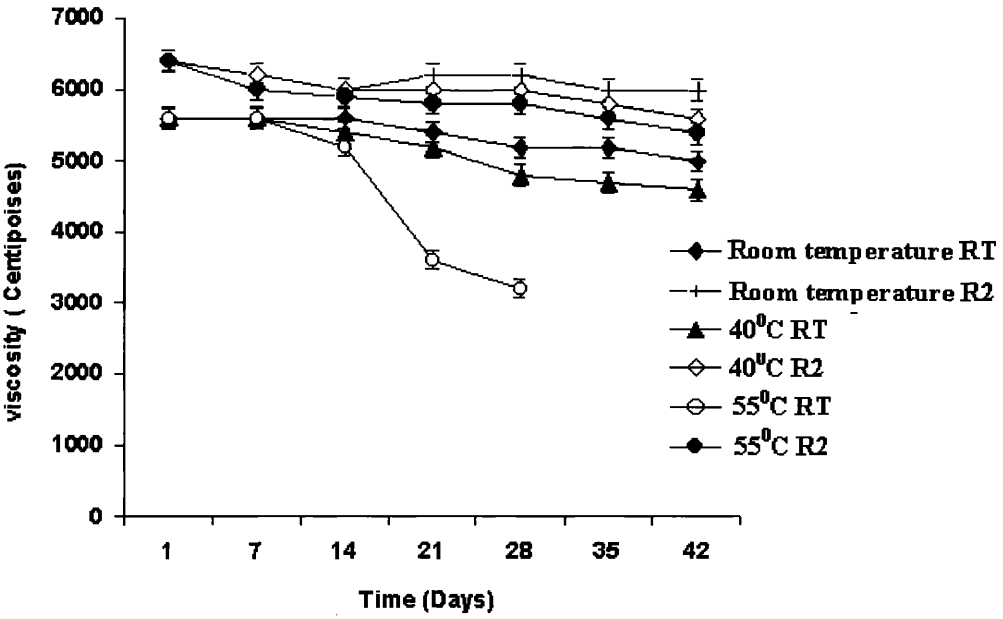

Figure 5. The changes in viscosity of the prepared creams during aging. RT: cream with Tween 60. R2: cream with polymer 2.

Though the initial viscosity of the cream containing polymer 2 (6400 centipoises) was greater than that of the marketed preparation (6000 centipoises), the overall release pattern of the drug from the cream containing polymer 2 was similar. However, there are similar findings in earlier published literature (15), which has indicated that a gel formulation (containing Carbopol 940 or emulsion base) with higher viscosity showed a better release profile than one with lower viscosity.

CONCLUSION

On the basis of the release parameters and storage stability, it seems that the cream prepared by using polymer 2 shows a good release pattern and storage stability and that it can be used successfully as hydrophilic cream base.

REFERENCES

(1) P. Balakrishnan, S. S. Sangole and B. B. Gogte, *Paintindia,* 44, 37 (1994).
(2) B. N. Mundhe, S. P. Morey, and B. B. Gogte, *Paintindia,* 44, 77 (1993).
(3) G. Melin, Antiwrinkle beauty cream composition, Fr. Demande FR 2,693,371, *Chem. Abs.,* 120, (1994).
(4) D. S. Sheorey and A. K. Dorle, *J. Microencapsulation,* 11, 11 (1994).
(5) Y. V. Pathak, R. L. Nikore, and A. K. Dorle, *Int. J. Pharm.* 24, 351 (1985).
(6) Y. V. Pathak, and A. K. Dorle, *Indian J. Pharm. Sci.,* 48, 16 (1986).
(7) P. Y. Klyuev, A. Y. Klyuev, I. V. Antonovich, A. K. Strakh, and O. A. Novikov, *U.S.S.R. SU 1810368 A1,* April 23, 1993.
(8) S. Icli, F. Uysal, *Turk. J. Chem.,* 16, 307–314 (1992).
(9) C. W. Chien, *J. Am. Chem. Soc.,* 62, 4762 (1960).
(10) Y. V. Pathak, R. L. Nikore, and A. K. Dorle, *Int. J. Pharm.,* 24, 351 (1985).
(11) Nakagava *et al., U.S. Patent, 5,478,567,* December 26, 1995.
(12) Oda *et al., U.S. Patent, 5,725,874,* March 10, 1998.
(13) N. H. Sahu, P. M. Mandaogade, A. M. Deshmukh, and A. K. Dorle, Biodegradation studies of rosin-glycerol ester derivative, *J. Bioactive Compatible Polymers,* 14, 344–360 (1999).
(14) Y. W. Chien and P. R. Keshary, *Drug. Dev. Ind. Pharm.,* 10, 883 (1984).
(15) S. P. Patvardhan, K. S. Joshi, R. V. S. V. Vadlamudi, and S. G. Deshpande, Development and in vitro evaluation of diclofenac hydroxyethyl pyrrolidine formulations containing penetration enhancers, *Indian J. Pharm. Sci.,* 61, 7–11 (1999).