ความสัมพันธ์ของคุณสมบัติวิสโคอิลาสติกของยาพื้นเจลคาร์โบพอล 940 กับสัมประสิทธิ์การแพร่ของไพรอกซีแคมในยาพื้นเจล และความรู้สึกสัมผัส

นาย รัฐพล อาษาสุจริต

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต
สาขาวิชาเภสัชกรรม ภาควิชาเภสัชกรรม
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2544

ISBN 974-03-1030-3

RELATIONSHIP OF VISCOELASTIC PROPERTIES OF CARBOPOL 940 GEL BASES TO PIROXICAM DIFFUSION COEFFICIENTS IN GEL BASES AND PERCEPTUAL ATTRIBUTES

Mr. Rathapon A-sasutjarit

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Pharmacy
Department of Pharmacy
Faculty of Pharmaceutical Sciences
Chulalongkorn University
Academic Year 2001

ISBN 974-03-1030-3

Thesis Title	Relationship of Viscoelastic Properties of Carbopol 940 Gel Bases to Piroxicam Diffusion Coefficients in Gel Bases and Perceptual Attributes
By	Mr. Rathapon A-sasutjarit
Field of Study	Pharmacy
Thesis Advisor	Assistant Professor Panida Vayumhasuwan, Ph.D.
Thesis Co-advisor	Associate Professor Anuvat Sirivat, Ph.D.

Accepted by the Faculty of Pharmaceutical Sciences, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree

……………………………………………. Dean of Faculty of
Pharmaceutical Sciences
(Associate Professor Boonyong Tantisira, Ph.D.)

Thesis Committee

……………………………………………. Chairman
(Associate Professor Porntip Nimmannitya, M.Sc. in Pharm.)

……………………………………………. Thesis Advisor
(Assistant Professor Panida Vayumhasuwan, Ph.D.)

……………………………………………. Thesis Co-advisor
(Associate Professor Anuvat Sirivat, Ph.D.)

……………………………………………. Member
(Associate Professor Parkpoom Tengamnuay, Ph.D.)

……………………………………………. Member
(Asira Fuongfuchat, Ph.D.)

รัฐพล อายาสุจริต : ความสัมพันธ์ของคุณสมบัติวิสโคอิลาสติกของยาพื้นเจลคาร์โบพอล 940 กับสัมประสิทธิ์การแพร่ของไพรอกซีแคมในยาพื้นเจลและความรู้สึกสัมผัส (RELATIONSHIP OF VISCOELASTIC PROPERTIES OF CARBOPOL 940 GEL BASES TO PIROXICAM DIFFUSION COEFFICIENTS IN GEL BASES AND PERCEPTUAL ATTRIBUTES) อ.ที่ปรึกษา : ผศ.ดร.พนิดา วยัมหสุวรรณ, อ.ที่ปรึกษาร่วม : รศ.ดร.อนุวัฒน์ ศิริวัฒน์, 197 หน้า. ISBN 974-03-1030-3.

งานวิจัยครั้งนี้ศึกษาความสัมพันธ์ระหว่าง คุณสมบัติวิสโคอิลาสติกของเจลไพรอกซีแคมที่ความเข้มข้น 1.0 เปอร์เซนต์โดยน้ำหนัก กับสัมประสิทธิ์การแพร่ของไพรอกซีแคมในยาพื้นเจล และความสัมพันธ์ระหว่างคุณสมบัติวิสโคอิลาสติกของยาพื้นเจลคาร์โบพอล 940 กับความรู้สึกสัมผัสในอาสาสมัครที่ได้รับการอบรม เจลไพรอกซีแคมและยาพื้นเจลแสดงคุณสมบัติของแข็งที่ยืดหยุ่นได้อย่างเด่นชัด ซึ่งพฤติกรรมนี้ขึ้นกับปริมาณของคาร์โบพอล 940 ในตำรับ เมื่อเก็บเจลไพรอกซีแคมไว้ในภาชนะที่ไม่ได้ป้องกันแสง ค่ามอดุลัสสะสมและความหนืดลดลงภายใน 14 วัน ส่วนตำรับที่เก็บไว้ในภาชนะป้องกันแสงจะไม่พบการเปลี่ยนแปลง เจลไพรอกซีแคมที่มีตัวทำละลายที่ดีแสดงคุณสมบัติของแข็งที่ยืดหยุ่นได้มากขึ้น ในทางตรงกันข้ามเจลไพรอกซีแคมที่มีโซเดียมคลอไรด์ปริมาณสูงแสดงคุณสมบัติของเหลวที่ข้นหนืดมากกว่า จากการวิเคราะห์ความสัมพันธ์โดยใช้วิธีของเพียร์สันที่ระดับนัยสำคัญน้อยกว่า 0.05 พบค่าสัมประสิทธิ์การแพร่ของไพรอกซีแคมในยาพื้นเจล แปรผันโดยตรงกับแทนเจนปลดปล่อย แต่แปรผกผันกับ มอดุลัสสะสม มอดุลัสปลดปล่อย มอดุลัสเชิงซ้อน และความหนืด ความแข็ง ความเหนียว ความสูงของเจลและความเหนียวเหนอะหนะแปรผันโดยตรงกับมอดุลัสสะสม มอดุลัสปลดปล่อย มอดุลัสเชิงซ้อน และความหนืด ในทางตรงกันข้ามความเปียกและการกระจายตัวแปรผกผันกับ มอดุลัสสะสม มอดุลัสปลดปล่อย มอดุลัสเชิงซ้อน และความหนืด ส่วนความมันวาวและส่วนเจลที่เหลือบนผิว จะแปรผันโดยตรงกับความหนืดเท่านั้น อย่างไรก็ตาม ไม่พบความสัมพันธ์ของความรู้สึกสัมผัสใดๆกับค่าแทนเจนปลดปล่อย รวมทั้งไม่พบความสัมพันธ์ระหว่างการดูดซึมและความพึงพอใจกับคุณสมบัติการไหลของยาพื้นเจล อย่างไรก็ตามพบว่ามีแนวโน้มในการทำนายสัมประสิทธิ์การแพร่ของยา และความรู้สึกสัมผัสจากความสัมพันธ์ระหว่างพารามิเตอร์ดังกล่าว กับพารามิเตอร์การไหล ดังนั้นความสัมพันธ์ที่ได้จึงมีประโยชน์ในการออกแบบสูตรตำรับยาทาภายนอก และเครื่องสำอาง

ภาควิชา	เภสัชกรรม	ลายมือชื่อนิสิต…………………………….………..
สาขาวิชา	เภสัชกรรม	ลายมือชื่ออาจารย์ที่ปรึกษา……………………….…
ปีการศึกษา	2544	ลายมือชื่ออาจารย์ที่ปรึกษาร่วม…………..…...……

4376604033 MAJOR: PHARMACY

KEY WORD: CARBOPOL 940 / DIFFUSION COEFFICIENTS / GEL BASES / PERCEPTUAL ATTRIBUTES / PIROXICAM / RELATIONSHIP / RHEOLOGY / VISCOELASTIC

RATHAPON A-SASUTJARIT: RELATIONSHIP OF VISCOELASTIC PROPERTIES OF CARBOPOL 940 GEL BASES TO PIROXICAM DIFFUSION COEFFICIENTS IN GEL BASES AND PERCEPTUAL ATTRIBUTES. THESIS ADVISOR: ASST. PROF. PANIDA VAYUMHASUWAN, Ph.D., THESIS CO-ADVISOR: ASSOC. PROF. ANUVAT SIRIVAT, Ph.D. 197 pp. ISBN 974-03-1030-3.

Relationships between viscoelastic properties of 1.0 %w/w piroxicam gels and piroxicam release were determined. Correlations between viscoelastic properties of carbopol 940 gel bases and perceptual attributes perceived by trained panelists were also studied. The piroxicam gels and their gel bases exhibited predominantly elastic solid behavior which depended on carbopol 940 concentration. Their storage modulus (G') and viscosity (η) decreased after they had been kept unprotected from light for 14 days. However, their rheological properties had not changed within 14 days if they were protected from light. Preparations containing good solvent exhibited more elastic solid characters. In contrast, the piroxicam gels containing higher sodium chloride contents possessed more viscous fluid behavior. Analyzed by Pearson's test at a p-value of less than 0.05, piroxicam diffusion coefficients (D) were directly proportional to loss tangent ($\tan \delta$), but were inversely proportional to G', loss modulus (G''), complex modulus (G^*) and η. Firmness, stickiness, peaking and tackiness attributes were directly proportional to G', G'', G^* and η. On the contrary, wetness and spreadability attributes were inversely proportional to G', G'', G^* and η. Gloss and residue were directly proportional to only η. However, neither relationships between all perceptual attributes versus $\tan \delta$ nor relationships between absorbency and liking versus rheological parameters could be found. Consequently, there was the potential for predicting drug diffusion coefficients and perceptual attributes from their correlations to rheological parameters, and therefore it could be beneficial to the formulation design of topical dosage forms design including cosmetic products.

Department	Pharmacy	Student's signature…………………….………
Field of study	Pharmacy	Advisor's signature…………………….………
Academic year	2001	Co-advisor's signature……….……………....

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to Assistant Professor Dr. Panida Vayumhasuwan, my thesis advisor, for her invaluable advice, guidance, kindness and encouragement throughout this study.

I also wish to express my gratitude to Associate Professor Dr. Anuvat Sirivat, my thesis co-advisor, and Dr. Asira Fuongfoochart for his and her suggestion, guidance and kindness.

My grateful appreciation is expressed to Petroleum and Petrochemical College, Chulalongkorn University for support of a fluid rheometer used throughout this study.

And I would like to give my thanks to Ms. Supaporn Wongkhongkhathep, head of Department of Pharmacy, Thammasart Chalermprakiat Hospital who provided me a chance to continue my study in this master program.

To the graduate school, Chulalongkorn University for a partial support in term of research grant.

To all the staff members of the Department of Pharmacy for their assistance and kindness.

To all my friends for their assistance, understanding and encouragement, especially Ms. Duangrat Duangta.

To my parents and my sister for their inspiration, understanding and great encouragement.

Finally, I would like to express my thanks to all of those whose names have not been mentioned and to those who in one way or another have helped to make this thesis a reality.

CONTENTS

Page

CHAPTER

LIST OF TABLES

LIST OF FIGURES

FIGURE **PAGE**

ABBREAVIATIONS AND SYMBOLS

$^{\circ}$C = degree celcius
cm = centimetre
CV = coefficient of variation
D = diffusion coefficient
dyn = dyne
δ = phase angle
η = viscosity
g = gram
G = shear modulus
G* = complex modulus
G' = storage modulus
G'' = loss modulus
γ = strain
γ^* = complex strain
γ' = in-phase strain
γ'' = out-of- phase strain
γ = rate of strain
γ_o = amplitude of strain
i = out-of- phase unit vector
J = flux
k_B = Boltzmann's constant
μg = microgram
mg = milligram
ml = millilitre
mm = millimetre
min = minute
NaCl = sodium chloride
ω = angle frequency

P = poise

r = coefficient of correlation

r^2 = coefficient of determination

rad = radian

s = second

SD = standard deviation

T = absolute temperature

tan δ = loss tangent

τ = stress

τ^* = complex stress

τ' = in-phase stress

τ'' = out-of-phase stress

v/v = volume by volume

v/w = volume by weight

w/w = weight by weight

CHAPTER I

INTRODUCTION

Viscoelasticity is one of mechanical properties of materials which possesses combined behavior of elastic solid and viscous fluid. In other words, viscoelastic materials have both elastic and flowing characters. These materials include melt polymers, some kinds of food such as cream, butter, ice cream, and yoghurt and pharmaceutical semi-solid dosage forms such as cream, ointment, and gels.

The viscoelasticity can be categorized as either linear or nonlinear, but only the linear viscoelasticity can be described theoretically with uncomplicated mathematics. The fundamental viscoelastic parameters of a linear viscoelastic system do not depend on the magnitude of the stress or strain (Radebaugh and Simonelli, 1983). Therefore, the linear viscoelastic regime is always used for study of mechanical properties of the viscoelastic material.

One of the accepted techniques for investigation of the viscoelastic behaviors of materials is the "dynamic mechanical testing" which is based on the fundamentally different responses of viscous and elastic elements to a sinusoidally varying stress or strain (Rosen, 1993). This technique provides informations about structure of sample without structure deformation.

The viscoelastic properties of pharmaceutical semi-solid dosage forms affect the physical characters of preparations that may influence patient or consumer perceptions (Wang, Kislalioglu and Breuer, 1999). The viscoelastic properties also affect contact times of an ophthalmic gel which are related to bioavailability and therapeutic efficacy of the preparations (Edsman, Carlfors and Harju, 1996). Semenzato et al. (1994) found that the viscoelastic properties of vitamin A palmitate emulsions were related to their chemical and physical stability. In addition, Bonferani et al. (1995) pointed out that there were relationships between drug releases from gel matrices by a mechanism of gel erosion and viscoelastic properties.

Recently, carbopol, a synthetic polymer, is often used as a component of drug delivery systems because it provides transparent and elegant gels with mucoadhesive behavior. Its rheological properties are usually explored by a technique of continuous shear that can deform the gel structure, thus the obtained data do not represent the intact gel structure.

A lot of researchers have tried to investigate the effect of viscosity obtained by continuous shear methods on drug release. Some of them found inverse relationships between viscosity of preparations and diffusion coefficients of diffusant consistent to the Stoke - Einstein equation ($D = k_BT/6\pi\eta R$ where D is the diffusion coefficient, k_B is the Boltzmann's constant, T is the absolute temperature, η is the viscosity and R is the radius of diffusant) (Colo et al., 1980; Realdon et al., 1998; Shin, Cho and Choi, 1999). Since viscoelastic properties were more related to the intact structure of products than the viscosity, the correlation of viscoelastic properties to release characteristics of drug should be more accurate.

In this study, the rheological properties of gel preparations using carbopol 940 as a gelling agent were determined by methods of continuous shear and dynamic shear. Piroxicam was used as a model drug for study of release characteristics.

There have been many studies on relationships between perceptual attributes and rheological parameters obtained by continuous shear technique. However, only a few studies were about the correlations between perceptual attributes and viscoelastic parameters (Wang, Kislalioglu and Breuer, 1999). Therefore, it would be interesting to investigate the perception of panelists on gel bases possessing different viscoelastic properties.

The purposes of this study were:

1. To determine the effect of aging time on viscoelastic properties of piroxicam gels using carbopol 940 as a gelling agent.
2. To determine the effect of formula compositions on viscoelastic properties of piroxicam gels using carbopol 940 as a gelling agent.
3. To determine the relationship between viscoelastic properties of carbopol 940 gel bases and diffusion coefficients of piroxicam in gel bases.
4. To determine the relationship between viscoelastic properties of carbopol 940 gel bases to perceptual attributes.

CHAPTER II

LITERATURE REVIEW

Linear Viscoelasticity (Rosen, 1993)

Scientists have traditionally dealt with two separate and distinct classes of materials: the viscous fluid and the elastic solid. Design procedures based on these concepts have worked pretty well because most traditional materials such as water, air, steel and concrete, at least to a good approximation, fit into one of these categories. The realization has grown, however, that these categories represent only the extremes of a broad spectrum of material response. Polymer systems fall somewhere in between, giving rise to some of the unusual properties of melts and solutions. Consequently, the word "viscoelastic" was created. It means the simultaneous existence of viscous and elastic properties within a material (Barnes, Hutton and Walters, 1989).

To visualize a viscoelastic response, two linear mechanical models are introduced to represent the extremes of the mechanical response spectrum. A spring represents a linear elastic or Hookean solid of which constitutive equation can be presented as follows:

$$\tau = G\gamma \tag{2.1}$$

where τ is the stress, G is the shear modulus and γ is the strain. Similarly, a linear viscous or Newtonian fluid is represented by a dashpot which constitutive equation can be explained as:

$$\tau = \eta\overset{\circ}{\gamma} \tag{2.2}$$

where η is the viscosity and $\overset{\circ}{\gamma}$ is the rate of strain.

The Hookean spring responds instantaneously to reach an equilibrium strain γ upon application of a constant stress τ_0, and the strain remains constant as long as the stress is maintained constant. Sudden removal of the stress results in instantaneous recovery of the strain. Doubling the stress on the spring simply doubles the resulting strain, so the spring is linear. In assuming that the spring instantaneously reaches an equilibrium strain under the action of a suddenly applied constant stress, the inertial effect is neglected.

If the constant stress τ_0 is suddenly applied to the dashpot, the strain increases with time assuming that the strain is zero when the stress is initially applied. Doubling the stress doubles the slope of the strain-time line at any time. So the dashpot is also linear.

Any combination of linear elements must be linear, so any models based on these linear elements, no matter how complex, represent only linear responses.

Dynamic Rheological Testing

The linear viscoelastic behaviors can be determined with dynamic and transient tests. The transient tests involve the imposition of a step change in stress (or strain) and the observation of the subsequent development in time of the strain (or stress). The dynamic tests involve the application of a harmonically varying strain or stress. Oscillation tests are dynamic methods for determining the rheological properties of the material in its rheological ground state. It does not alter the static structure of the materials (Korhonen et al., 2000). Consequently, these tests are used for study of pharmaceutical semi-solid dosage forms by many authors.

If a sinusoidal strain, γ, is applied to a purely elastic solid, the resulting stress, τ, is in phase with the strain which can be explained as follows:

$$\gamma = \gamma_o \sin \omega t \qquad (2.3)$$

Since $\tau = G\gamma$,

$$\tau = G\gamma_o \sin \omega t \qquad (2.4)$$

where γ_o is the amplitude of strain, ω is the angular frequency (rad/s) and t is the time (s). For a purely viscous fluid, however, the stress is 90° out of phase with the strain because the stress is proportional to the rate of strain rather than the strain.

$$\tau = \eta\overset{\circ}{\gamma} = \eta\omega\gamma_o \cos \omega t \qquad (2.5)$$

As it might be expected, viscoelastic materials exhibit some sort of intermediate response. This can be thought of as being a projection of two vectors, τ^* and γ^*, rotating in a complex plane. The angle between these vectors is the phase angle, δ, which is equal to 0° for a purely elastic material and 90° for a purely viscous material. It is customary to resolve the vector representing the dependent variable into components in phase (designated by a prime) and 90° out of phase (designated by a double prime) with the independent variable. In this example, the applied strain is the independent variable, so the stress vector (τ^*) is resolved into its in-phase (τ') and out-of-phase (τ'') components. In complex notation,

$$\tau^* = \tau' + i\tau'' \tag{2.6}$$

where i is the out-of-phase unit vector.

An in-phase or storage modulus (G') is defined as

$$G' = \frac{\tau'}{\gamma^*} \tag{2.7}$$

and an out - of - phase or loss modulus (G'') is defined by

$$G'' = \frac{\tau''}{\gamma^*} \tag{2.8}$$

The complex modulus (G*) is the vector sum of the in-phase and out-of-phase moduli as shown in Equation (2.9):

$$G^* = G' + iG'' = \frac{\tau^*}{\gamma^*} = \frac{\tau' + i\tau''}{\gamma^*} \tag{2.9}$$

The loss tangent ($\tan\delta$) is defined as:

$$\tan\delta = \frac{\tau''}{\tau'} = \frac{G''}{G'} \tag{2.10}$$

The G' represents the energy stored elastically in the material during its straining. Hence, G' is the "storage modulus". If the applied mechanical energy (work) is not stored elastically, it must be "lost" converted to heat through molecular friction, that is, viscous dissipation, within the material. It is represented by G'' which is known as the "loss modulus".

The instruments for dynamic/oscillating tests are dynamic oscillating type rheometer such as a controlled strain rheometer. The sample is deformed in shear strain by an oscillating driver, which may be either mechanical or electromagnetic in nature. The amplitude of the sinusoidal deformation is measured by a torque transducer. Most dynamic/oscillating rheometers are capable of operating over a wide frequency range (Nielsen, 1977).

Davis (1971) studied model ointments and creams by oscillatory methods, using the Weissenberg rheogoniometer and a digital transfer function analyzer. The obtained fundamental rheological parameters such as G' and G'' provided a useful consistency spectrum for characterization of pharmaceutical products.

The viscoelastic properties of dispersions of powdered zinc oxide in anhydrous lanolin, and of colloidal sulfur in anhydrous lanolin were investigated by Radebaugh and Simonelli (1985). The G', G'' and tan δ were determined as a function of shear frequency, temperature and volume fraction of powder. The constitutive mathematical models to predict the mechanical behavior of solid-filled polymeric materials were proposed. These models were useful in explaining differences in viscoelastic behaviors of powder-filled semi-solids due to surface characteristics of the fillers.

Oscillatory parameters (G', $G''$and δ) of 20.0 %w/w poloxamer 407 thermoreversible gels with and without 10.0 % morphine acetate were studied (Dumortier et al., 1991). The viscoelastic properties of the samples were greatly influenced by temperature. The temperature interval corresponding to the sol-gel transition ranged between 22-25 °C and between 23-26 °C for the gel with and without morphine acetate, respectively. Edsman, Carlfors and Petersson (1998) found that an increase in concentration of poloxamer 407 resulted in a slight increase in G' of ophthalmic gels and a decrease in sol-gel transition temperature. The contact time increased with increasing concentration of poloxamer which could be explained and correlated with the viscoelasticity of poloxamer solution/gel mixed with simulated tear fluid.

Manufacturing procedures can affect the viscoelastic parameters as well (Segers, Zatz and Shah, 1997). Phenol ointments manufactured with different procedures including slow cooling, slow mixing (SCSM); slow cooling, fast mixing (SCFM); fast cooling, slow mixing (FCSM); and fast cooling, fast mixing (FCFM) were examined. The rank order of tan δ values was similar to that of release data which was SCSM < SCFM < FCSM < FCFM.

Korhonen et al. (2000) studied the effect of surfactant on the rheological properties of model cream formulae. The model cream containing polyethylene glycol 10 soya sterol and sorbitan trioleate possessed the greatest elasticity with the greatest G'. It was also presumed to be able to maintain structural stability and resistance to external forces for longer periods of time.

In addition, the oscillatory rheometry was used for characterization and selection of topical bioadhesive, chlorhexidine-containing semi-solid formulations for clinical evaluation (Jones, Woolfson and Brown 1998). Kantaria, Rees and Lawrence (1999) studied the effect of formula compositions on the viscoelasticity of gelatin-containing microemulsion based organogels (MBGs). They were capable of conducting electricity and had been successfully employed in the study of iontophoretic delivery of sodium salicylate through excised pig skin. The authors used a CarriMed CSL 100 controlled stress rheometer for determination of G' and G''. Bonferoni et al. (1995) also found that the oscillatory tests provided the reliable and complete information about polymer network structure. Tests are therefore especially suitable for characterizing polymer and polymer-solvent properties relevant to matrix systems which affected drug release.

Carbopols

Recently, polymers have been used extensively in the formulation and manufacture of pharmaceutical dosage forms because they satisfy a number of unique needs such as lowering surface tension, thickening, stabilization, and so on. Their wide ranging physical/chemical properties and lack of reactivity, taste, and irritation make them preferred excipients for formulating dosage forms as well as advanced dosage delivery systems such as topical, oral, and nasal controlled-release dosage forms (Lieberman, Rieger and Banker, 1998).

One kind of polymers which is more favorable for drug delivery system development is "carbopols". Carbopols are highly soluble polymers of acrylic acid cross-linked with allyl ethers of pentaerythritol or sucrose to form high molecular weight anionic hydrophilic polymers. They swell rapidly without heat with highly efficient thickening and provide sparkling clear gels possessing the plastic behavior. In acid forms, carbopols do not swell significantly due to limited solubilizing power of carboxylic acid groups. When solubilized, carbopols form a three-dimensional microgel structures.

There are two techniques for solubilization of carbopols (Laba, 1993):

1. Neutralization.

This technique is most often used to convert carbopols to salt forms. The selection of neutralizing agent is critical since the salt formed must be soluble in the solvent used. Divalent bases should be avoided to prevent insoluble salts formed. However, the over neutralization results in viscosity loss.

The enhancing solubility of neutralization technique is achieved by the repulsion of like anionic charges resulting in rapidly uncoiled chains, and instantaneous thickening.

2. Hydroxyl donor.

An addition of a hydroxyl donor results in thickening due to hydrogen bonding between hydroxyls and polymer carboxyl groups. Polyhydroxy and polyethoxy reagents in the formulation such as ethoxylated nonionic surfactants and polyols may undergo hydrogen bonding with unneutralized carbopols. Its thickening process is time dependent and can take up to 5 minutes to several hours. The presence of nonionic surfactant in formulation may increase viscosity. However, functional properties such as viscosity build-up may differ due to the use of alternative solvent. This technique is rarely used as the primary mechanism to solubilize carbopols.

Carbopols were introduced in the mid-to-late 1950s by B.F. Goodrich Co. The synthetic nature of these polymers, which allows close quality control and provides marked thickening and suspending properties at relatively low concentrations, has led to their wide usage in the pharmaceutical and cosmetic industries (Barry and Meyer, 1979). In addition, they are quite stable to heat, do not support bacterial or fungal growth, and are neither toxic nor irritating. Thus, carbopols have been used in gel formulations for topical use by several workers (Adams and Davis, 1973; Macedo, Block and Shukla, 1993; Ho et al., 1994; Lieberman, Rieger and Banker, 1998; Peppas et al., 2000). Recently, carbopols have been used as mucoadhesive polymers. They can prolong the contact time between a dosage form and adsorbing mucus membrane (Chu et al., 1992; Tamburic and Craig, 1995; Peppas et al., 2000); therefore, they can improve drug bioavailability.

Diffusion (Martin, 1993)

Diffusion is defined as a process of mass transfer of individual molecules of a substance, brought about by random molecular motion, and associated with a concentration gradient. Flow of molecules through a barrier such as a polymeric membrane is particularly convenient for diffusion process study. The passage of matter through a barrier may occur by simple molecular permeation or by movement through pores and channels. Molecular diffusion or permeation through nonporous media depends on dissolution of the permeating molecule in the bulk membrane. The diffusion through solvent-filled pores of membrane is influenced by the relative sizes of the penetrating molecules and the diameter of the pores.

Fick's First Law. The amount, M, of material flowing through a unit cross-section, A, of a barrier in a unit time, t, is known as flux, J.

$$J = \frac{dM}{Adt} \tag{2.11}$$

The flux in turn is proportional to the concentration gradient, dC/dx:

$$J = -D\frac{dC}{dx} \tag{2.12}$$

in which D is the diffusion coefficient of a penetrant (also called the diffusant) in cm^2/s, C is concentration in g/cm^3, and x is the distance in cm of movement perpendicular to the surface of the barrier. In Equation (2.11), the mass, M, is usually given in grams or moles, the barrier surface, A, in cm^2, and the time, t, in seconds. Thus, the units on J are $g\ cm^{-2}s^{-1}$. The SI units of kilogram and meter are sometimes used, and the time may be given in minutes, hours, or days. The negative sign in Equation (2.12) signifies that diffusion occurs in a direction (the positive x direction) opposite to that of increasing concentration. That is to say diffusion occurs in the direction of decreasing concentration of diffusant.

The diffusion constant or diffusivity as it is occasionally called does not ordinarily remain constant, for its value may change at higher concentrations. D is also affected by temperature, pressure, solvent properties, and the chemical nature of the diffusant. Therefore, D is referred to more correctly as a diffusion coefficient rather than as a constant. Equation (2.12) is known as Fick's first law.

Fick's Second Law. One often wants to examine the rate of change of diffusant concentration at a point in the system. An equation for mass transport that emphasizes the change in concentration with time at a definite location rather than the mass diffusing across a unit area of barrier in unit time is known as Fick's second law. However, this expression is not usually needed in pharmaceutical problems of diffusion.

If a diaphragm separating two compartments of a diffusion cell has a cross-sectional area, A, and thickness, h, and if the concentrations in the membrane on the donor and receptor sides are C_1 and C_2, respectively, the first law of Fick may be written as:

$$J = \frac{dM}{Adt} = \frac{D(C_1 - C_2)}{h} \tag{2.13}$$

in which $(C_1 - C_2)/h$ approximates dC/dx. The gradient $(C_1 - C_2)/h$ within the diaphragm must be assumed to be constant for a quasi-stationary state to exist. Equation (2.13) presumes that the aqueous boundary layers on both sides of the membrane do not significantly affect the total transport process.

The concentrations C_1 and C_2 within the membrane are not ordinarily known but can be replaced by the partition coefficient multiplied by the concentration C_d on the donor side or C_r on the receiver side. The distribution or partition coefficient, K, is given by

$$K = \frac{C_1}{C_d} = \frac{C_2}{C_r} \tag{2.14}$$

Hence,

$$\frac{dM}{dt} = \frac{DAK(C_d - C_r)}{h} \tag{2.15}$$

and, if a sink condition holds in the receptor compartment, i.e, $C_r \cong 0$,

$$\frac{dM}{dt} = \frac{DAKC_d}{h} = PAC_d \tag{2.16}$$

in which

$$P = \frac{DK}{h} \tag{2.17}$$

where P is the permeability coefficient. Integrating Equation (2.16) yields.

$$M = PAC_d\,t \tag{2.18}$$

providing that C_d remains relatively constant. It is noteworthy that the permeability coefficient, also called the permeability has a unit of linear velocity (cm/s). The determination of permeability is useful when it is not possible to determine D, K, or h independently. It is relatively easy to calculate P from the slope of a linear plot of M versus t as presented in Equation (2.18).

Drug delivery from topical formulations for both local and systemic effects essentially involves passive diffusion of the drug through the skin. The diffusion of a drug molecule from a vehicle into and across the skin is controlled by physicochemical factors sensitive to the molecular properties of the permeant, the vehicle, and the membrane (Osborne and Amann, 1990).

A theoretical basis for the study of release kinetics of drugs from both suspension and solution ointments, providing that the release from the vehicle is rate-limiting, was established by Higuchi. Higuchi (1961) first depicted the situation in which the ointment vehicle is initially saturated with solute, with excess solute uniformly suspended as tiny particles. The exact assumptions for the derivation of the time dependency of release are as follows:

1. The particles are present in a fine enough state so that the dissolution of the particles in not rate-limiting.
2. Q, which is the total concentration (mass/volume) of dissolved and undissolved drug, is much greater than C_S, the solubility (mass/volume) of the drug in the ointment.
3. A sink condition prevails at the ointment-receiver phase interface.
4. Release occurs through a planar surface.
5. There is no significant boundary layer adjacent to the ointment (assumed implicitly).

6. Quasi-steady-state diffusion exists between the dissolution interface at the edge of the particle field and the interface with the sink.

7. Although it is not explicitly stated, the model is semi-infinite, as in the original derivation no limit was placed on how far the boundary could recede.

An equation describing the release of solute was derived and obtained as:

$$M = \sqrt{2DC_S\left(Q - \frac{C_S}{2}\right)t} \tag{2.19}$$

After differentiation with time, an expression for the instantaneous rate of release is obtained.

$$\frac{dM}{dt} = \frac{1}{2}\sqrt{\frac{D(2Q - C_S)C_S}{t}} \tag{2.20}$$

when Q >> C_S, the amount of drug released into a sink bears the following relationship to time:

$$M = \sqrt{2QDC_S t} \tag{2.21}$$

and the rate becomes

$$\frac{dM}{dt} = \sqrt{\frac{QDC_S}{2t}} \tag{2.22}$$

Equation (2.21) predicts that a plot of the amount of drug released (per unit area) versus the square root of time should be linear, whereas Equation (2.22) predicts that the rate of drug release is proportional to the reciprocal of the square root of time.

Higuchi (1962) proposed a relationship characterizing the release of drug from "solution ointment", i.e., no excess solid drug, from a planar surface directly into a diffusional sink. Providing the diffusion of drug to the releasing interface being the rate-limiting step, the following mathematical description of the process can be presented:

$$M = hC_0 \left[1 - \frac{8}{\pi^2} \sum_{m=0}^{\infty} \frac{\left[\exp\left[-\frac{D(2m+1)^2 \pi^2 t}{4h^2} \right] \right]}{(2m+1)^2} \right] \tag{2.23}$$

In this expression, h is the thickness of the ointment phase and C_0 is the initial drug concentration in the ointment. The following simplified equation closely describes diffusion for the first 30 % of release.

$$M = 2C_0 A \sqrt{Dt/\pi} \tag{2.24}$$

The solutions to the release of drug from "solution ointment" showed in Equations (2.23) and (2.24) assume a semi-infinite geometry for the ointment phase. In practice, the amount of drug released is proportional to the square root of time for up to 30 % of total release.

Sensory Evaluation

Sensory evaluation is a growing discipline in the cosmetic and personal care product industries today. Having its root in the food industry where most of the original methodology was developed, sensory evaluation was challenged by applying these principles to skin care, hair care, fragrance, etc. Water content, pH, viscosity and active ingredient levels of cosmetic and personal care products have been traditionally controlled. Some companies have even paid cursory attention to color, fragrance, odor, skinfeel, etc. In fact, sensory characteristics of a skin care product are much more important and are worthy of much more attention at the quality control level than they usually were. This is because a motivation for purchasing a specific cosmetic or personal care product is influenced by senses of consumers. Color, fragrance and texture are key elements stimulating the desire to buy. The sensory properties of skin care products are the first signals consumers receive regarding product performance, and they are often the most important reason for purchase (Close, 1994).

For skin care products, an important group of perceptions is "touch". The sense of touch can be divided into "somesthesis" (tactile sense, skinfeel) and "kinesthesis" (deep pressure sense or proprioception), both of which vary in physical pressure. The surface nerve endings are responsible for the somesthetic sensations called touch, pressure, heat, cold, itching, and tickling. Deep pressure, kinesthesis, is felt through nerve fibers in muscles, tendons, and joints whose main purpose is to sense the tension and relaxation of muscles. Kinesthetic perceptions corresponding to the mechanical movement of muscles (heaviness, hardness, stickiness, etc.) result from stress exerted by muscles of the hand, jaw, or tongue and the sensation of the resulting strain (compression, shear, rupture) within the sample being handled, masticated, etc. The surface sensitivity of the lips, tongue, face, and hands is much greater than that of other areas of the body, resulting in an ease of detection of small force differences, particle size differences, and thermal and chemical differences from hand and oral manipulation of products (Meilgaard, Civille and Carr, 1991).

Sensory data usually fall under one of the following headings:

- Nominal data: items examined are placed in two or more groups which differ in name but neither obey any particular order nor any quantitative relationship, for example: the numbers carried by football players.
- Ordinal data: a panelist places the items examined into two or more group which belong to an ordered series, for example: slight, moderate, strong.
- Interval data: panelists place the item into numbered groups separated by a constant interval, for example: three, four, five, six.
- Ratio data: panelists use numbers which indicate how many times the stimulus in question is stronger (or saltier, or more irritating) than a reference stimulus presented earlier.

The nominal data contain the least information. The ordinal data carry more information and can be analyzed by most non-parametric statistical tests. The interval and ratio data are even better; they can be analyzed by all non-parametric and often by parametric methods. The ratio data are preferred by some researchers because they are free from end-of- scale distortions. In practice, the combination of ratio and interval data is often used by dividing the ratio data into different intervals because it is easier to collect data, yet results evaluated are similar to the non-divided ratio data.

The most used methods for measuring sensory response to a sample are, in order of increasing complexity:

- Classification :items evaluated are sorted into groups which differ in a nominal manner, for example, marbles sorted by color.
- Grading : time-honored methods used in commerce which depend on expert graders who learn their craft from other grader, for example, "USDA Choice" grade of meat.
- Ranking : samples (usually three to seven) are arranged in order of intensity or degree of some specified attributes; the scale is used in ordinal.
- Scaling : subjects who have been trained judge the sample by referring to a scale of numbers (often from 0 to 10); category scaling yields ordinal data or sometimes interval data, linear scaling usually yields interval data, and magnitude estimation yields ratio data.

Correlations between ease of rubbing of white soft paraffin and discrete viscoelastic parameter, and between ease of rubbing of white soft paraffin and continuous shear yield stresses were found (Barry and Grace, 1971). The discrete viscoelastic parameters studied included initial elastic compliance and residual viscosity obtained by analysis of creep parameter curves. Twelve untrained subjects were asked to rank the materials in order of ease of rubbing. A point system was used; 4 points for the easiest, and 0 point for the most difficult. The mean of rated points was analyzed for correlation studies.

Barry and Meyer (1973) used two preference scoring techniques to assess spreadability of a series of preparations. Technique I was a five-point semantic hedonic scale. The rating scores are shown as follows:

Score	Sensation during spreading
1	Too fluid, disagreeable
2	Fluid but all right
3	Agreeable
4	Stiff but all right
5	Too stiff, disagreeable

technique II was a five-point facial hedonic scale. The panel members were asked to indicate the face that most closely agreed with their feeling with regard to the spreadability of each sample. The faces depicted the degree of "agreeable" or "disagreeable" experienced by the subject, the neutral face being the median interval. Technique II was developed to overcome problems in semantics, which could arise with the use of descriptive rating scales experienced in technique I. However, technique II was considered by the panelists to be more sensitive than technique I when it was used for tasting tests.

The sensory firmness and viscousness was found to change continuously depending upon changes in hardness and viscosity of cream base measured instrumentally (Morosawa et al., 1974). The sensory evaluation was performed by 10 trained panelists using standard references. The relationships between firmness and hardness, and between viscousness and viscosity were indicated by their correlation coefficients (r). Changes in skin friction coefficient immediately after using an emollient measured instrumentally were found to be inversely proportional to the subjective after-feel of greasiness; that was the greater the skin friction coefficient, the less greasy the product was perceived (Nacht et al., 1981). However, viscoelastic properties of model creams and lotions investigated by Wang, Kislalioglu and Breuer (1999) did not seem to have a major effect on their tactile perceptual attributes evaluated by eight untrained women. In addition to the rheological parameters, skin hydration measured instrumentally was also found to correlate with subjective assessment of volunteers. Bimczok et al. (1994) assessed the efficacy of skin care products by objective and subjective methods. A total of 368 healthy female volunteers were asked to evaluate two different all-purpose skin care creams at eleven centers in Germany. Measurement of skin hydration with a corneometer demonstrated a fundamental improvement of skin condition and the skin hydration measured could be correlated with subjective assessment by the volunteers. Results were statistically highly significant, and there was a fair correlation between the different centers.

Panelists, trained or untrained, can play an important role in the results of skinfeel attributes obtained. Aust et al. (1987) evaluated skinfeel attributes of products perceived by 9 trained descriptive panelists. They were capable of identifying and defining attributes of test products through reference materials, and were able to reproducibly measure the relative intensities of product attributes on a numerical scale. The data for each attribute evaluated by analysis of variance (ANOVA) and least significant difference test (LSD) was performed whenever significant product differences were observed.

S - Replicated Latin Square Experimental Design (Dean and Voss, 1999)

The Latin square designs are often used in experiments where the time effect is thought to have a major effect on the response. Treatments allocated to subjects are sequential as a function of time. One requirement of the Latin square design is that the population must distribute normally. Since number of subjects and number of treatments must be equal in the case of a single Latin square, a multiple Latin square has an advantage in that the normal distribution of population can be made by increasing the number of subjects while the number of treatments remains the same. An S-replicated Latin square is used to represent the multiple Latin square with S replications.

For example, 2-replicated Latin squares can be obtained by using two 3 × 3 Latin squares in order to get normally distributed population. The 3 × 3 Latin square is presented as follows:

column

	A	B	C
row	B	C	A
	C	A	B

Columns represent treatments and time sequence, while rows represent subjects.

The 2-replicated Latin square presented below shows arrangements of subjects and treatments.

column

	A	B	C
	B	C	A
row	C	A	B
	A	B	C
	B	C	A
	C	A	B

Details of the analysis of variance for S – replicated Latin square design is shown in Table 2.1 with the following assumptions:

Null hypothesis, **Ho** : $\mu_{T1} = \mu_{T2} = \mu_{T3} = \ldots = \mu_{Ti}$

Alternative hypothesis, **Ha** : at least two of the μ_{Ti}'s differ.

where μ_{Ti} is the treatment mean of the i^{th} treatment.

A test of the null hypothesis against the alternative hypothesis is given by a decision rule; that is, Ho would be rejected if $F_{calc} > F_{(\upsilon-1),(\upsilon S-2)(\upsilon-1)}$ for a chosen significant level α. If any treatment means are significantly different from any of the others, multiple comparisons such as Tukey's method of all pairwise comparisons can be applied to determine which pair is different. In Tukey's method, critical coefficients, Q_{α}, are used to indicate the difference and the minimum significant difference for pairwise difference (HSD) is

$$\mathrm{HSD} = Q_{\alpha}\sqrt{\frac{\mathrm{MSE}}{n}} \tag{2.25}$$

where MSE is the mean square error obtained from the ANOVA table and n is number of subjects.

Table 2.1 ANOVA table of S - replicated Latin square design

Source of variation	**df**	**SS**	**MS**	**Ratio**
Total (TO)	$\upsilon^2 S - 1$	$\sum\sum\sum Y_{hqi}^2 - G^2/\upsilon^2 S$		
Row (Subject : R)	$\upsilon S - 1$	$1/C\sum B_h^2 - CT$		
Column (Time : C)	$C - 1$	$1/\upsilon S \sum C_q^2 - CT$		
Treatment (TMT)	$\upsilon - 1$	$1/\upsilon S \sum T_i^2 - CT$	SSTMT/df	STMT/MSE $= F_{calc}$
Error (E)	$(\upsilon S - 2)(\upsilon - 1)$	SSTO - SSR - SSC - SSTMT	SSE/df	

Where df is degree of freedom,

SS is sum square,

MS is mean square,

υ is number of treatments,

S is number of replications,

C is number of times (column),

b is number of subjects (row) ($b = \upsilon$),

h is row block (from the 1st to the bth block),

q is column block (from the 1st to the cth block),

i is treatment (from the 1st to the υth treatment),

Y_{hqi} is the observation on the hth row block, qth column block, ith treament,

T_i is sum of observations on the ith treament,

B_h is sum of observations on the hth row block,

C_q is sum of observations on the qth column block,

G is grand total,

CT is correction term = $G^2/\upsilon^2 S$.

CHAPTER III

MATERIALS AND METHODS

Materials

Piroxicam, Lot No. 931052, S. Tong Chemicals Co., Ltd.

Carbopol 940, Lot No. 1500, Goodrich Co., Ltd.

Glycerin, Lot No. 12-00, Srichand United Dispensary Co., Ltd.

Methyl paraben, Lot No. MFB 47/947, Srichand United Dispensary Co., Ltd.

Propyl paraben, Lot No. LI 2011, Srichand United Dispensary Co., Ltd.

Propylene glycol, Lot No. PL90/925, Srichand United Dispensary Co., Ltd.

Sodium chloride, Lot No. K28431204045, Merck.

Triethanolamine, Lot No. TF 15/912, Srichand United Dispensary Co., Ltd.

Disodium hydrogen phosphate, Lot No. FOJ067, APS Finechem.

Potassium dihydrogen phosphate, Lot No. 1890I 100, Carlo Erba.

Light mineral oil (Baby oil®), Lot No. 061001B20140, Johnson and Johnson.

White soft petrolatum, Lot No. VC 130/790, Srichand United Dispensary Co., Ltd.

Cellulose dialysis tubing, Molecular weight cut-off 12,000, Lot No. 28 H0141, Sigma.

Equipment

Analytical balance, Model PC 440, Mettler.

Analytical balance, Model 1615 MP, Sartorius.

pH meter, Model SA 520, Orion Research Inc.

UV Spectrophotometer, Model 7800, Jasco Corp.

Modified Franz diffusion cell apparatus.

Disposable needles and syringes.

Rheometer model ARES, Rheometric Scientific Inc.

Methods

1. Preparations of 1.0 %w/w Piroxicam Gel.

Compositions of 1.0 %w/w piroxicam gel formulae are presented in Table 3.1.

Table 3.1 1.0 %w/w piroxicam gel formulae[a]

Formula[b]	Piroxicam (g)	Carbopol 940 (g)	Paraben Conc.[c] (ml)	PG[d] (ml)	NaCl (g)	Glycerin (ml)	TEA[e] (ml)
C.4	1.0	0.4	1.0	10.0	-	-	2.8
C.6	1.0	0.6	1.0	10.0	-	-	3.2
C.6/S.09	1.0	0.6	1.0	10.0	0.09	-	3.2
C.6/S.9	1.0	0.6	1.0	10.0	0.9	-	3.2
C.6/G5	1.0	0.6	1.0	10.0	-	5.0	3.2
C.6/G10	1.0	0.6	1.0	10.0	-	10.0	3.2
C.6/G15	1.0	0.6	1.0	10.0	-	15.0	3.2
C1	1.0	1.0	1.0	10.0	-	-	4.0
C1/S.09	1.0	1.0	1.0	10.0	0.09	-	4.0
C1/S.9	1.0	1.0	1.0	10.0	0.9	-	4.0

[a] All piroxicam gels were adjusted to 100 g by using purified water.

[b] C is carbopol 940.
S is sodium chloride.
G is glycerin.
Numerical code is the concentrations in %w/w or %v/w.

[c] Paraben concentrate is a mixture of 20.0 %w/v methyl paraben and 2.0 %w/v propyl paraben dissolved in propylene glycol.

[d] Propylene glycol.

[e] Triethanolamine.

There were 3 steps to prepare 1.0 %w/w piroxicam gels.

1. Preparation of piroxicam solution.

One gram of piroxicam powder was dispersed in a mixture of 10 ml propylene glycol and a portion of water, then 2 ml of triethanolamine was added to the dispersion and it was stirred until the dispersion became clear. Paraben concentrate, sodium chloride (in the case of formulae C.6/S.09, C.6/S.9, C1/S.09 and C1/S.9) and glycerin (in the case of formulae C.6/G5, C.6/G10 and C.6/G15) were added to the clear solution and stirred until homogeneous.

2. Preparation of carbopol 940 gel bases.

Carbopol 940 powder was dispersed in an appropriate amount of water with continuous stirring until uniform. An accurate amount of triethanolamine was slowly added to the dispersion with continuous stirring thus resulting in a stiff gel.

3. Preparation of piroxicam gel.

The piroxicam solution was slowly incorporated to the carbopol 940 gel base and the mixture was stirred continuously until it was homogeneous. Purified water was added to make the total weight of 100 g with continuous stirring. The gel was stored in an air-tight glass jar wrapped with aluminium foil to protect from light.

2. Preparation of Carbopol 940 Gel Bases.

Compositions of carbopol 940 gel bases formulae are presented in Table 3.2.

Table 3.2 Carbopol 940 gel base formulae[a]

Formula	Carbopol 940 (g)	Paraben Conc[b]. (ml)	NaCl (g)	Glycerin (ml)	TEA[c] (ml)
T1	0.3	1.0	-	-	0.3
T2	0.4	1.0	-	-	0.4
T3	0.6	1.0	-	-	0.6
T4	0.6	1.0	0.9	-	0.6
T5	0.6	1.0	-	30	0.6
T6	1.0	1.0	-	-	1.0

[a] All gel bases were adjusted to 100 g by using purified water.

[b] Paraben concentrate.

[c] Triethanolamine.

The preparation procedure of carbopol 940 gel bases was as follows:

1. Carbopol 940 powder was dispersed in an appropriate amount of water with continuous stirring until uniform. An accurate amount of triethanolamine was slowly added to the dispersion with continuous stirring thus resulting in a stiff gel.

2. Paraben conconcentrate, sodium chloride (in the case of formula T4) and glycerin (in the case of formula T5) were added to the carbopol 940 gel base and stirred until homogeneous.

3. Purified water was added to make the total weight of 100 g with continuous stirring. The gel was stored in an air-tight glass jar wrapped with aluminium foil to protect from light.

3. Analysis of Content Uniformity of Piroxicam Gels.

Drug content of the gels was determined by dissolving an accurate quantity of gel (about 0.02 g) using 20.0 %v/v propylene glycol in pH 7.4 isotonic phosphate buffer. The solution was transferred to a 10 ml volumetric flask and the volume was then adjusted. The composition of pH 7.4 isotonic phosphate buffer is shown in Appendix I. The solution was quantitatively transferred to a volumetric flask and an appropriate dilution was made with 20.0 %v/v propylene glycol in pH 7.4 isotonic phosphate buffer. The solution was analyzed spectrophotometrically for piroxicam content using a wavelength of 355 nm and having 20.0 %v/v propylene glycol in pH 7.4 isotonic phosphate buffer as a blank. The contents of piroxicam were calculated from a calibration curve.

All samples were analyzed in triplicate. Only samples with piroxicam content that lied within 100 ± 10 % of the labeled amount were accepted.

4. Calibration Curve Determination.

A stock solution was prepared by weighing accurately 0.01 g piroxicam powder in 100 ml volumetric flask. The 20.0 %v/v propylene glycol in pH 7.4 isotonic phosphate buffer was used as a solvent and was used to adjust the volume to 100 ml. The stock solution 0.5, 2, 4, 6, 8 and 10 ml was pipetted and transferred to 50 ml volumetric flasks then, the volumes were adjusted to 50 ml by using the 20.0 %v/v propylene glycol in pH 7.4 isotonic phosphate buffer resulting in piroxicam concentrations of 1, 4, 8, 12, 16 and 20 μg/ml, respectively. The standard solutions were analyzed spectrophotometrically for piroxicam at 355 nm in triplicate. The absorbance of piroxicam versus known concentrations were fit to a straight line using the linear regression. The concentrations of the piroxicam samples were calculated by using this linear equation.

5. pH Measurement.

The pH of all preparations were measured by using Orion pH-meter. The electrode was immersed into the gel preparation. The pH value was read when it appeared constant.

6. Solubility Determination of Piroxicam in Vehicles of Formulae C.6 and C.6/G15.

The saturated concentrations of piroxicam in vehicles of formulae C.6 and C.6/G15 were determined as follows. An excess amount of piroxicam was added into a screw–capped test tube containing 10 ml of the vehicles of which compositions were similar to those of formulae C.6 and C.6/G15 except that carbopol 940 was excluded. The test tubes were tightly sealed and wrapped with aluminium foil. They were slowly and continuously turned upside-down in a water bath controlled at 33 ± 1 °C. The mixtures were allowed to equilibrate for 48 hours. An aliquot portion of supernatant was diluted with an appropriate amount of 20.0 %v/v propylene glycol in pH 7.4 isotonic phosphate buffer and its absorbance was measured spectrophotometrically at a wavelength of 355 nm. The piroxicam concentrations were determined by using the calibration curve performed previously. The solubility of piroxicam in each vehicle was determined in 4 replications.

7. Rheological Property Measurements.

7.1 Dynamic strain sweep test.

The measurements were performed by a fluid rheometer using the cone and plate geometry with a cone angle of 0.04 radian and a diameter of 25 mm. The gap range was 0.051 ± 0.001 mm. The experiments were carried out at a frequency of 1.0 rad/s at 27 ± 1 °C. The initial and final strain values were set at 0.05 and 500%, respectively. Only formula C.6 was selected as a representative of all formulae and tested in this category.

The level of strain was determined in order to ensure that all dynamic measurements were made within the linear viscoelastic regime.

7.2 Dynamic frequency sweep test.

The measurements were performed by a fluid rheometer using the cone and plate geometry with a cone angle of 0.04 radian and a diameter of 25 mm. The gap range was 0.051 $\pm$ 0.001 mm. The experiments were carried out at a strain value below the critical strain. The studies of aging time and formula composition effects were performed at 27 $\pm$ 1 °C and the studies of diffusion and perceptual attributes were performed at 33 $\pm$ 1 °C. The initial and final frequencies were set at 100 and 0.1 rad/s, respectively. The value of strain used was chosen to be within the linear viscoelastic regime. In this case, G', G'' and tan δ were determined as a function of frequency.

7.3 Steady rate sweep test.

The measurements were performed by a fluid rheometer using the cone and plate geometry with a cone angle of 0.04 radian and a diameter of 25 mm. The gap range was 0.051 $\pm$ 0.001 mm. The experiments were carried out at 27 $\pm$ 1 °C for the effect of aging time and formula composition studies and at 33 $\pm$ 1 °C for the diffusion and perceptual attributes studies. The initial and final shear rates were set at 0.05 s^{-1} and 100 s^{-1}, respectively, for the effect of aging time, formula composition, and diffusion studies. Some perceptual attributes were studied at the initial and final shear rate of 0.05 s^{-1} and 100 s^{-1}, respectively while some were studied at 0.05 s^{-1} and 500 s^{-1}, respectively. In these cases, viscosity and shear stress were determined as a function of shear rate.

The determination of the rheological characteristics of all samples was performed by applying about 0.5 g of the samples to the lower plate of the rheometer. The gap between cone and plate was adjusted to 0.051 $\pm$ 0.001 mm. A thin layer of silicone oil was applied along the edges of the cone and plate device to prevent excessive solvent evaporation especially during low frequency scans. The rheological properties of all samples were measured in triplicate.

8. Aging Time Effect Study.

Formulae C.4, C.6, and C1 were selected as representatives of piroxicam gels. The rheological properties had been determined at different time periods from the gel preparation date until the date that the equilibrium of gel structures were reached. G', tan δ and viscosity were determined at 27 ± 1 °C (room temperature) by the method explained in 7.2 and 7.3.

9. Formula Composition Effect Study.

G', G'', tan δ, viscosity, and shear stress of all piroxicam gels were determined at 27 ± 1 °C. These studies were carried out by the method explained in 7.2 and 7.3.

10. Piroxicam Diffusion Coefficient Determination.

Gel formulae C.4, C.6, C1, C.6/S.09, C.6/S.9, C1/S.9, C.6/G10 and C.6/G15 were selected to investigate the relationship between viscoelastic properties and piroxicam diffusion coefficients in the gel preparations. The rheological parameters studied were G', G'', G^*, tan δ and viscosity, which had been determined at 33 ± 1 °C before the piroxicam release studies.

A semi-permeable cellulose membrane with a molecular weight cut-off of 12,000 was soaked overnight in pH 7.4 isotonic phosphate buffer solution. The membrane was washed with purified water, blotted with a tissue paper, and placed between the donor and receptor units of a modified Franz diffusion cell. The attachment of the donor and receptor units was locked by using a metal clamp. The receptor part was filled with about 14 ml pH 7.4 isotonic phosphate buffer solution maintained at 37 ± 1 °C by means of the water jacket around the receiving cell. The exact volume of receptor part was calculated from weight and density of distilled water at corresponding temperature. The system was equilibrated for 30 minutes and any air bubbles in receiving solution were removed. Then, about 5 g of the gel preparation was placed over the membrane in the donor part. An accurate amount of the receiving solution, 5 ml, was withdrawn at 15, 30, 60, 90, 120, 150 and 180 minutes, respectively. The volume of the receiving solution was maintained by replacing the amount withdrawn with an equal volume of pH 7.4 isotonic phosphate buffer solution. The receiving solution was kept well stirred with a magnetic stirrer throughout the time of diffusion studies. All piroxicam release characteristic studies were carried out in triplicate.

The receiving solution withdrawn was analyzed spectrophotometerically at a wavelength of 355 nm. The concentration of piroxicam in each sample was calculated by referring to the previously constructed calibration curve described in the calibration curve determination part. The amount of piroxicam released was calculated by multiplying the concentration obtained by the exact receiving volume. Diffusion coefficients were calculated from the slope of cumulative amount released versus square root of time plot.

11. Perceptual Attributes Study.

The protocol of this study was approved by the Ethics Committee of the Faculty of Pharmaceutical Sciences, Chulalongkorn University.

11.1 Subjects.

Subjects consisted of 30 healthy panelists. Criteria for subject recruitment were as follows:

1. Interest in full participation in the rigors of practice and ongoing work phase of the panel.
2. Availability to participate in all phase of the panel's work.
3. Generally good health and no illness related to the sensory properties being measured such as central nervous system disorders or reduced nerve sensitivity due to the use of drugs affecting the central nervous system.
4. No hypersensitivity reaction to any formula compositions.
5. Ability to detect and describe differences and ability to apply abstract concept which can be determined through a series of tests including:
    - A set of prescreening questionnaires as shown in Appendix VII indicating that the recruited candidates neither took any medicines nor had illnesses that could cause limited perception, were not hypersensitive to any formula compositions, were available for the training and test sessions, and could answer at least 80% of the questions in the prescreening questionnaires correctly.
    - A triangle test for recruiting candidates who could detect small product variables. A set of three coded samples (1, 2 and 3) was presented randomly to the

candidates as shown in Table 3.3. The candidates were then directed that two samples were identical and one was different and asked to examine each product from 1 to 3, respectively, and selected the odd sample. The candidates would have been recruited if their answers were correct. Although they failed in their first attempts, they might still be recruited if they could pass both of their second and third attempts.

Table 3.3 Coding of sample sets for prescreening purpose

Sample set number	**Rank order of samples to be examined**		
	1st	**2nd**	**3rd**
1, 7, 13, 19, 25, 31	T1	T3	T3
2, 8, 14, 20, 26, 32	T3	T1	T3
3, 9, 15, 21, 27, 33	T3	T3	T1
4, 10, 16, 22, 28, 34	T3	T1	T1
5, 11, 17, 23, 29, 35	T1	T3	T1
6, 12, 18, 24, 30, 36	T1	T1	T3

11.2 Training

An important aspect of any training sequence is to provide a structured framework for learning based on demonstrated facts and to allow the panelist to grow both in skill and confidence.

11.2.1 Terminology development and scaling.

The panelists were introduced to physical properties which influenced the perception of each product attribute. Definitions of perceptual attributes were also explained in Table 3.4. Reference products used for scaling the perceptual attributes are shown in Table 3.5.

11.2.2 Practice

The test process was explained to the panel. They were allowed to practice and memorize the scales by using the reference products. Then, the panel received 6 products to practice how to evaluate. The first set of products used to practice were fairly different in perceptual attributes. These included preparations T1, T2, T4, and T6. The second set of products used to practice possessed similar perceptual attributes, and these included preparations T2, T3, T5, and T6. The final set of products used to practice were all products to be tested, i.e., T1, T2, T3, T4, T5 and T6. During the training program, the panelists were allowed to discuss at the end of each session so that problems and controversies could be resolved.

Table 3.4 Definitions of perceptual attributes (Meilgaard, Civille and Carr, 1991)

Attribute Group	**Attributes**	**Descriptions**
Pick up	Firmness	Force required to fully compress the product between thumb and forefinger
	Stickiness	Force required to separate the fingers
	Peaking	Peak height after the fingers have been separated
Rub out	Wetness	Amount of water perceived while rubbing
	Spreadability	Ease of moving the product over the skin surface
	Absorbency	Number of rubs at which product loses wet and moist feeling
After feel	Tackiness	Force required to separate forefinger from the skin while trying to lift the finger from the skin
	Gloss	Degree of glitter perceived
	Amount of residue	Amount of remaining product perceived on the skin after absorption
	Liking	Degree of overall acceptance

Table 3.5 Scale of perceptual attributes evaluated of reference products (Meilgaard, Civille and Carr, 1991)

Attributes	Scale value	Reference Product	Manufacturer
Firmness	0	Baby Oil	Johnson & Johnson
	8.4	White Soft Petrolatum	Generic
Stickiness	0.1	Baby Oil	Johnson & Johnson
	8.4	White Soft Petrolatum	Generic
Peaking	0	Baby Oil	Johnson & Johnson
	9.6	White Soft Petrolatum	Generic
Wetness	2.2	White Soft Petrolatum	Generic
	9.9	Water	-
Spreadability	2.9	White Soft Petrolatum	Generic
	9.7	Baby Oil	Johnson & Johnson
Amount of residue	0	Untreated Skin	-
	8.8	White Soft Petrolatum	Generic

11.3 Sample evaluation.

Rank order of samples to be evaluated by the panelists were coded according to the 5-replicated Latin square design as shown in Table 3.6. Each panelist must evaluate the assigned set of samples 3 rounds.

Table 3.6 Coding of sample sets for panelist evaluation

Sample set number	Rank order of samples to be examined					
	1st	2nd	3rd	4th	5th	6th
1, 7, 13, 19, 25	T1	T2	T3	T4	T5	T6
2, 8, 14, 20, 26	T2	T3	T4	T5	T6	T1
3, 9, 15, 21, 27	T3	T4	T5	T6	T1	T2
4, 10, 16, 22, 28	T4	T5	T6	T1	T2	T3
5, 11, 17, 23, 29	T5	T6	T1	T2	T3	T4
6, 12, 18, 24, 30	T6	T1	T2	T3	T4	T5

The rheological properties including G', G'', G^*, tan δ, stress and viscosity of freshly prepared gel bases had been determined before their attributes were evaluated.

The panelists were asked to wash their hands and arms and dry them before the evaluation process. The sites of application which were forearms were carefully cleaned and dried between sample applications. Each panelist evaluated all samples independently and was not allowed to discuss anything during the entire evaluation process. The scores recorded could be any integers or fractions or decimals between 0 and 15 (0 = minimum score and 15 = maximum score). The answer sheets are shown in Appendix VII.

CHAPTER IV

RESULTS AND DISCUSSION

The main purposes of this study were to investigate the relationships of viscoelastic properties of carbopol 940 gel bases to piroxicam release characteristics through gel bases and perceptual attributes in subjects, therefore 1.0 %w/w piroxicam gels and carbopol 940 gel bases which possessed different viscoelastic properties were formulated.

1. Preparation of Test Products.

1.1 Preparations of 1.0 %w/w piroxicam gels

The 1.0 %w/w piroxicam gels were formulated using carbopol 940 as a gelling agent. Each formula contained different compositions to produce gels with different rheological properties.

Most of the preparations were transparent yellowish gels, except for the preparations containing sodium chloride (formula C.6/S.09, C.6/S.9, C1/S.09 and C1/S.9) which were slightly cloudy and became more fluid. The gels were yellowish as a result of the color of piroxicam.

Generally, in the manufacturing of a pharmaceutical product, the content uniformity of the product would be investigated as a part of quality assurance. The drug content of pioxicam gels was determined by the method described previously. The piroxicam concentration in every preparation was within ± 10 % of the labeled amount (Table 4.1). Therefore, they were accepted to use for further studies on release characteristics and rheological properties. Their pH values (Table 4.2) were slightly basic to provide a complete dissolution of piroxicam.

Table 4.1 Piroxicam content (mean ± SD) in gel preparations (n = 3)

Formula	Amount of piroxicam (mg/100 g)	%LA[a]
C.4	1.06 ± 0.02	105.86 ± 2.17
C.6	1.02 ± 0.03	101.90 ± 3.26
C.6/S.09	1.05 ± 0.02	104.87 ± 1.77
C.6/S.9	1.05 ± 0.01	104.78 ± 0.54
C.6/G5	1.00 ± 0.02	99.88 ± 1.57
C.6/G10	1.00 ± 0.04	99.65 ± 3.97
C.6/G15	1.00 ± 0.01	100.21 ± 0.65
C1	0.98 ± 0.00	98.06 ± 0.33
C1/S.09	1.02 ± 0.02	102.08 ± 2.06
C1/S.9	0.97 ± 0.02	97.20 ± 1.93

[a] Percent labeled amount.

Table 4.2 pH values of piroxicam gels

Formula	pH value
C.4	7.98
C.6	8.14
C.6/S.09	8.15
C.6/S.9	7.96
C.6/G5	8.18
C.6/G10	8.05
C.6/G15	8.16
C1	8.03
C1/S.09	8.05
C1/S.9	8.11

1.2 Preparation of carbopol 940 gel bases.

The carbopol 940 gel bases were used for perceptual attribute studies in subjects. All of them were transparent colorless gels except that the gel base T4 containing sodium chloride was slightly turbid.

The pH values of gel bases are shown in the Table 4.3. These pH values were adjusted to about 6 which was close to the pH value of normal human skin.

Table 4.3 pH values of carbopol 940 gel bases

Formula	pH value
T1	5.93
T2	6.10
T3	6.02
T4	6.03
T5	6.05
T6	5.99

2. Calibration Curve Determination.

The calibration curve of piroxicam in 20.0 %v/v propylene glycol in pH 7.4 isotonic phosphate buffer was constructed (Figure 4.1). Its linear equation obtained by linear regression method is shown as follows:

$$y = 0.0545x - 0.0141 \tag{4.1}$$

where y is the absorbance at the wavelength of 355 nm and x is piroxicam concentration (μg/ml).

The determination coefficient of the regression line (r^2) was 0.9998. This equation would be used for further calculations of piroxicam concentrations.

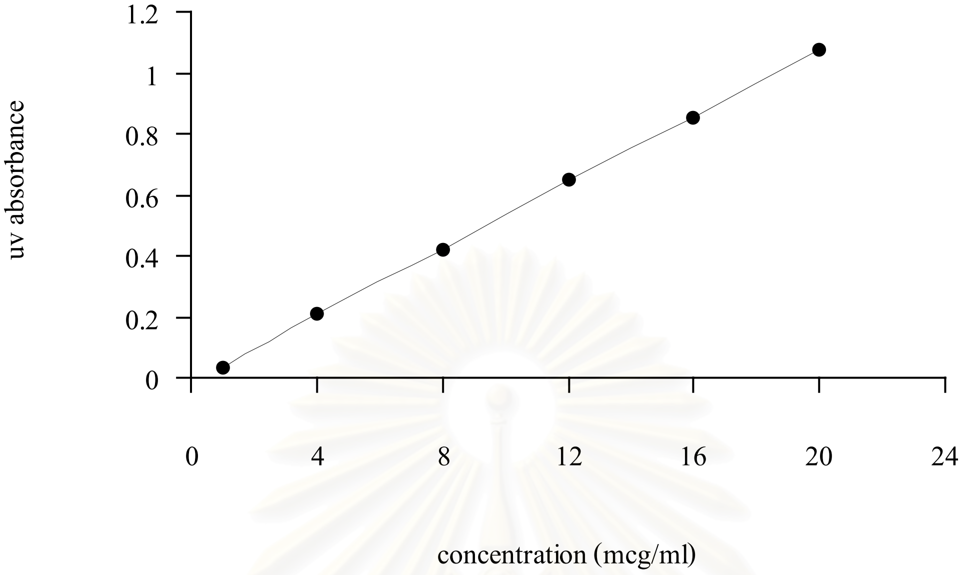

Figure 4.1 Calibration curve of piroxicam in 20.0 %v/v propylene glycol in pH 7.4 isotonic phosphate buffer at 355 nm (mean ± SD, n = 3).

3. Strain Sweep Test.

For dynamic measurements, the level of strain was determined at a fixed frequency in order to ensure that all dynamic measurements were carried out within a linear viscoelastic regime, of which viscoelastic parameters were independent of strain amplitude (Radebaugh and Simonelli, 1983). Because all preparations used the same gelling agent, only gel formula C.6 was initially selected as a representative for dynamic strain sweep test.

The result of strain sweep test of formulation C.6 is shown in the Figure 4.2. The storage moduli of formula C.6 were independent of strain up to a critical strain, i.e., 10 %strain. Beyond the critical strain level, the behavior of storage moduli was nonlinear and the moduli declined. From this result, the strain of 1% was chosen for subsequent dynamic tests.

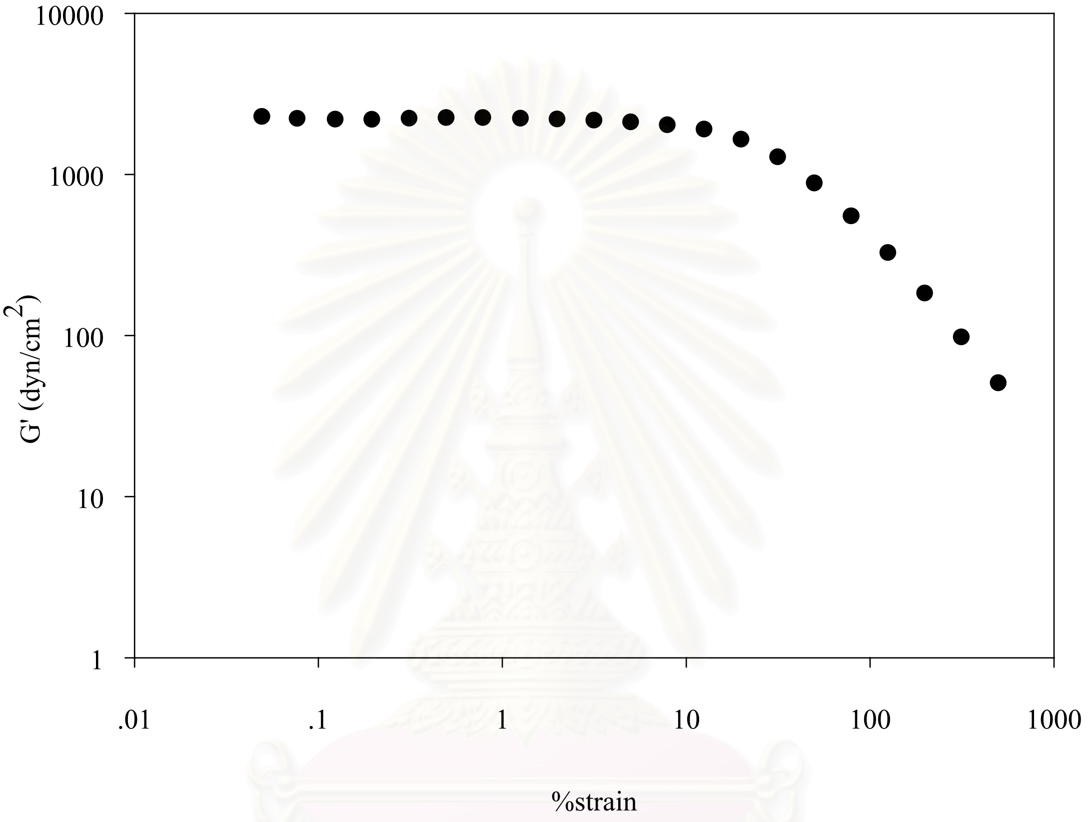

Figure 4.2. Double logarithmic plot of strain sweep test of piroxicam gel (formula C.6) at 27 °C. (mean ± SD, n = 3).

4. Effect of Light on Rheological Parameters.

The gel C.6 was selected as a representative because carbopol 940 concentration in this formula was in the middle range and its components were common to other formulae. It was stored in an air-tight colorless glass jar without wrapping with aluminium foil. Its rheological properties were examined at 2, 8 and 15 days, respectively. The rheological properties at initial time (at 0 day) were not observed since the significance of light effect was not expected. The storage moduli and viscosity decreased markedly after it had been prepared for 2 days but no change was noticed within 8-15 days as shown in Figures 4.3 and 4.4, respectively. These suggested that the structure of gel C.6 had altered and tended to lose its elastic solid properties within 8 days. It was possible that the alteration terminated or there might be slight change that could not be detected by the instrument. The tan δ values of gel C.6 changed slightly. This was not surprising since the decreasing values of G'' and G' were comparable, thus tan δ was affected only slightly since tan $\delta = G''/G'$. At high frequency, tan δ at 15 days tended to be slightly higher than others indicating that the structure of gel sample changed gradually to less elastic solid.

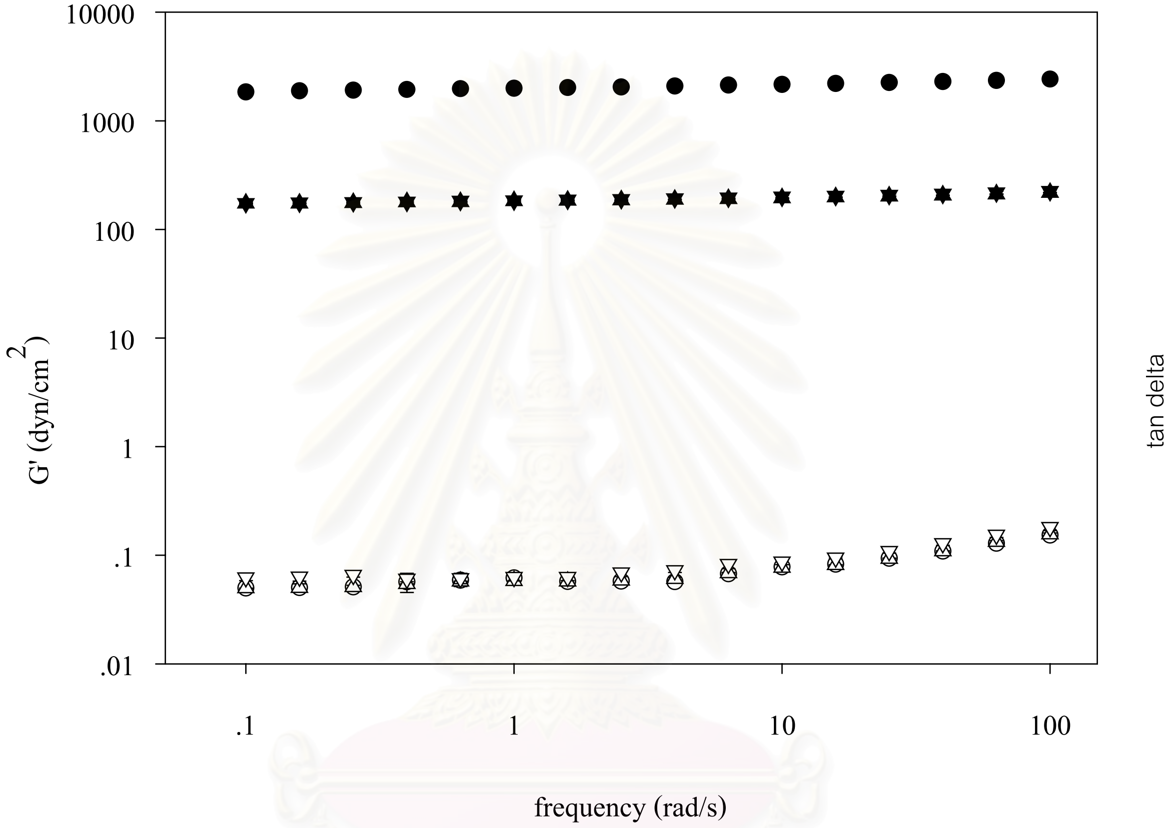

Figure 4.3 Double logarithmic plot of storage modulus (filled symbol) and semi-logarithmic plot of tan delta (unfilled symbol) against frequency of light exposed piroxicam gel (formula C.6) as a function of aging time (mean ± SD, n = 3) (●,○ : at 2 days; ▲,△ : at 2 days; ▼ ,▽ : at 15 days).

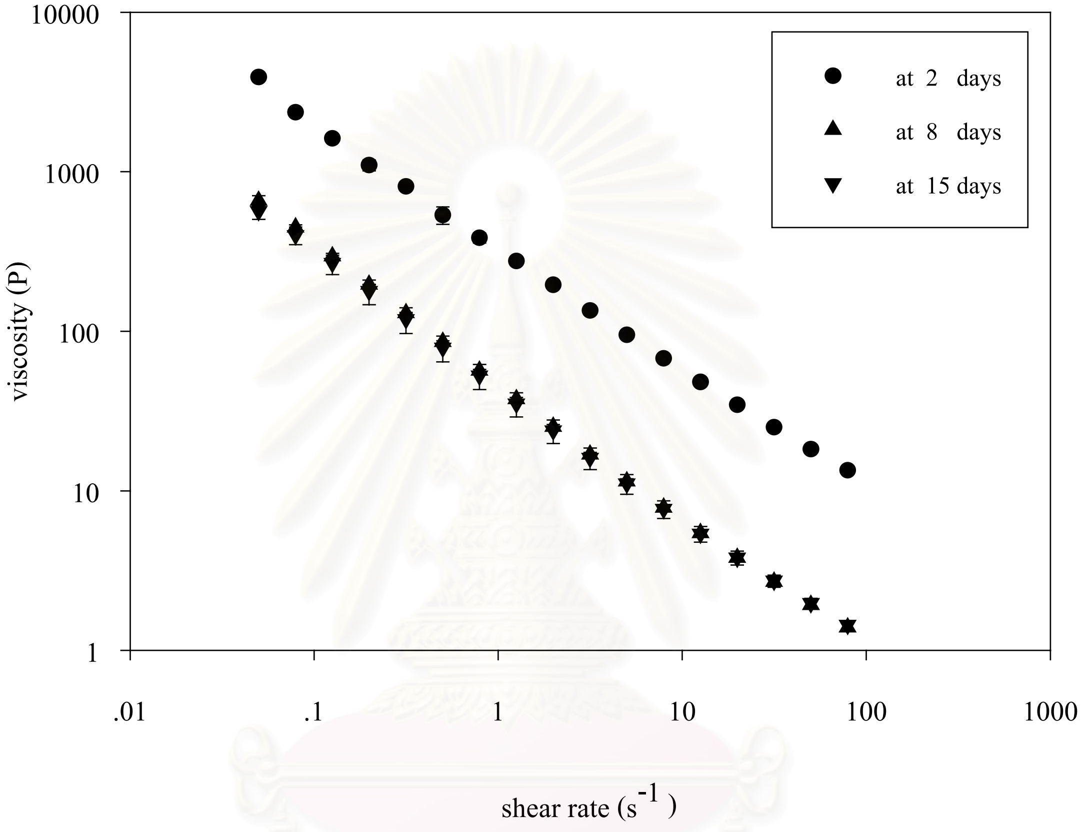

Figure 4.4. Double logarithmic plot of viscosity against shear rate of light exposed piroxicam gel (formula C.6) as a function of aging time. (mean ± SD, n = 3).

To confirm these results, the carbopol 940 gel base of formula C.6 (pH 8.12) was prepared to investigate the effect of light on gel structure. It was stored in both light protected and light exposed conditions. The sample was protected from light by wrapping its container with aluminium foil. Whereas, the other sample was stored in a transparent glass jar and placed in the sunlight exposed room, however, it was not exposed directly to the sunlight. Their rheological characters were determined at 0, 3, 7 and 14 days as shown in Figures 4.5 and 4.6. The results were similar to those of the previous studies. The storage moduli and viscosity decreased markedly while tan δ had tendency to increase slightly especially between 3 days and 14 days. On the contrary, the rheological parameters of the light protected gel base did not change appreciably within 14 days (Figures 4.7 and 4.8).

These findings are consistent with previous research by Barry and Meyer (1979). They explored the apparent viscosity of carbopol 940 gel stored in light resistant containers for 2 - 8 days. They found that there was no significant change in the apparent viscosity, but the systems stored in daylight exhibited marked photodegradation. Barry and Meyer referred to the research reported by Morimoto and Suzuki (1972) that the mechanism of photooxidation of a poly (acrylate) polymer, which is similar to carbopol, was an addition of oxygen molecules to the acrylic acid group followed by a scission of side chain and a formation of either cross-links or conjugate bonds. Especially, the formation of conjugate bond can reduce the molecular size of the polymer. Hence, the consistency of gels is reduced. Furthermore, the formation of conjugate bonds cause the gradual yellowing observed in poly(acrylate) and carbopol gels. However, the systems which are neutralized with triethanolamine yellow faster and more intensely than the unneutralized systems. Thus, it seems possible that this process is also due to the oxidation of the amine.

These results suggest that carbopol-based pharmaceutical or cosmetic products should be stored in light-resistant containers. Stabilizing agents such as a chelating agent combined with a water-soluble UV absorber should also be added for minimization of the oxidation reaction of carbopol (Lieberman, Rieger and Banker, 1998).

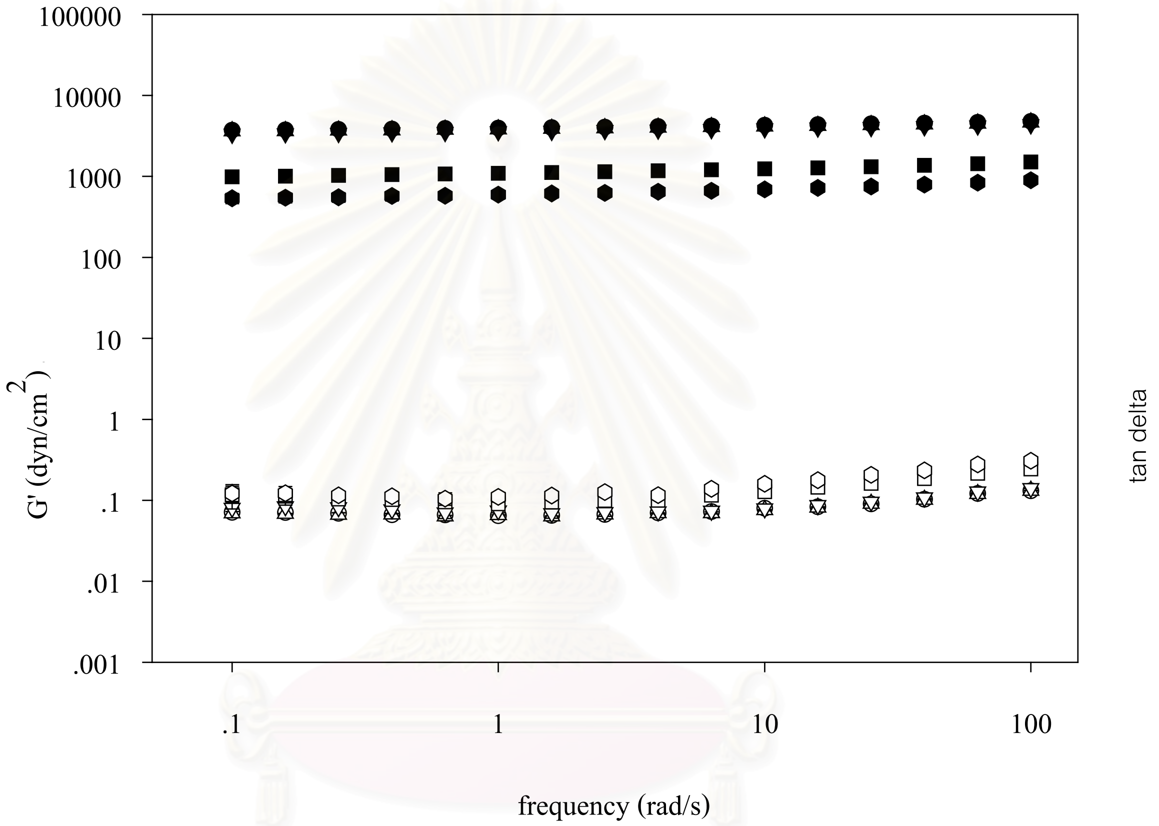

Figure 4.5 Double logarithmic plot of storage modulus (filled symbol) and semi-logarithmic plot of tan delta (unfilled symbol) against frequency of light exposed 0.6%w/w carbopol 940 gel base as a function of aging time (mean ± SD, n = 3) (●,○ : at 0 days; ▲,△ : at 1 days; ▼,▽ : at 3 days; ■,□ : at 7 days; ⯃,⯂: at 14 days).

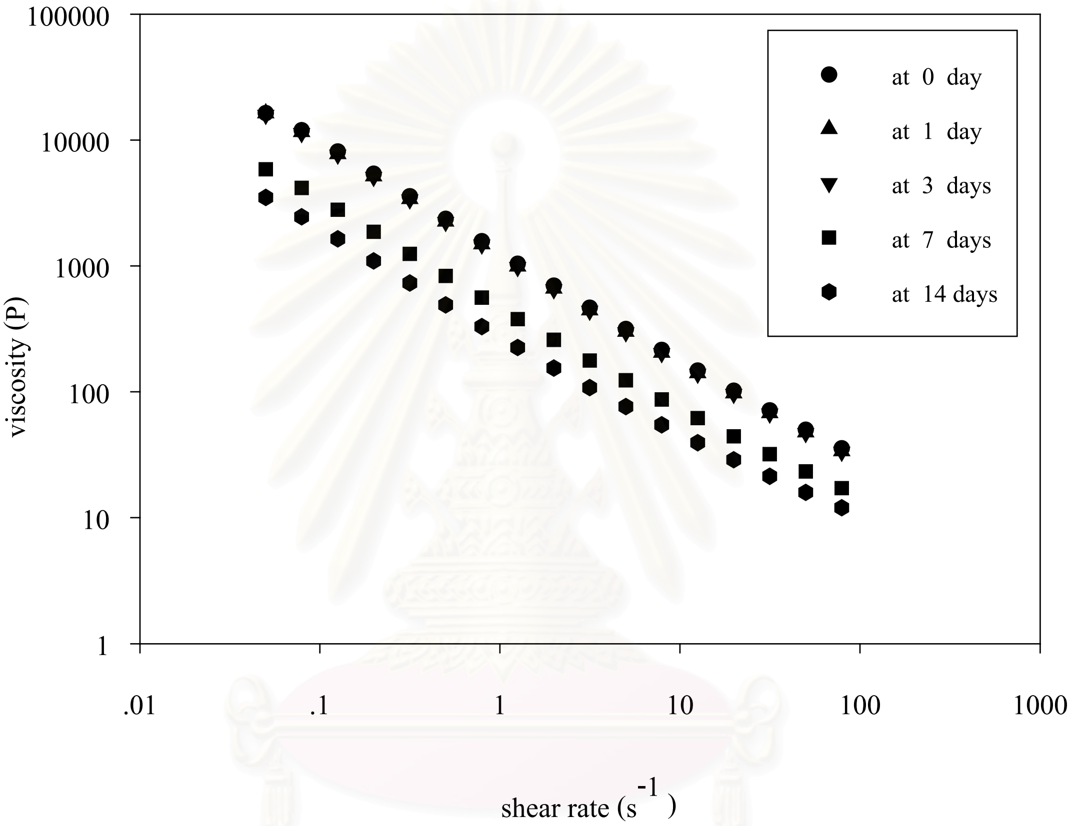

Figure 4.6. Double logarithmic plot of viscosity against shear rate of light exposed 0.6 %w/w carbopol 940 gel base as a function of aging time (mean ± SD, n = 3).

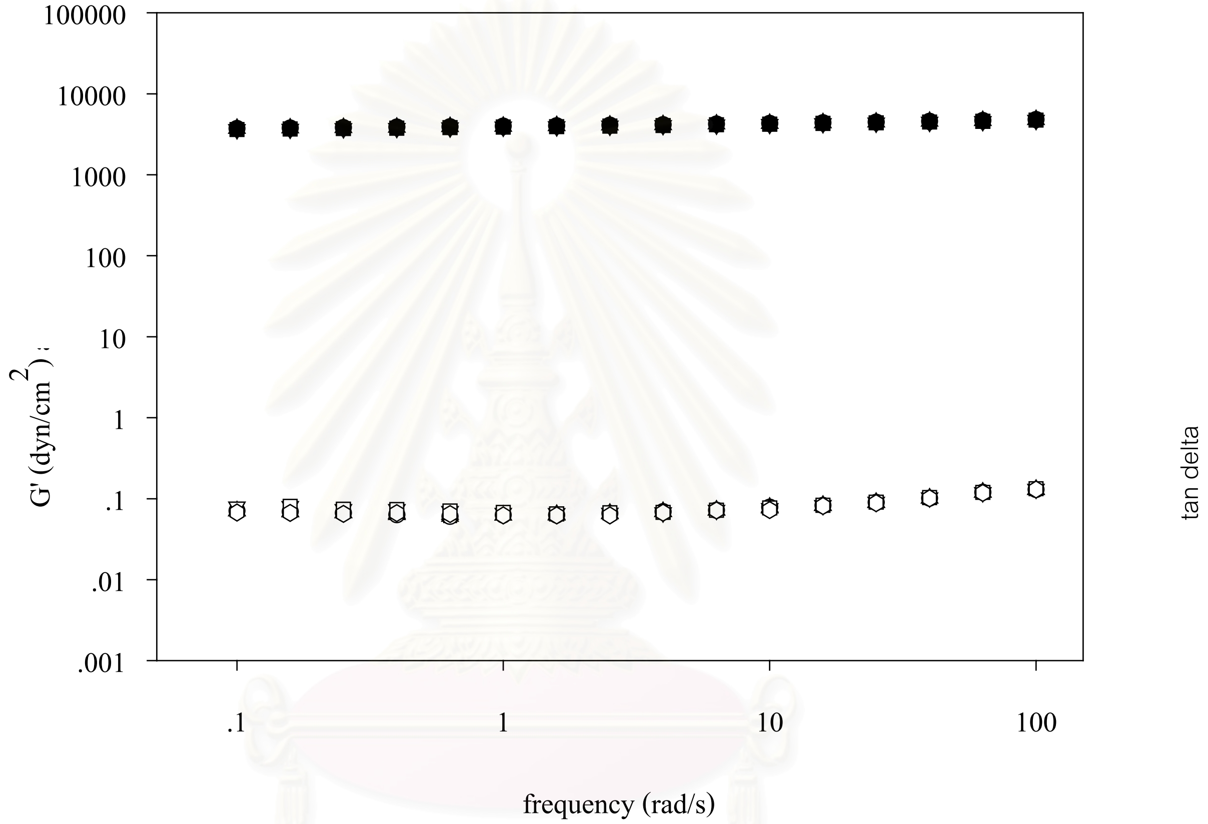

Figure 4.7 Double logarithmic plot of storage modulus (filled symbol) and semi-logarithmic plot of tan delta (unfilled symbol) against frequency of light protected 0.6 %w/w carbopol 940 gel base as a function of aging time (mean ± SD, n = 3) (●,○ : at 0 days; ▲,△ : at 1 days; ▼,▽ : at 3 days ;■,□ : at 7 days; ⯃,⯂: at 14 days).

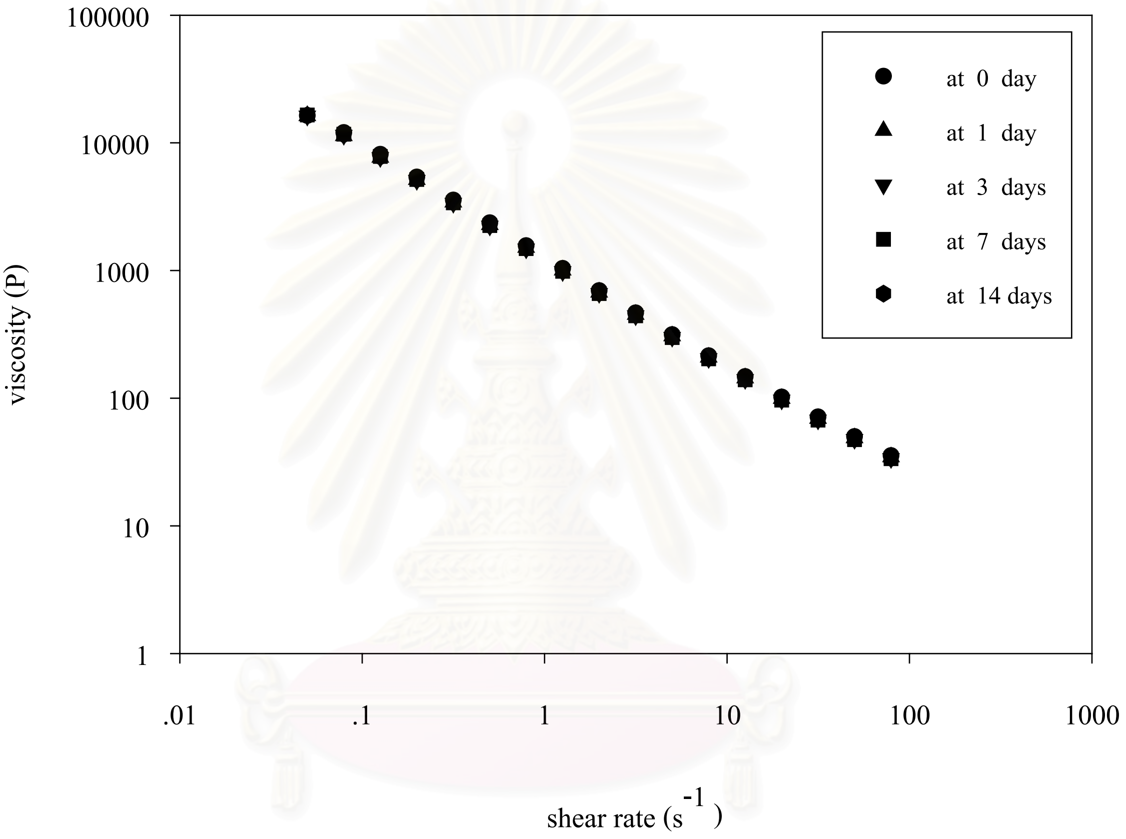

Figure 4.8. Double logarithmic plot of viscosity against shear rate of light protected 0.6 %w/w carbopol 940 gel base as a function of aging time. (mean ± SD, n = 3).

5. Effect of Aging Time on Rheological Parameters.

This study was undertaken to examine whether the aging time could influence gel structure; thus gel samples were characterized using a fluid rheometer for the determination of rheological properties as a function of aging time.

The rheological properties of gel formulae C.4, C.6 and C1 stored in air-tight glass jars wrapped with aluminium foil were determined at 1, 4, 7 and 14 days after they had been prepared. The results obtained were similar to the case of formula C.6. They are shown in Appendix II. The rheological properties of the samples such as storage moduli, tan δ and viscosity did not change within 14 days as shown in Figures 4.9 and 4.10 for the case of formula C.6. This indicated that the structure of all samples should reach the equilibrium state within 24 hours after they had been prepared. Thus, the gel samples which were protected from light could be used for subsequent studies within 1-14 days after they had been compounded.

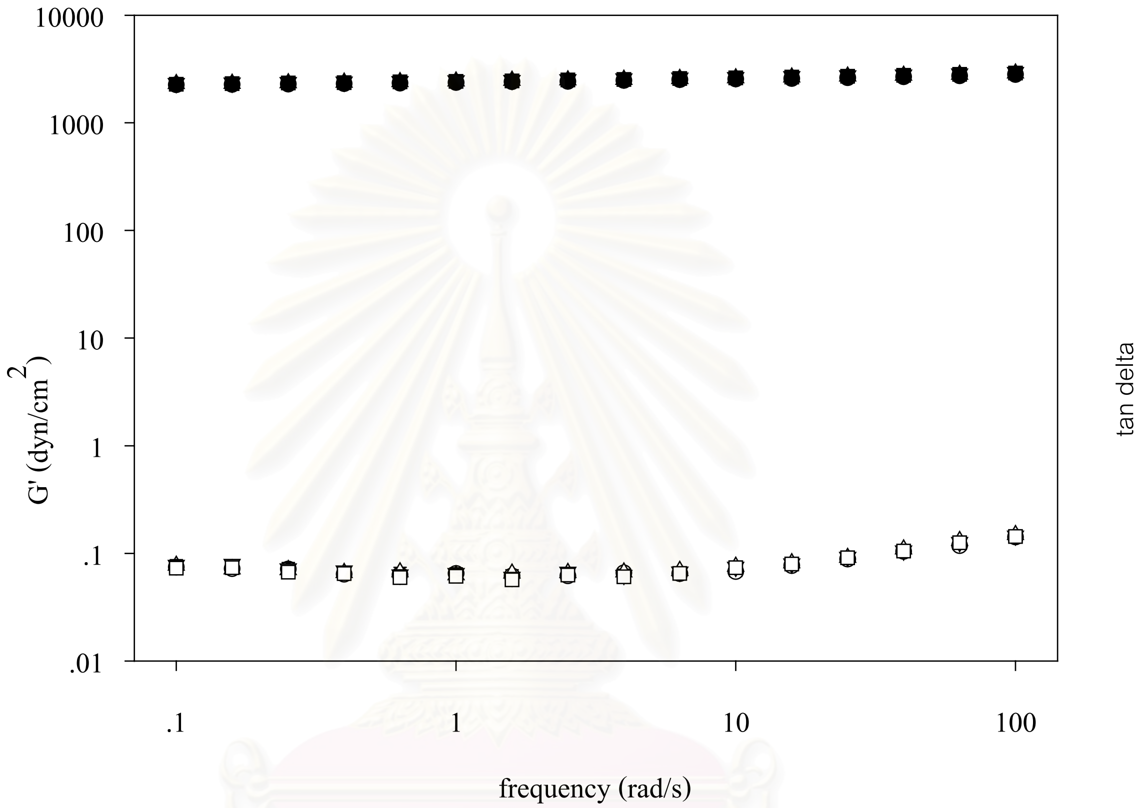

Figure 4.9 Double logarithmic plot of storage modulus (filled symbol) and semi-logarithmic plot of tan delta (unfilled symbol) against frequency of light protected piroxicam gel (formula C.6) as a function of aging time (mean ± SD, n = 3) (●,○ : at 1 days; ▲,△ : at 4 days; ▼ ,▽ : at 7 days; ■,□ : at 14 days).

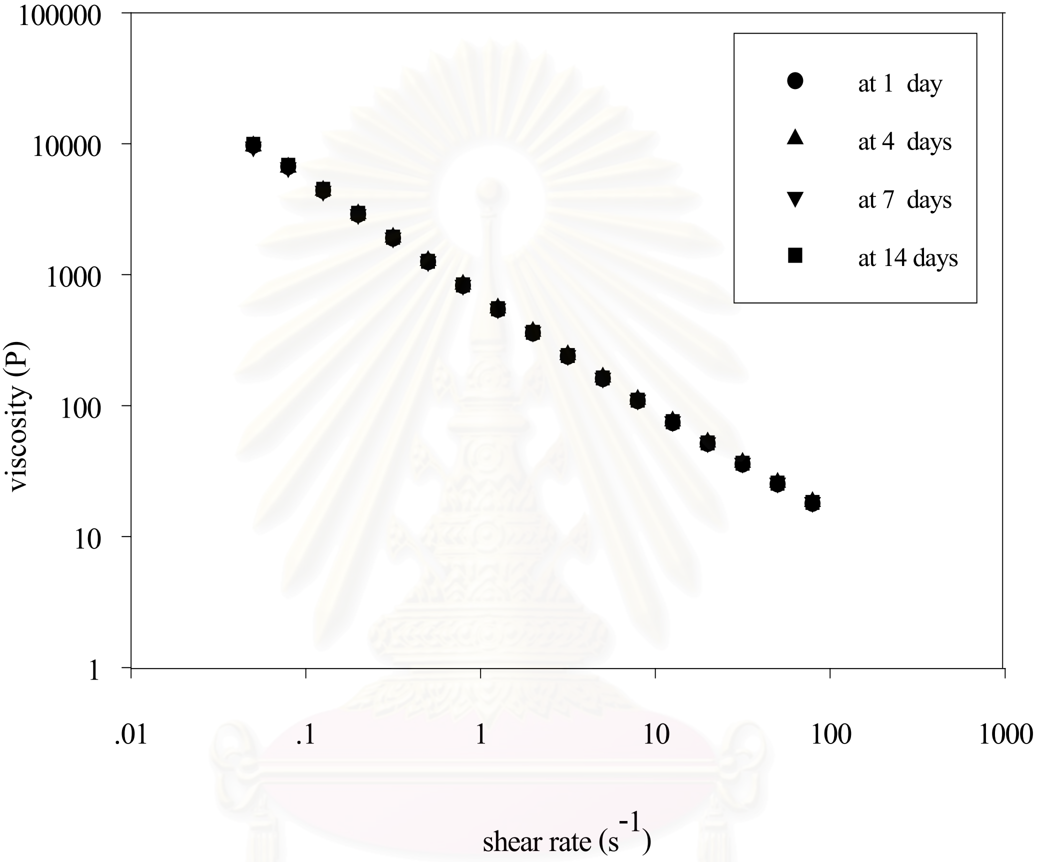

Figure 4.10. Double logarithmic plot of viscosity against shear rate of light protected piroxicam gel (formula C.6) as a function of aging time. (mean ± SD, n = 3).

6. Effect of Formula Compositions on Rheological Parameters.

6.1 Effect of carbopol 940 concentration.

The rheological parameters of gel formulae C.4, C.6 and C1, which contained 0.4, 0.6 and 1.0 %w/w carbopol 940, respectively, were characterized at 27 °C. They had predominant elastic solid behavior as their magnitudes of storage moduli were greater than that of loss moduli (Figure 4.11). In addition, tan δ, which is commonly described as the ratio of the energy lost (G'') to energy stored (G'), were less than 1 (Figure 4.12). This is in agreement with the work of Jones, Woolfson and Brown (1997). A typically cross-linked gel-network structure exhibits elastic solid behavior; their storage moduli are greater than their loss moduli and both moduli tend to increase at the higher frequencies (Clark and Ross-Murphy, 1987). The values of storage moduli and loss moduli increased with an increment of carbopol 940 concentration, and tan δ values tended to decrease. This suggests that the gel samples would perform predominantly elastic solid behavior when the concentration of gelling agent increased. It is possible that the more the polymer content, the more entanglement and the more interactions the polymer chains.

Figure 4.13 shows viscosity profiles of gel formulae C.4, C.6 and C1. Their viscosities decreased with increasing shear rates. This is generally called "shear-thinning" behavior (Barnes, Hutton and Walters, 1989). It means that the resistant of a material to flow decreases and the energy required to sustain at high shear rates is reduced (Laba, 1993). The viscosity of piroxicam gels increased with increasing carbopol 940 concentration. It was possible that more polymer chains entangled and interacted as polymer chains were increased. The flow profiles (rheogram) of piroxicam gels containing 0.4, 0.6, and 1.0 %w/w carbopol 940 show plastic behavior (Figure 4.14). This finding showed that at rest, the materials formed gel-network structure of which polymer chains might entangle or interact. However, this structure was deformed under the influence of the shear force, resulting in the shear-thinning behavior. The flow profiles also exhibit yield values. The yield value is the external force required to overcome the internal force and to initiate the flow of the material. Beyond the yield point, the material changes its viscosity as a function of increased shear rate (Laba, 1993). In this study, the critical stress needed to do so is defined as the yield value obtained by the extrapolation of stress data at low shear rate region.

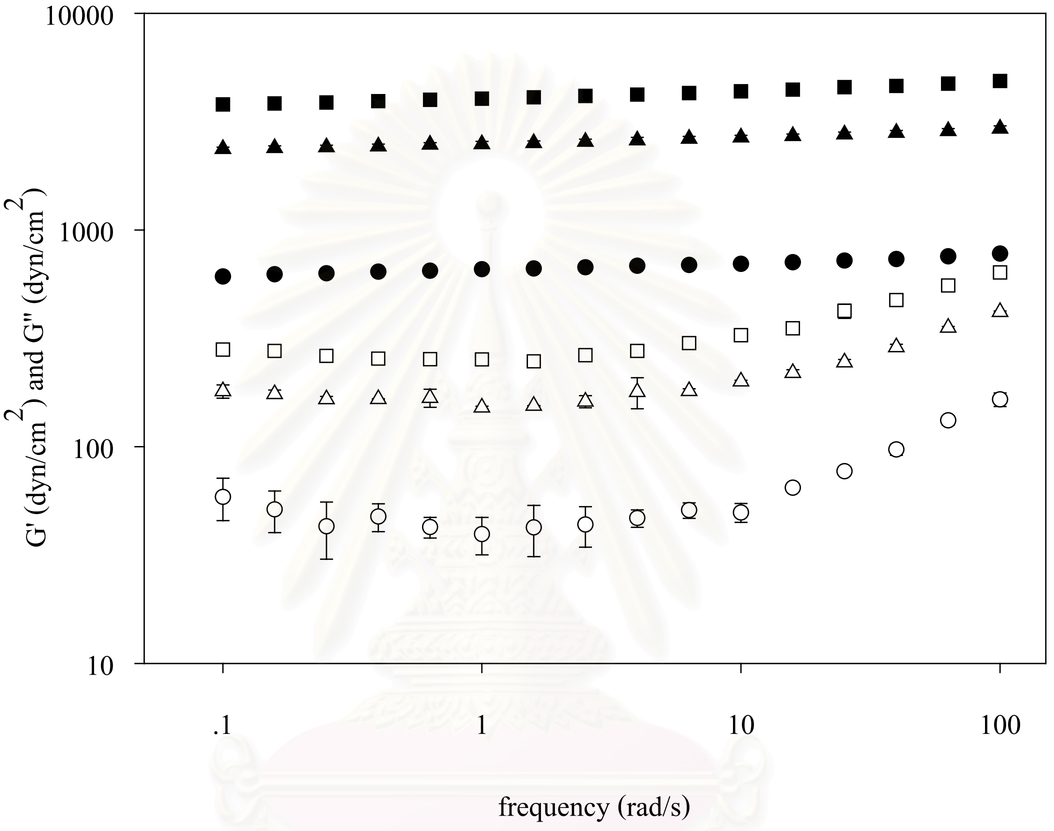

Figure 4.11 Double logarithmic plot of storage modulus (filled symbol) and loss modulus (unfilled symbol) against frequency of piroxicam gel with varied carbopol 940 concentrations at 27°C (mean ± SD, n = 3) (●,○ : 0.4%w/w; ▲,△ : 0.6%w/w; ■,□ : 1.0%w/w).

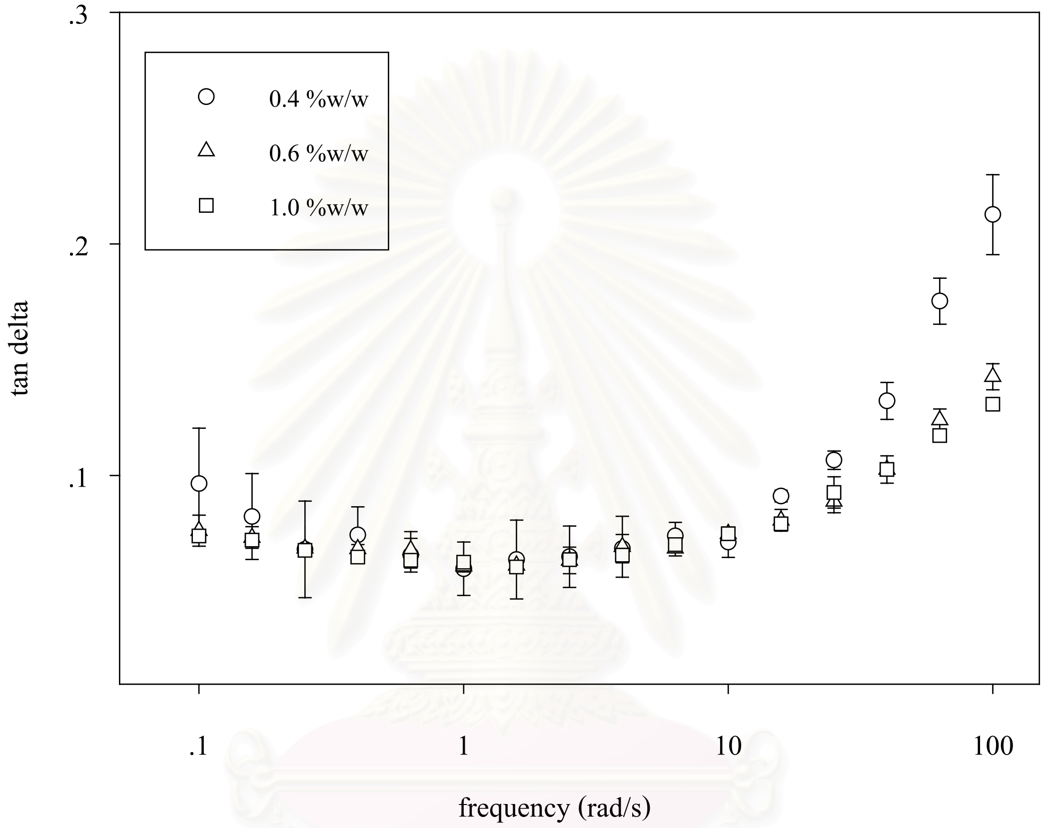

Figure 4.12. Semi-logarithmic plot of tan delta against frequency of piroxicam gels with varied carbopol 940 concentrations at 27 °C (mean ± SD, n = 3).

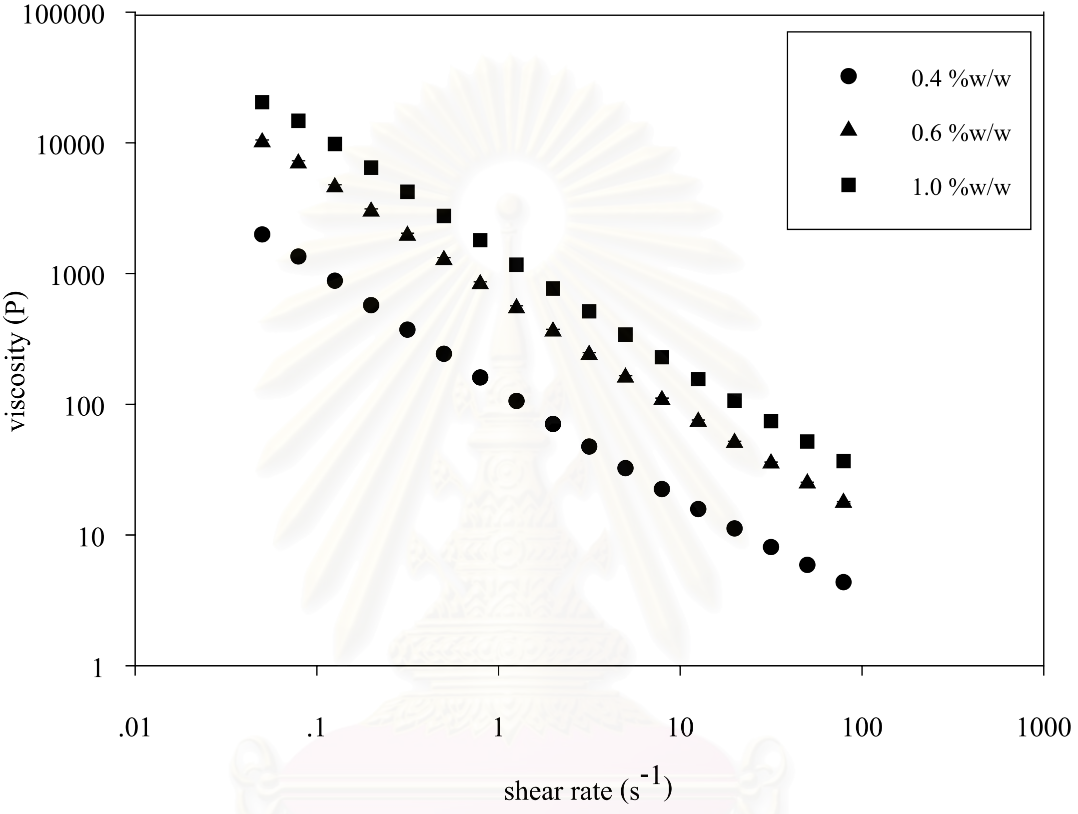

Figure 4.13. Double logarithmic plot of viscosity against shear rate of piroxicam gels with varied carbopol 940 concentrations at 27 °C. (mean ± SD, n = 3).

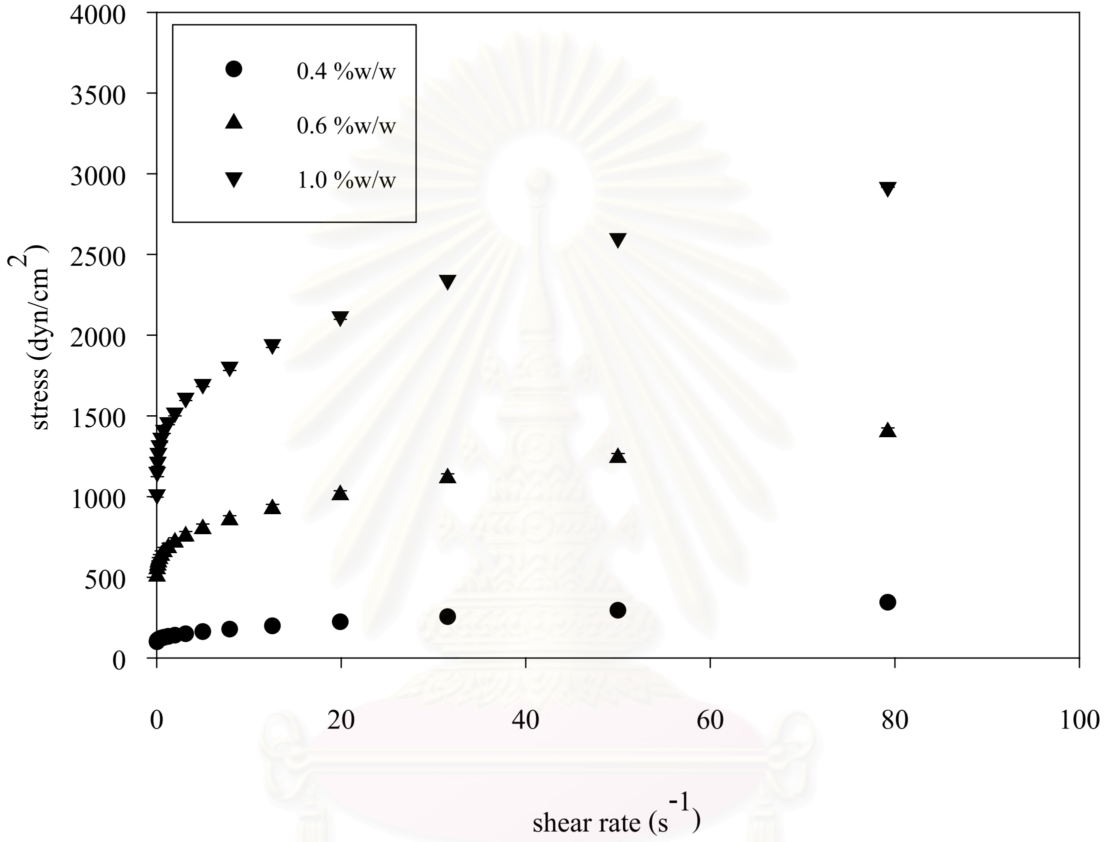

Figure 4.14. Plot of stress against shear rate of piroxicam gels varied carbopol 940 concentrations at 27 °C. (mean ± SD, n = 3).

6.2 Effect of solvent compositions.

One objective of this study is to determine the rheological properties of 1.0 %w/w piroxicam gels containing mixed solvents. The solvents studied included water, propylene glycol and glycerin (formulae C.6, C.6/G5, C.6/G10 and C.6/G15) as shown in Table 4.4. Carbopol 940 at a concentration of 0.6 %w/w was used throughout this study.

Table 4.4 Ratios of solvent compositions

Formula	Water : Propylene glycol : Glycerin
C.6	90 : 10 : 0
C.6/G5	85 : 10 : 5
C.6/G10	80 : 10: 10
C.6/G15	75 : 10 : 15

The storage moduli and loss moduli values of gel formulae C.6, C.6/G5 and C.6/G10 containing 0.0, 5.0 and 10.0 %v/w glycerin, respectively, were comparable (Figure 4.15). However, the gel formula C.6/G15 containing 15.0 %v/w glycerin had lower storage moduli and decreasing tendency of loss moduli values. Furthermore, the tan δ profiles shown in Figure 4.16 of gel formulae C.6, C.6/G5 and C.6/G10 showed that their tan δ values were comparable, but those of the gel formula C.6/G15 possessed higher values. This indicates that the gel formula C.6/G15 had more viscous fluid behavior than the others.

From the dynamic testing data, the decrease in water content of the solvent mixtures to lower than 80% with an increase in glycerin content to over than 10% would yield more viscous fluid behavior of the gel structure. Generally, the viscoelasticity of neutralized carbopol polymers is obviously affected by the degree of entanglement between different polymer chains; the entanglement is greater when the polymer chains are more extended. In a "good" solvent composition such as solvent with a higher water content, polymer-solvent interactions are favored over the polymer chain-chain interactions, thus polymer chains are well expanded. In a "poor" solvent composition, the intermolecular interactions between the polymer segments are greater than the segment-solvent affinity, and the molecular chain would tend to be more contracted. Thus in a good solvent, the neutralized carbopol polymer chain is more extended and the elastic solid behavior of the polymer is more obvious (Chu et al., 1992; Lin et al., 1993). In addition, the glycerin added can play a platicizer role that increases the flexibility of polymer chains, and therefore, the gel elastic behavior decreases.

The viscosity of gel formula C.6/G15 were slightly lower than those of other gels (Figure 4.17). It was possible that the degree of entanglement of gel formula C.6/G15 was decreased. However, their rheograms (Figure 4.18) show plastic behaviors with yield values.

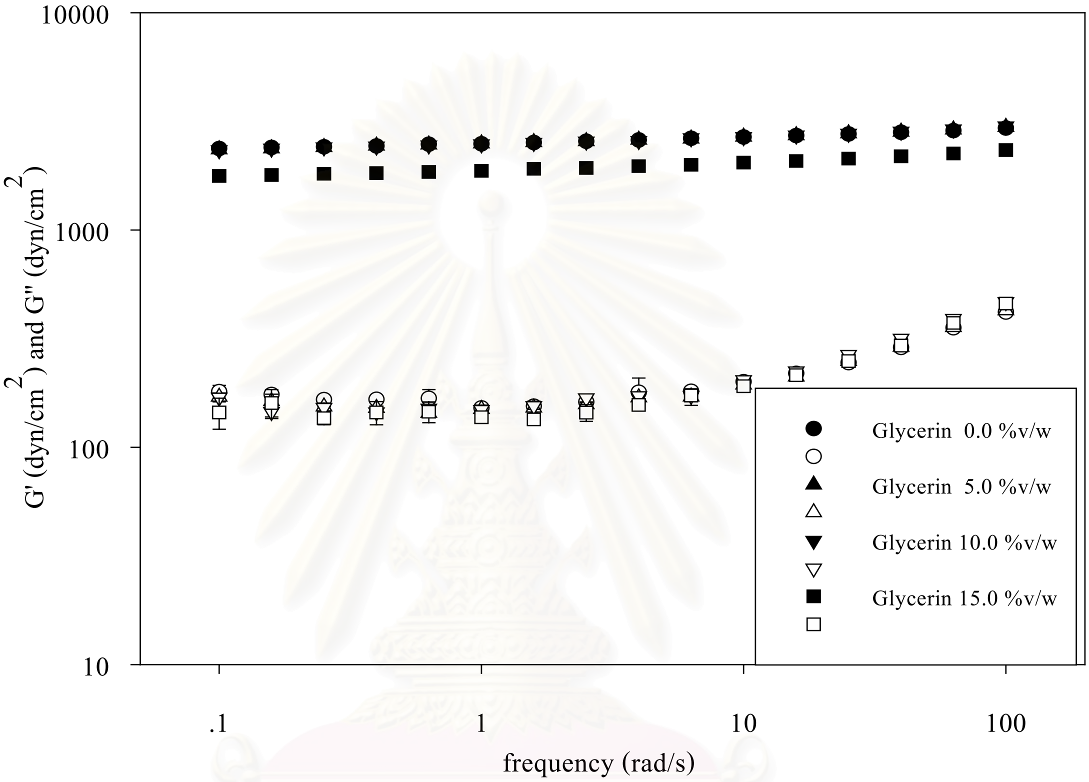

Figure 4.15. Double logarithmic plot of stroage modulus (filled symbol) and loss modulus (unfilled symbol) against frequency of piroxicam gels containing 0.6 %w/w carbopol 940 and varied concentrations of glycerin at 27 °C. (mean ± SD, n = 3).

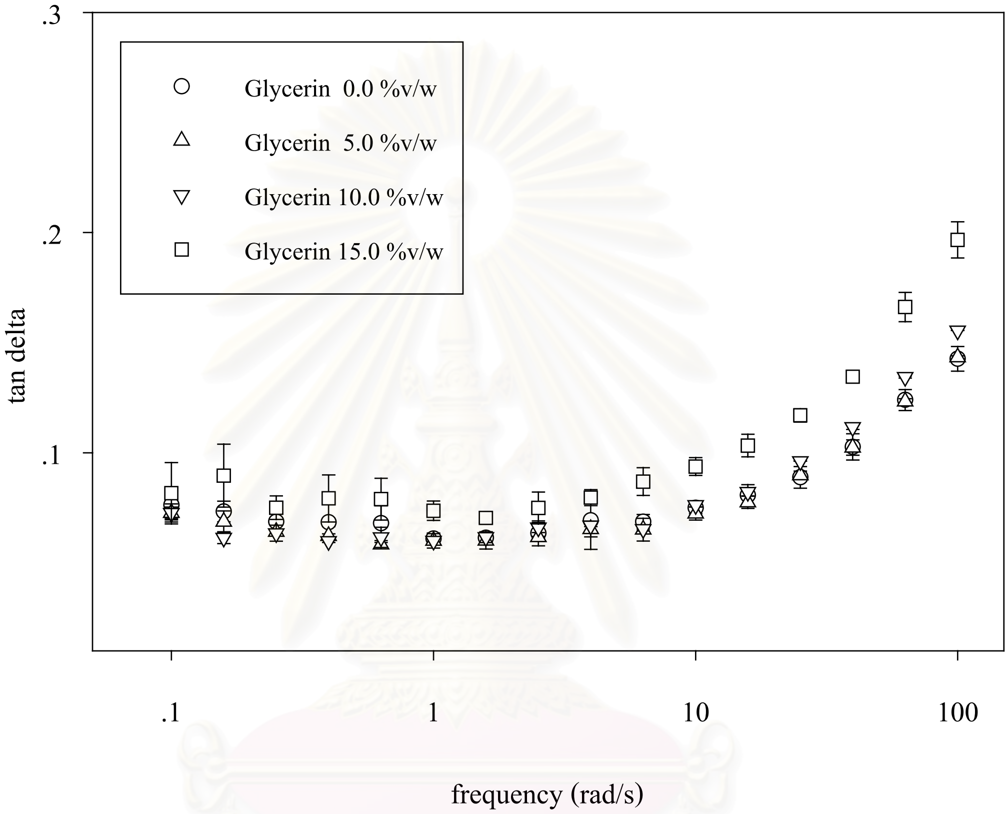

Figure 4.16 Semi-logarithmic plot of tan delta against frequency of piroxicam gels containing 0.6 %w/w carbopol 940 and varied concentrations of glycerin at 27 ^{o}C (mean ± SD, n = 3).

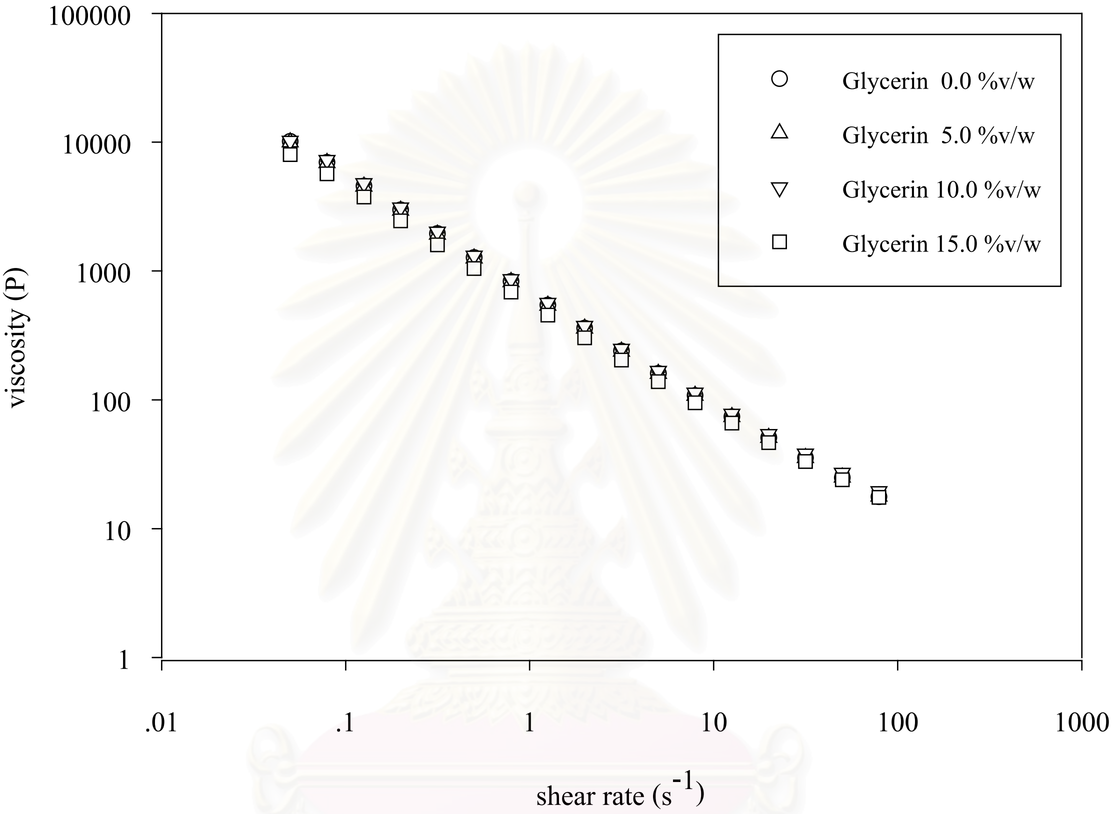

Figure 4.17. Double logarithmic plot of viscosity against shear rate of piroxicam gels containing 0.6 %w/w carbopol 940 and varied concentrations of glycerin at 27 °C. (mean ± SD, n = 3).

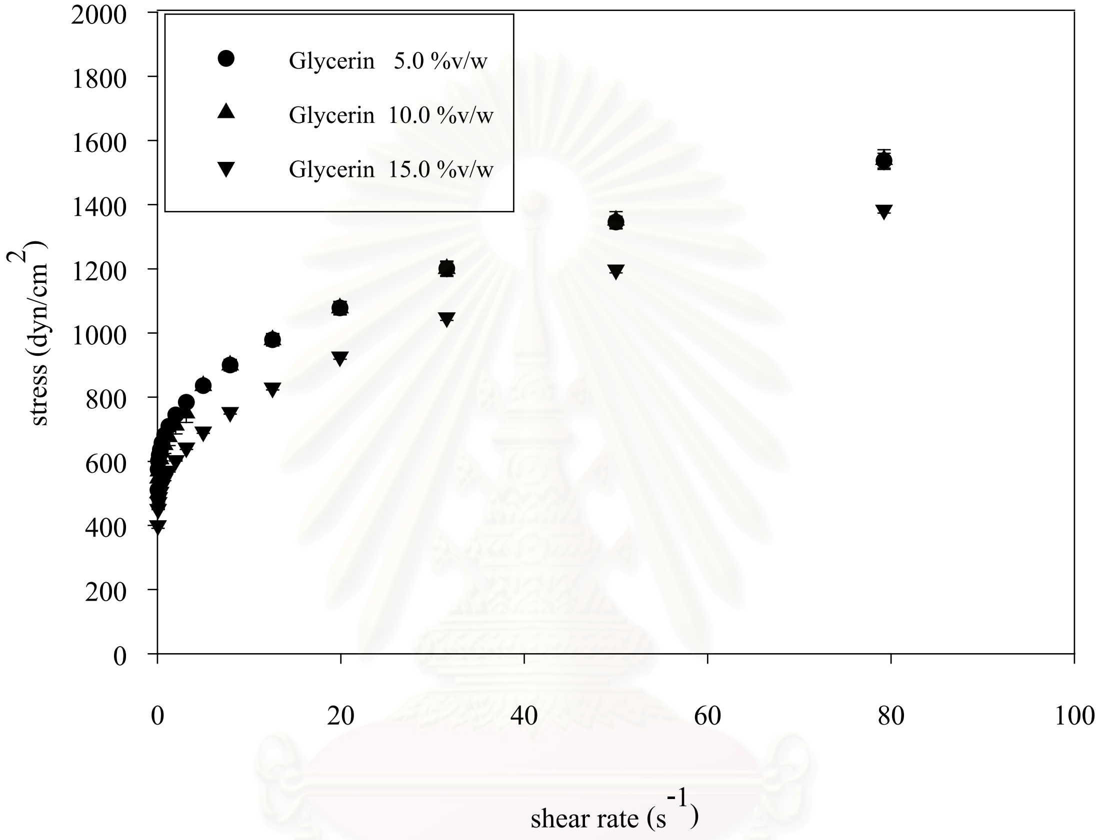

Figure 4.18. Plot of stress against shear rate of piroxicam gels containing 0.6 %w/w carbopol 940 and varied concentrations of glycerin at 27 °C. (mean ± SD, n = 3).

6.3 Effect of electrolyte.

Carbopol is a polymer of acrylic acid cross-linked with allyl ethers of pentaerythritol or sucrose to form a high molecular weight anionic hydrophilic polymer. In the acid form, carbopol does not swell significantly due to the limited solubilizing power of carboxylic acid groups. When it is solubilized, the hydration occurs and it forms a three-dimensional microgel structure. The most often used technique for solubilization of carbopol is neutralization which converts carbopol to a salt form (Laba, 1993). Gels are formed on neutralization to pH 5 - 10 with metal hydroxides or amines. The neutralization expands the long chains of carbopol by charge repulsion to produce an entangled gel network. Because the electrostatic repulsion plays a critical role in forming the gel structure, viscoelastic properties, viscosity and gel strength depend on both pH and salt content (Swarbrick and Boylan, 1996).

The rheological properties of preparations containing sodium chloride were thus examined. Sodium chloride influenced the carbopol gel structure markedly and it cause slightly cloudy appearance of the preparations. The storage moduli and loss moduli values of the preparations studied decreased with increments of sodium chloride content; the effect was greater in the case of formulation containing lower concentration of carbopol 940 (Figures 4.19 - 4.22). Tan δ profiles (Figure 4.20) show that the structure of gel containing 0.6 %w/w carbopol 940 with 0.9 %w/w sodium chloride possessed more viscous fluid behavior. However, the structure of gel containing higher concentration of carbopol 940, i.e., 1.0 %w/w had a slight change in its behavior as its tan δ values did not change as much as those of 0.6 %w/w carbopol 940 (Figure 4.22).

Sodium chloride could affect the hydration of carbopol 940 due to its greater solubilizing power. Thus the polymer-solvent interactions were lessened and the polymer chains tended to contract. Consequently, the preparations tended to lose their elastic solid characters and their viscosity were decreased (Figures 4.23 and 4.24); particularly the preparation containing lower concentration of carbopol 940 (0.6 %w/w) and high concentration of sodium chloride (0.9 %w/w) became slightly turbid. This might occur as a result of polymer flocculation. Their rheograms depicted plastic behavior with yield values (Figure 4.25). In conclusion, the preparations containing high concentrations of carbopol 940 were more tolerant to electrolyte than the preparations containing low concentrations of carbopol 940.

Edsman, Carlfors and Harju (1996) found that there was a good correlation of the human ocular contact time and the elastic solid properties of ophthalmic gels using carbopol as a gelling agent. Thus, preparations containing high carbopol 940 concentration should be chosen for using in ocular drug delivery dosage forms and mucoadhesive dosage forms because they would prolong the contact time and are tolerant of electrolyte in biological fluids such as tear, saliva and mucus. The increment of contact time would result in an increase in drug bioavailability. However, the gel structure should be optimally strong because too strong a gel structure could result in irritation.

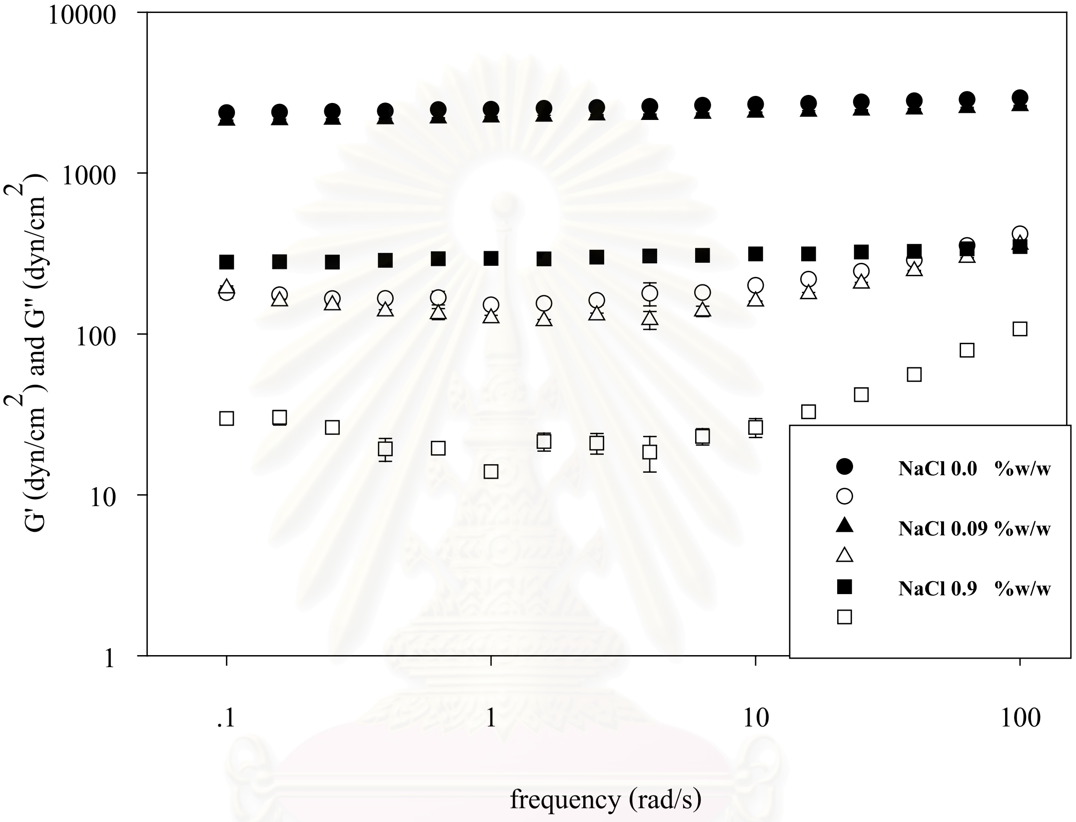

Figure 4.19. Double logarithmic plot of storage modulus (filled symbol) and loss modulus (unfilled symbol) against frequency of piroxicam gels containing 0.6 %w/w carbopol 940 and varied concentrations of sodium chloride at 27 °C. (mean ± SD, n = 3).

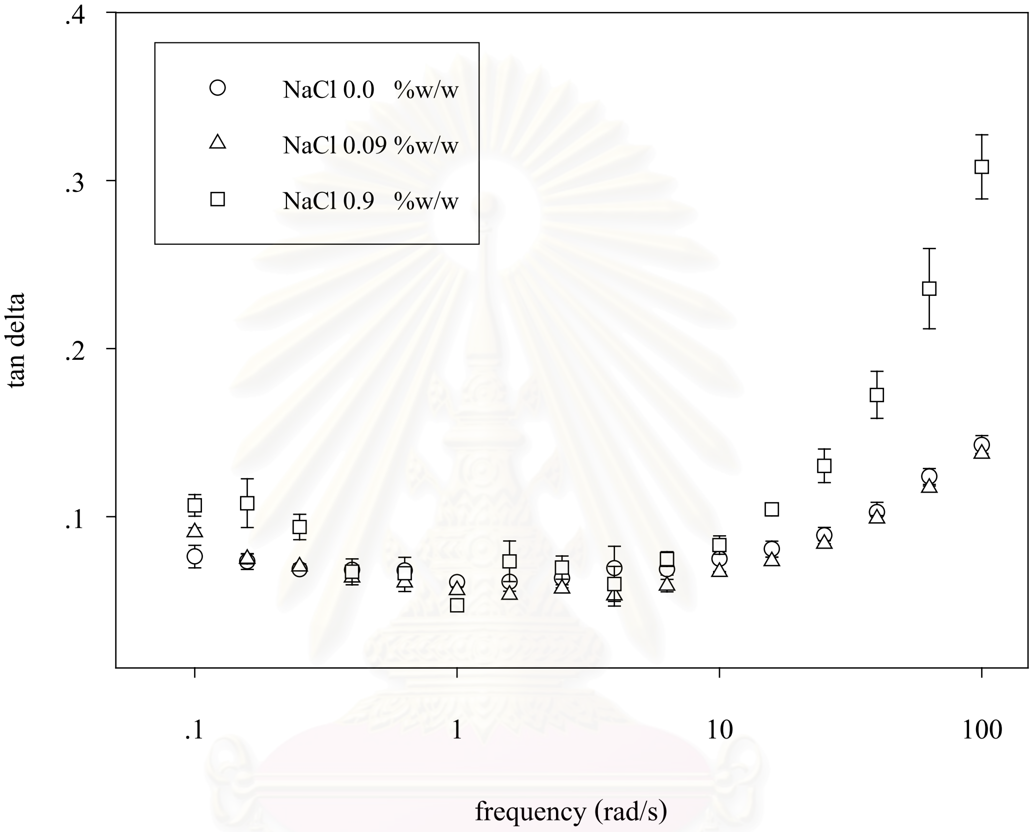

Figure 4.20 Semi-logarithmic plot of tan delta against frequency of piroxicam gels containing 0.6 %w/w carbopol 940 and varied concentrations of sodium chloride at 27 °C (mean ± SD, n = 3).

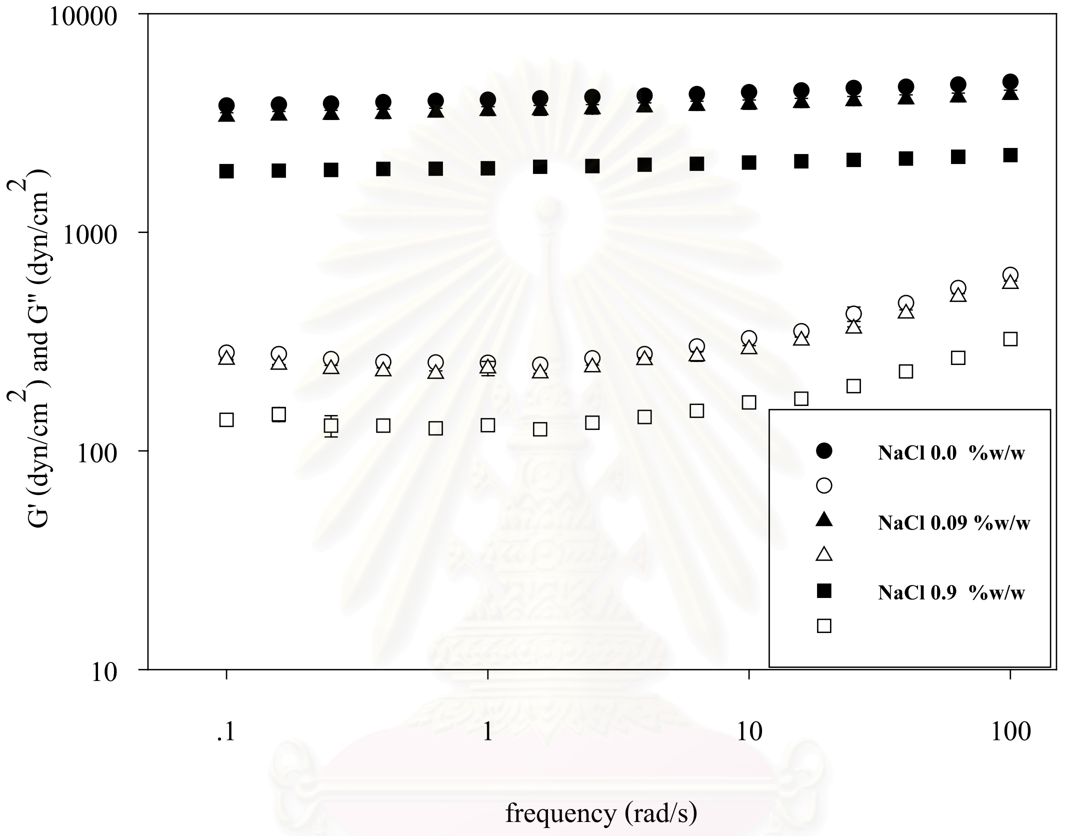

Figure 4.21. Double logarithmic plot of storage modulus (filled symbol) and loss modulus (unfilled symbol) against frequency of piroxicam gels containing 1.0 %w/w carbopol 940 and varied concentrations of sodium chloride at 27 °C. (mean ± SD, n = 3).

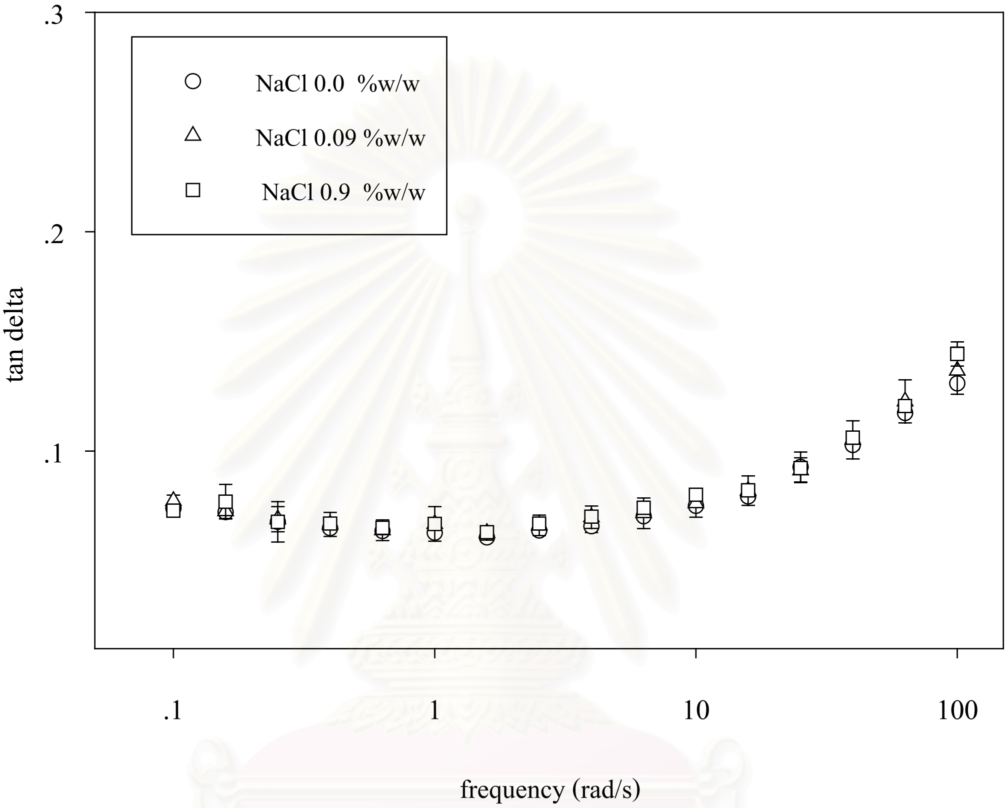

Figure 4.22 Semi-logarithmic plot of tan delta against frequency of piroxicam gels containing 1.0 %w/w carbopol 940 and varied concentrations of sodium chloride at 27 °C (mean ± SD, n = 3).

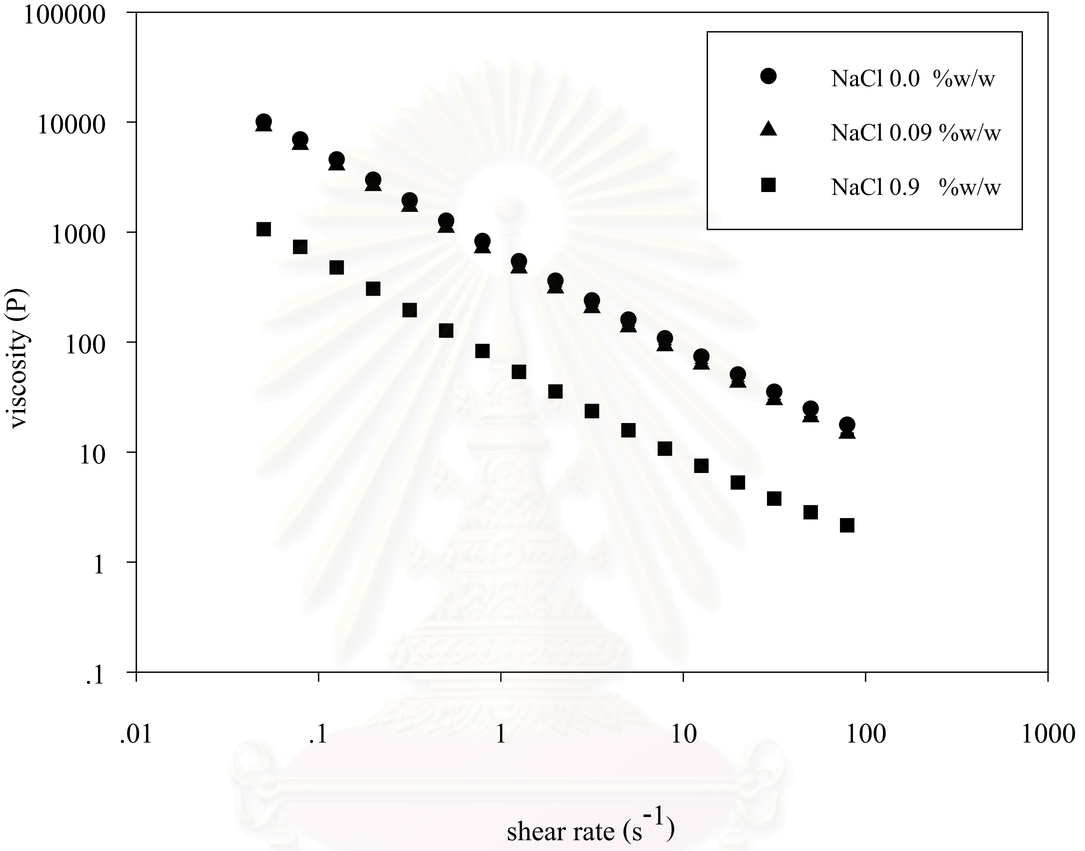

Figure 4.23. Double logarithmic plot of viscosity against shear rate of piroxicam gels containing 0.6 %w/w carbopol 940 and varied concentrations of sodium chloride at 27 °C. (mean ± SD, n = 3).

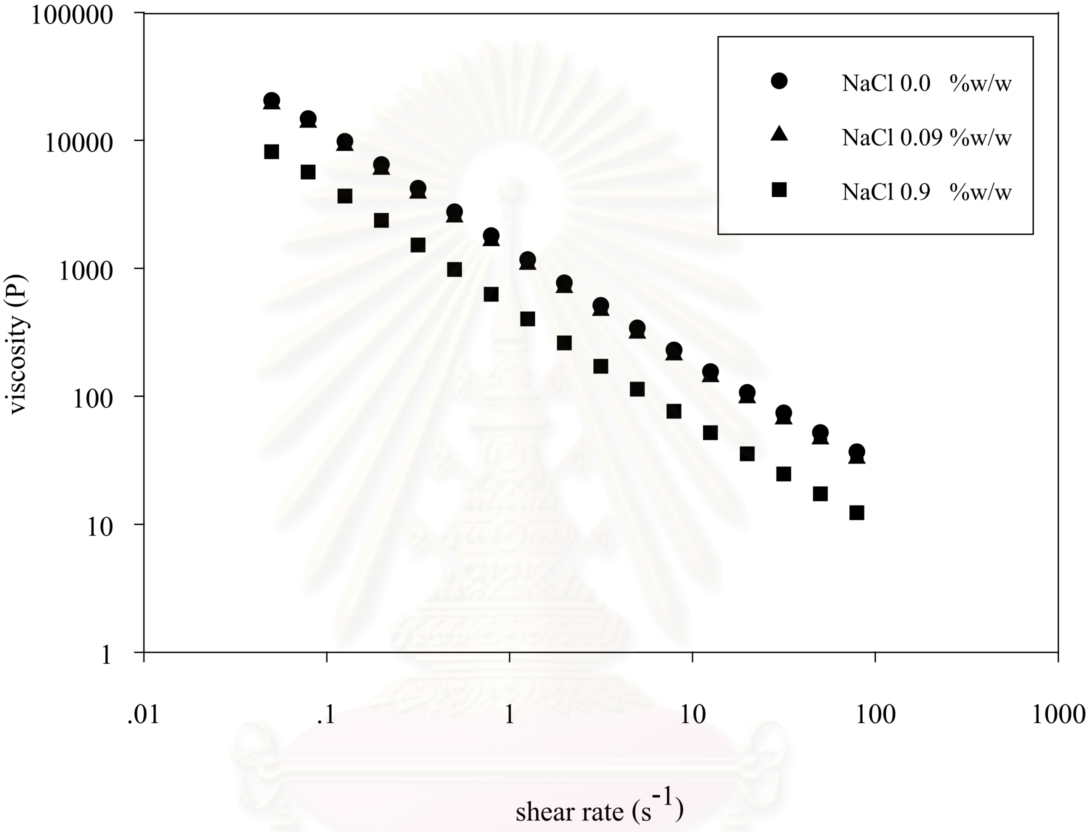

Figure 4.24. Double logarithmic plot of viscosity against shear rate of piroxicam gels containing 1.0 %w/w carbopol 940 and varied concentrations of sodium chloride at 27 °C. (mean ± SD, n = 3).

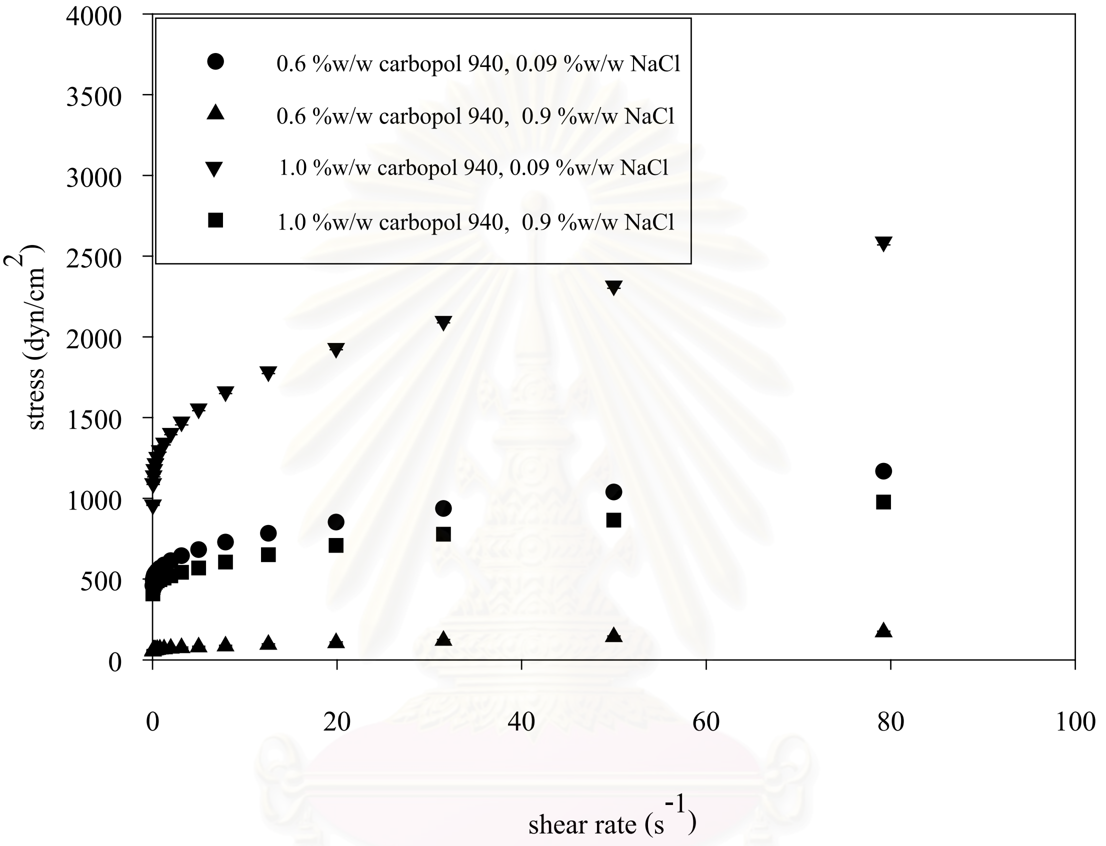

Figure 4.25. Plot of stress against shear rate of piroxicam gels containing 0.6 % and 1.0 %w/w carbopol 940 and varied concentrations of sodium chloride at 27 °C. (mean ± SD, n = 3).

7. Piroxicam Diffusion Coefficient Determination.

Diffusion coefficients of piroxicam in some preparations possessing different viscoelastic behaviors were calculated from the slopes of plots of cumulative amount released versus square root of time according to Higuchi's equation (Equation 2.24) and are presented in Table 4.5.

Table 4.5 Diffusion coefficients of piroxicam in carbopol 940 gel bases at 33 °C

Formula	Diffusion coefficient [a] (cm^2/min)
C.4	$1.17\times10^{-4} \pm 7.99\times10^{-6}$
C.6	$9.07\times10^{-5} \pm 1.97\times10^{-6}$
C1	$8.58\times10^{-5} \pm 1.54\times10^{-6}$
C.6/G10	$8.86\times10^{-5} \pm 2.29\times10^{-6}$
C.6/G15	$7.45\times10^{-5} \pm 4.88\times10^{-6}$
C.6/S.09	$1.13\times10^{-4} \pm 3.69\times10^{-6}$
C.6/S.9	$1.48\times10^{-4} \pm 1.88\times10^{-6}$
C1/S.9	$1.00\times10^{-4} \pm 7.01\times10^{-6}$

[a] mean ± SD (n = 3).

The rank order of piroxicam diffusion coefficients in gel bases is C.6/S.9 > C.4 > C.6/S.09 > C1/S.9 > C.6 > C.6/G10 > C1 > C.6/G15. However, using the one-way ANOVA with Tukey multiple comparison at a p-value of less than 0.05, the diffusion coefficients of piroxicam of formulae C.6 and C.6/G10 were not different significantly; those of formula C.6/G10 and C1 were also not different significantly.

The rheological properties of these formulations were examined at low frequency (0.1 rad/s) and minimum shear rate (0.05 s^{-1}) (Table 4.6) in order to interfere the gel structure to the least extent.

Table 4.6 Rheological data of the test products at 33 °C (mean ± SD, n = 3)

Formula	Viscoelastic Parameters[a]				Viscosity[d] (P)
	G'^{b}	G''^{b}	$\tan \delta^{c}$	G^{*b}	
C.4	608.78	58.55	0.0965	611.70	1986.61
C.6	2365.59	180.14	0.0762	2372.48	10108.05
C1	3799.99	280.72	0.0739	3809.35	20452.20
C.6/G10	2348.25	170.62	0.0727	2339.08	10018.18
C.6/G15	1773.69	144.60	0.0816	1779.69	7997.01
C.6/S.09	2120.43	192.61	0.0908	2129.16	9179.54
C.6/S.9	279.81	29.83	0.1067	281.40	1060.90
C1/S.9	1897.29	135.08	0.0713	1902.10	8158.80

[a] viscoelastic parameters were obtained at the frequency of 0.1 rad/s.

[b] the units of G', G'' and G^* are dyn/cm^2.

[c] $\tan \delta$ is dimensionless.

[d] viscosity was obtained at the shear rate of 0.05 s^{-1}.

Generally, the drug mobility in aqueous dispersions of polymers is basically restricted by mechanical impediments of polymers and reductions in free volume with increases in medium viscosity (Lorenzo et al., 1999). Thus, there is an inverse relationship between the diffusion coefficient and gel viscosity as predicted by the Stokes–Einstein equation

$$D = k_B T / 6\pi\eta R \qquad (4.2)$$

where D is the diffusion coefficient, k_B is the Boltzmann's constant, η is the viscosity and R is the radius of diffusant.

In this study, the rank order of viscosity of test products was as follows: C.6/S.9 < C.4 < C.6/G15 < C1/S.9 < C.6/S.09 < C.6/G10 < C.6 < C1. Since there was a trend of inverse relationship between piroxicam diffusion coefficients (D) in carbopol 940 gel bases and their viscosity (η), the simple regression with Pearson's test at a p-value of less than 0.05 was performed. Equation (4.3) was obtained with the correlation coefficient (r) of 0.8835 and its plot is shown in Figure 4.26.

$$D = 0.0659/\eta + 9 \times 10^{-5} \tag{4.3}$$

Despite of the trend of the inverse relationship, the correlation coefficient of this relationship was quite far from ±1. Thus, the gel viscosity was not the only parameter affecting the diffusion coefficients.

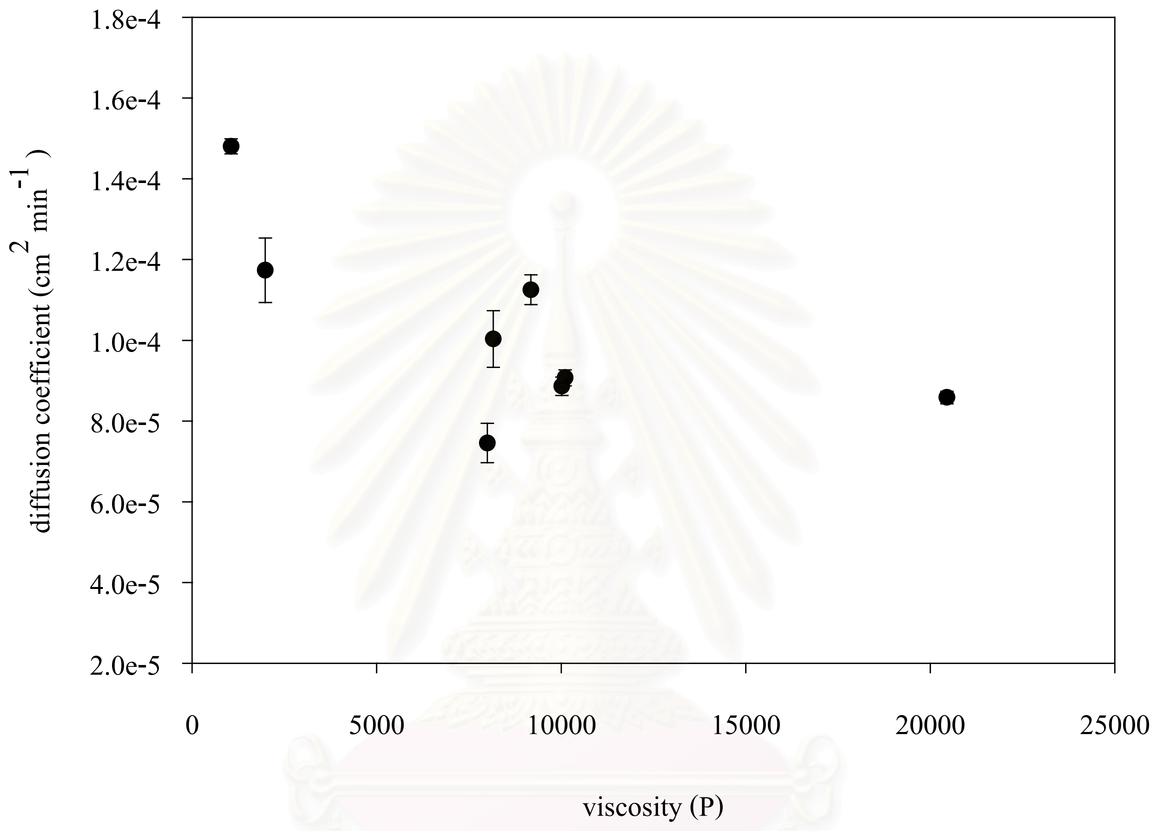

Figure 4.26 Plot of piroxicam diffusion coefficients in carbopol 940 gel bases against viscosity at a shear rate of 0.05 s^{-1} of piroxicam gel at 33 °C (mean ± SD, n = 3).

The plot of D versus η in Figure 4.26 shows some deviations. The addition of glycerin could reduce the gel viscosity as seen in the cases of C.6, C.6/G10 and C.6/G15. However, the decrease in viscosity did not make increases in piroxicam diffusion coefficients. The diffusion coefficient of formula C.6/G15 was the lowest although its viscosity was in the middle region. The polymer concentrations of formulae C.6 and C.6/G15 were the same; the only difference was the glycerin content which could increase the vehicle lipophilicity, thus piroxicam would like to stay in the donor part and diffused less to the hydrophilic receiving solution. This could be confirmed by the increase in piroxicam solubility by an addition of glycerin as shown in Table 4.7. The solubility of the piroxicam in pH 7.4 isotonic phosphate buffer used as a receiving medium is 0.48 ± 0.07 mg/ml at 37 °C (Jittida, 1994). Therefore, piroxicam was more likely to stay in the donor part as its solubility in the donor part was greater than that in the receiving solution.

Table 4.7 The solubility of piroxicam in the vehicles of formulae C.6 and C.6/G15 at 33 °C

Formula	Solubility[a] (mg/ml)
C.6	12.32 ± 0.17
C.6/G15	15.64 ± 0.42

[a]mean±SD, (n = 4).

The effect of glycerin on viscosity was less than that on diffusion coefficient. This was more prominent in the case of C1 and C.6/G10. The viscosity of gel base C1 was about twice as much as that of C.6/G10 because C1 contained greater amount of carbopol 940. However, the diffusion coefficients of piroxicam in both gel bases were not significantly different. This should be because the increase in lipophilicity of glycerin added gel base would make more drug molecule stay in the donor part or would lessen the diffusion coefficient of drug.

Carbopol 940 was very sensitive to sodium chloride as it was explained previously. This was obvious in the case of C.6/S.09 and C.6/S.9. The increase in carbopol 940 could reduce the salt effect as seen in the case of C.6/S.9 and C1/S.9. The diffusion coefficient of C1/S.9 was less than that of C.6/S.09 although its viscosity was less. Barry (1983) explained that the polymer can impede the movement of drug molecules by adsorbing them on the polymer surface and/or modify the observed diffusivity of solute by a mechanical obstruction effect, which depended on the size of the solute molecule. In this case, piroxicam should have negative charge in the solution pH studied, therefore the adsorption of drug molecules on carbopol chain should not be significant because charges on polymer were also negative.

The relationships between D and viscoelastic parameters were studied by using simple regression with Pearson's test at a p-value of less than 0.05 as shown in Equations (4.4) - (4.7).

$$D = 0.0181/G' + 8\times10^{-5} \qquad r = 0.8787 \tag{4.4}$$

$$D = 0.002/G'' + 8\times10^{-5} \qquad r = 0.8721 \tag{4.5}$$

$$D = 0.0015(\tan\delta) - 3\times10^{-5} \qquad r = 0.8525 \tag{4.6}$$

$$D = 0.0182/G^{*} + 8\times10^{-5} \qquad r = 0.8787 \tag{4.7}$$

The moduli G', G'' and G^* was inversely proportional to D, while tan δ was directly proportional to D. Since the coefficient value of Equation (4.4) was greater than that of Equation (4.5), the effect of G' on D was greater than that of G''. This was also confirmed by the small value of coefficient in Equation (4.6). Therefore, the carbopol 940 gel structure possessing predominantly elastic solid behavior, in addition to the adsorption of drug molecule on the polymer surface, the entanglement between different polymer chains which was high could act as a fine mesh that impeded the diffusant movement. Thus, G' was inversely proportional to D. An increase in carbopol 940 concentration also increased the amount of drug adsorbed on the polymer surface. Since G^* was dominated by the moduli that had greater effect which was G' in this case, the coefficient of Equation (4.7) was very close to that of Equation (4.4).

The correlation coefficients of Equations (4.4) - (4.7) which were not close to ±1 meant that the linear regression equations that described the relationships between viscoelastic parameters and D were not the best. Walkow and McGinity (1987) proposed that it was not possible to correlate any single physical or chemical property of either the drug or the vehicle with the resulting diffusion profiles. Instead, it appeared that a combination of factors were responsible for the unique diffusion of diffusant. Thus, to construct equations for describing diffusivity of diffusant, more than one independent variables should be considered such as parameters describing vehicle structure, solubility of diffusant in the vehicle and interactions between vehicle components and the diffusant.

8. Perceptual Attribute Studies.

A triangle test was used for recruiting candidates. It is usually used when the test objective is to determine whether perceptual attributes of two products are different. This method is useful in situations where treatment effects may cause changes in products, which cannot be characterized simply by one or two attributes. It is effective in certain situations especially for selecting and monitoring panelists for capability of discriminating given attributes.

The candidates who passed the required criteria and the screening test were recruited. There were a total of 30 healthy panelists consisting of 3 males and 27 females, ranging in age from 18 to 40.

After they had been trained, they were asked to evaluate the perceptual attributes of test products and scored in answer sheets as directed. Their rating scores were used to determine the correlations between the rheological properties of test products and sensory perceptions. The rheological properties studied in this case were G', G'', tan δ, and G^* (Table 4.8); viscosity (Tables 4.9 and 4.10); and yield value (Table 4.10). The mean scores of perceptual attributes evaluated by the panelists are shown in Table 4.11.

Table 4.8 Viscoelastic data of the test products at 33 °C (n = 3)

Gel base	**Frequency 0.1 rad/s**[a]				**Frequency 1.0 rad/s**[b]				**Frequency 100 rad/s**[c]			
	G'^{d}	G''^{d}	tan δ^{e}	G^{*d}	G'^{d}	G''^{d}	tan δ^{e}	G^{*d}	G'^{d}	G''^{d}	tan δ^{e}	G^{*d}
T1	**3497.62**	**249.25**	**0.0713**	**3506.49**	**3691.57**	**237.89**	**0.0644**	**3699.23**	**4358.56**	**529.51**	**0.1215**	**4390.61**
T2	**3860.98**	**296.58**	**0.0768**	**3872.35**	**4113.37**	**254.67**	**0.0619**	**4121.25**	**4903.67**	**558.98**	**0.1140**	**4935.43**
T3	**4150.38**	**295.91**	**0.0713**	**4160.92**	**4419.07**	**271.22**	**0.0614**	**4427.69**	**5253.76**	**609.70**	**0.1161**	**5289.02**
T4	**219.82**	**16.74**	**0.0759**	**220.46**	**235.10**	**11.75**	**0.0500**	**235.39**	**264.06**	**60.11**	**0.2280**	**270.82**
T5	**4152.68**	**323.81**	**0.0780**	**4165.29**	**4452.06**	**302.88**	**0.0680**	**4462.35**	**5788.52**	**779.84**	**0.1347**	**5840.81**
T6	**4762.55**	**344.94**	**0.0724**	**4775.03**	**5036.99**	**307.56**	**0.0611**	**5046.37**	**5961.66**	**673.95**	**0.1130**	**5999.63**

[a] Used in correlation to the attribute group of pick up.

[b] Used in correlation to spreadability.

[c] Used in correlation to the attribute groups of rub out (except for spreadability) and after feel.

[d] in dyn/cm^2.

[e] dimensionless.

Table 4.9 Viscosity of the test products at 33 °C (n = 3)

Gel base	Viscosity (P)	
	shear rate[a] 0.05 s^{-1}	shear rate[b] 500 s^{-1}
T1	6123.13	5.65
T2	9305.26	6.66
T3	14471.47	8.35
T4	796.72	0.40
T5	17066.47	11.45
T6	26244.80	11.66

[a] Used in correlation to the attribute group of pick up.

[b] Used in correlation to the attribute groups of rub out (except for spreadability) and after feel.

Table 4.10 Yield values and viscosity near the yield values of test products at 33 °C (n = 3)

Gel base	Yield value[a] (dyn/cm^2)	Viscosity (P) near the yield value[a]
T1	959.36	298.29
T2	1136.32	357.11
T3	1450.62	464.07
T4	42.49	13.72
T5	1633.85	530.15
T6	1912.94	619.68

[a] Used in correlation to spreadability.

Table 4.11 Mean scores rated by panelists (n = 30)

Attribute group	Mean scores[a]						
	Attributes	T1	T2	T3	T4	T5	T6
Pick up	Firmness	4.66	5.22	6.29	1.31	7.47	8.66
	Stickiness	4.05	5.14	6.18	1.76	7.43	8.80
	Peaking	4.91	5.66	6.28	1.70	7.37	7.96
Rub out	Wetness	7.33	6.62	5.50	8.52	3.92	4.84
	Spreadability	8.18	7.37	6.55	9.63	5.53	4.81
	Absorbency	5.76	5.72	5.72	7.06	9.90	8.48
After feel	Tackiness	4.24	5.15	6.02	2.82	8.59	7.22
	Gloss	2.77	3.24	3.32	2.18	6.26	4.72
	Amount of residue	2.50	2.93	3.21	1.70	6.33	4.94
	Liking	10.94	10.63	11.42	7.25	5.47	8.67

[a]Minimum and maximum scores are 0 and 15, respectively.

The rank orders of mean scores of attributes evaluated when the panelists picked gel up from the containers including firmness, stickiness and peaking were similar as follows:T6 >T5 > T3 > T2 > T1 > T4. The ANOVA for Latin square with Tukey HSD at a p-value of less than 0.05 indicated that all mean scores were significantly different.

To determine the relationships between the mean scores of these attributes and the rheological properties of test products, the value of rheological parameters at low frequency (0.1 rad/s) and low shear rate (0.05 s^{-1}) were considered because the pick up attribute group involved initial destruction of the gel structure. Simple regression and Pearson's test at a p-value of less than 0.05 were taken for data analysis.

$$\log(\text{firmness}) = 0.5506 \log G' - 1.855 \qquad r = 0.9666 \qquad (4.8)$$

$$\log(\text{firmness}) = 0.5566 \log G'' - 0.5775 \qquad r = 0.9678 \qquad (4.9)$$

$$\log(\text{firmness}) = -3.5877 \log(\tan\delta) - 3.3667 \qquad r = -0.2105 \qquad (4.10)$$

$$\log(\text{firmness}) = 0.5506 \log G^* - 1.1863 \qquad r = 0.9665 \qquad (4.11)$$

$$\log(\text{firmness}) = 0.5442 \log \eta - 1.4433 \qquad r = 0.9951 \qquad (4.12)$$

$$\log(\text{stickiness}) = 0.4409 \log G' - 0.803 \qquad r = 0.9166 \tag{4.13}$$

$$\log(\text{stickiness}) = 0.4466 \log G'' - 0.3181 \qquad r = 0.9196 \tag{4.14}$$

$$\log(\text{stickiness}) = -2.1138 \log(\tan \delta) - 1.6923 \qquad r = -0.1470 \tag{4.15}$$

$$\log(\text{stickiness}) = 0.4409 \log G^* - 0.8036 \qquad r = 0.9167 \tag{4.16}$$

$$\log(\text{stickiness}) = 0.4598 \log \eta - 1.1033 \qquad r = 0.9957 \tag{4.17}$$

$$\log(\text{peaking}) = 0.4602 \log G' - 0.857 \qquad r = 0.9722 \tag{4.18}$$

$$\log(\text{peaking}) = 0.4657 \log G'' - 0.3499 \qquad r = 0.9744 \tag{4.19}$$

$$\log(\text{peaking}) = -2.591 \log(\tan \delta) - 2.2197 \qquad r = -0.1830 \tag{4.20}$$

$$\log(\text{peaking}) = 0.4602 \log G^* - 0.8577 \qquad r = 0.9722 \tag{4.21}$$

$$\log(\text{peaking}) = 0.4511 \log \eta - 1.058 \qquad r = 0.9927 \tag{4.22}$$

The relationships between firmness, stickiness, and peaking and the rheological parameters are presented in Equations (4.8) - (4.12), (4.13) - (4.17), and (4.18) - (4.22), respectively. Except for tan δ, other attributes correlated to the rheological parameters as indicated by their r values. The comparable values of coefficients of all moduli, (G', G'' and G^*) indicated that the elastic solid and viscous fluid behaviors exerted the comparable extent to the pick up attributes. The relationships of these attributes and the rheological parameters could be explained by Stevens' equation (Wang, Kislalioglu and Breuer, 1999). Stevens concluded that the magnitude of sensory attributes, S, can be expressed as a power function of the corresponding physical property, P, as follows:

$$S = P^{\alpha} \tag{4.23}$$

where the magnitude of the exponent, α, is a characteristic quantity for a given attribute property relationship. When the mean scores obtained for each attribute were plotted against the values of rheological parameters on a log - log scale, the values of α were obtained from the slope. The exponent, α, is a measure of the rate of growth of perceived intensity as a function of stimulus intensity. When α is larger than 1, the sensation grows faster than the stimulus, e.g., electric shock. Conversely, when α is smaller than 1, the sensation grows more slowly than the stimulus. Since the α values in this study indicated by the coefficients of the independent variables were all less than 1, the attributes perceived by the panelists grew more slowly than the change in values of rheological parameters (Meilgaard, Civille and Carr, 1991).

Since firmness was defined as a force required to fully compress the product between thumb and forefinger, this attribute had relationships with the moduli G', G'' and G^*. These were because the great magnitudes of G', G'' or G^* meant that the test products were hard to be deformed. Because G', G'' and G^* were defined as corresponding stress/strain as it was described previously, they could be explained similarly to the “modulus of deformability” as in the case of Young’s modulus, which was stress/strain, for elastic materials. Therefore, the greater the moduli, the harder the gel to deformed, i.e., the more firmness the gel possessed. The test products possessing high values of moduli exhibited higher stiffness. Their gel-network structure were formed with highly entangled polymer, thus the viscosity at low shear of these products were great and more force was required to break the structure.

Stickiness and peaking were quite related to cohesion which is the attractive force acting between molecules of the same substance (De Man et al., 1976). The test products requiring more force to separate the fingers had a great magnitude of cohesion originated by the gel-network structure. Thus, the products with high values of G', G'', G^* and η made the panelist perception of stickiness be high. If the test products had great cohesion, the gel would maintain its high peak after separating the fingers. Consequently, the panelists perceived high peaks of the remaining gel on their fingers.

Because $\tan \delta$ is a ratio of G''/G', it explains how viscous fluid behavior is inferior or superior to the elastic solid behavior. In this study, the $\tan \delta$ values of test products were comparable and not related to the pick up attributes.

While gel was being rubbed on the skin, the wetness, spreadability and absorbency were evaluated. The rank order of wetness perception was as follows: T4 > T1 > T2 > T3 > T6 > T5, and they were different significantly as analyzed by using ANOVA for Latin square with Tukey HSD at a p-value of less than 0.05. It was probable that the panelists could perceive the amount of free water in test products while they were rubbing. The rheological data were obtained at high frequency (100 rad/s) and at high shear rate ($500\ s^{-1}$) since the attributes were evaluated at high frequency and shear rate.

In a restful state of gel products, the polymer chains entangled and trapped water within their networks. This water seemed to be decreased. When the shear stress was applied, the polymer chains elongated and disentangled and the trapped water was released, thus free water was increased. If the panelists rubbed gels on their forearms with equivalent forces for each test, they would perceive less wetness in the case of the test product with higher concentration of carbopol 940 because less free water was released. However, the small values of coefficients of the moduli indicate that the panelists hardly perceived different wetness of products with different values of rheological parameters. The correlations are shown in Equations (4.24) - (4.28) which were analyzed by using Pearson's test at a p-value of less than 0.05.

$$\text{wetness} = -0.0007\, G' + 9.1396 \qquad r = -0.8535 \qquad (4.24)$$

$$\text{wetness} = -0.0061\, G'' + 9.392 \qquad r = -0.8990 \qquad (4.25)$$

$$\text{wetness} = 23.57\, (\tan \delta) + 2.8722 \qquad r = 0.6241 \qquad (4.26)$$

$$\text{wetness} = -0.0007\, G^{*} + 9.1457 \qquad r = -0.8544 \qquad (4.27)$$

$$\text{wetness} = -0.3891\, \eta + 8.9863 \qquad r = -0.9636 \qquad (4.28)$$

The wetness of gel base T5 containing 30.0 %v/w of glycerin perceived by the panelists was the lowest because it contained the lowest amount of water.

The spreadability was evaluated by considering are ease of moving the product over the skin surface. The rank order of spreadability was as follows: T4 > T1 > T2 > T3 > T5 > T6, they were different significantly as analyzed by ANOVA of Latin square with Tukey HSD at a p-value of less than 0.05. Since the spreadability in this case was evaluated only in the first step of the rubbing process, the initial force to move the product over the skin was considered and the viscosity around the yield value was measured.

Generally, a product containing tight gel-network structure required more initial force to break than the one containing loose gel-network structure. Therefore, the product possessing more prominent elastic solid behavior was harder to be moved over the skin surface. The relationship between spreadability and rheological parameters are presented in Equations (4.29) - (4.34), where σ_y is the yield value. These parameters were inversely correlated to spreadability except for tan δ as analyzed by Pearson's test at a p-value of less than 0.05. Since the correlation coefficient of Equation (4.31) was insignificant according to the Pearson's test, tan δ could not be related to the spreadability attribute. The viscous fluid behavior influenced the wetness and spreadability attributes more than the elastic solid due to much greater absolute values of coefficient of G''.

$$\text{spreadability} = -0.0009\,G' + 10.255 \qquad r = -0.8703 \qquad (4.29)$$

$$\text{spreadability} = -0.0139\,G'' + 10.221 \qquad r = -0.8707 \qquad (4.30)$$

$$\text{spreadability} = -193.86(\tan\delta) + 18.862 \qquad r = -0.6624 \qquad (4.31)$$

$$\text{spreadability} = -0.0009\,G^* + 10.256 \qquad r = -0.8703 \qquad (4.32)$$

$$\text{spreadability} = -0.0081\,\eta + 10.098 \qquad r = -0.9810 \qquad (4.33)$$

$$\text{spreadability} = -0.0026\,\sigma_y + 10.13 \qquad r = -0.9755 \qquad (4.34)$$

The higher scores of absorbency meant that more numbers of rubs was required for the panelists to perceive that no moisture was left on their forearms. The ANOVA for Latin square with Tukey HSD at a p-value of less than 0.05 were used for data analysis. The rank order of absorbency was as follows: T5 > T6 ~ T4 > T1 ~ T2 ~ T3. The gel base T5 containing 30.0 %v/w glycerin required more numbers of rubs than others because the high concentration of glycerin made the product more hygroscopic than others. Since gel base T6 contained the highest concentration of carbopol 940 (1.0 %w/w), there would be more water attached to the polymer chains as water of hydration and the gel-network structure could trap more free water within its structure. Consequently, the panelists needed more number of rubs before the polymer released water completely. Because the gel base T4 contained sodium chloride, the preparation was much more fluid, slightly cloudy though homogeneous. It appeared as a little viscous solutions with high water content and the panelists perceived incomplete absorption. The compositions of gel bases T1, T2 and T3 were similar; only polymer concentrations were different. T1, T2 and T3 contained carbopol 940 in concentrations of 0.3, 0.4 and 0.6 %w/w respectively. Therefore, their absorbency attribute were not significantly different. However, there was no correlations between absorbency and rheological parameters obtained at high frequency (100 rad/s) or at high shear rate (500 s^{-1}) analyzed by the Pearson's test at a p-value of less than 0.05.

After the panelist had rubbed gel on their forearms, after feeling attributes were evaluated. Tackiness was defined as a force required to separate a finger from the forearm skin while the panelists tried to lift the finger from the skin. The rank order of tackiness perceived by panelists was as follows: T5 > T6 > T3 > T2 > T1 > T4.

Tackiness might result from residual product that could not be absorbed completely. The gel base T5 contained high concentration of glycerin which possessed tacky and hygroscopic character thus the panelists could feel high intensity of tackiness on their skins after rubs. A product containing high concentration of polymer such as gel base T6 could result in the perception of high viscosity with more elastic solid behavior. When the more concentrated carbopol 940 gel bases had been rubbed for a long time on the skin until the panelists could not perceive moist feeling, the polymer was left on the applied area as a tackier thin film and it needed more force to separate the cohesion in the film structure. Thus, the rank order of tackiness was consistent with rank order of carbopol 940 concentration, i.e.,T6 > T3 > T2 > T1. However, the gel base T4 containing the same carbopol 940 concentration as T3 and T5 had the lowest tackiness perception. The gel base T4 was more fluid than others and appeared like a liquid with low viscosity. This was probable that gel structure exhibited more viscous fluid behavior. Consequently, the panelists perceived it like a low viscosity solution with the lowest tackiness.

The correlations between rheological parameters and tackiness with a p-value of less than 0.05 are presented in Equations (4.35) - (4.39). Only tan δ could not be related to tackiness attribute because the correlation coefficient of Equation (4.37) was not significant according to the Pearson's test. The viscous fluid behavior of polymer had more influence on the tackiness attribute than the elastic solid behavior since the coefficient value of G'' were greater than that of G'. An explanation was that the tackiness attribute was determined after the polymer structure had been deformed, therefore the elastic solid behavior was less dominant and the viscous fluid became prominent.

$$\text{tackiness} = 0.0008\ G' + 2.058 \qquad r = 0.8358 \qquad (4.35)$$

$$\text{tackiness} = 0.0074\ G'' + 1.7045 \qquad r = 0.8918 \qquad (4.36)$$

$$\text{tackiness} = -27.481\ (\tan \delta) + 9.4631 \qquad r = -0.5946 \qquad (4.37)$$

$$\text{tackiness} = 0.0008\ G^* + 2.05 \qquad r = 0.8368 \qquad (4.38)$$

$$\text{tackiness} = 0.4726\ \eta + 2.1952 \qquad r = 0.9564 \qquad (4.39)$$

The residue perceptions were evaluated by observation of residual product left on the panelist skin and the glitter of residual product was ranked as degree of gloss. The rank order of gloss and residue attributes perceived by the panelists were as follows: T5 > T6 > T1 ∼ T2 ∼ T3 ∼ T4 and T5 > T6 > T1 ∼ T2 ∼ T3 > T4, respectively. The gel base T5 containing 30.0 %v/w glycerin was evaluated as having the highest gloss and residue. The most concentrated carbopol 940 as in the case of T6 could have more thin film of polymer left on the panelist skins than the less concentrated products and the panelists perceived its high degree of glitter as more glossy with high residue. However, the gloss of gel bases T1, T2, T3 and T4 perceived by the panelists were not significantly different. This was because they did not contained glycerin and their polymer concentrations were low, i.e., 0.3 - 0.6 %w/w. The gel base T4 possessed low viscosity and behaved like a viscous fluid, thus the residue left was the least. The residue left from the gel bases T1, T2 and T3 were not significantly different. The reasons might be the same as previously described.

The correlation coefficients of correlation between viscosity and gloss, and between viscosity and residue are shown in Equation (4.40) - (4.41), respectively. As it was stated previously that gloss and residue were greatly influenced by glycerin and carbopol 940 contents in the preparations which, in turn, affected the viscosity, especially the effect of carbopol 940 on viscosity. However, the Pearson's test at a p-value of less than 0.05 indicated insignificant values of correlation coefficients of correlations between the other rheological parameters studied and both gloss and residue attributes. An explanation was that the viscosity values were obtained by continuous shear method which could destroy the gel structure continuously. This was similar to both attribute score which were obtained after the structure of products had been disrupted. However, the viscoelastic data of much less destroyed structure were obtained and thus not correlated to any attributes.

$$\text{gloss} = 0.306\,\eta + 1.495 \qquad r = 0.8615 \qquad (4.40)$$

$$\text{residue} = 0.3644\,\eta + 0.9188 \qquad r = 0.8929 \qquad (4.41)$$

The last attribute considered was liking. It was the degree of overall acceptance by the panelists. The correlations between rheological parameters and liking could not be found. This was probable that the product acceptance did not depend only on rheological factor, but also by other inherent properties of the formulation compositions. Since the formula composition influenced the rheological properties of the product, the formulators or the researchers might use the rheological data as a compass for success in topical drug or cosmetic formulations.

The rank order of liking attribute perceived by the panelists was as follows: T1 ~ T2 ~ T3 > T6 > T4 > T5. Most of the panelists accepted preparations T1, T2, T3 with insignificant difference. The preparations T1, T2 and T3 possessed optimum consistency; they were neither too hard nor too fluid. In addition, they were easy to spread, absorbed quite quickly, less gloss and left only small amount of residue. Because the preparation T4 was very fluid and T5 possessed the gloss character with tackiness, thus the liking scores were low.

When the correlation coefficients of all correlations were compared, the correlations of perception attributes to viscosity were the greatest. This should be because the score of attributes studied were obtained after the gel structures had been destroyed. All perception attributes were not correlated to tan δ. Since the tan δ values of all preparations were not different appreciably, the panelists might not able to perceive such a small difference. Both G' and G'' influenced the pick up attributes to about the same extent. In other words, both elastic solid and viscous fluid behaviors played important roles in the firmness, stickiness and peaking attributes perceived by the panelists. However, G'' had more effect on the rub on (wetness and spreadability) and after feel (tackiness) attributes than G'. Therefore, the viscous fluid played a significant role after the gel structure was more extensively destroyed.

CHAPTER V

CONCLUSION

Relationships between viscoelastic properties of piroxicam gels and piroxicam diffusion coefficients in gel bases and those between viscoelastic properties of carbopol 940 gel bases and their perceptual attributes can be concluded as follows:

1. The viscoelastic properties of the light protected piroxicam gels containing carbopol 940 as a gelling agent did not change within 14 days after they had been prepared. However, the viscoelastic properties of light exposed preparations altered with aging time.

2. The formula compositions influenced the viscoelastic properties of piroxicam gels using carbopol 940 as their gel bases.

2.1 Increases in carbopol 940 concentrations caused the preparations exhibited more elastic solid behavior; G', G'', G^*, and viscosity tended to increase, while $\tan \delta$ decreased.

2.2 The preparations containing optimum water and glycerin contents showed more elastic solid character than the preparations containing lower water content with higher glycerin concentrations; their G', G'', G^* and viscosity were greater while $\tan \delta$ was less.

2.3 The addition of sodium chloride affected the viscoelastic properties of piroxicam gels containing carbopol 940. The preparations containing higher sodium chloride content had lower values of G', G'', G^*, and viscosity, and higher values of $\tan \delta$. Higher concentrations of carbopol 940 could help tolerating concentrated electrolyte.

3. There were correlations between viscoelastic parameters of carbopol 940 gel bases and piroxicam diffusion coefficients (D) in gel bases analyzed by using the Pearson's test at a p-value of less than 0.05. The correlations indicated that the effect of G' on D was greater than those of G'', and $\tan \delta$ on D, respectively and the influenced of G^* on D was about the same as that of G'. The effect of viscosity on D was the greatest.

4. There were correlations between some viscoelastic parameters of carbopol 940 gel bases and some perceptual attributes analyzed by using the Pearson's test at a p-value of less than 0.05. The correlations between viscosity and perceptual attributes including firmness, stickiness, peaking, wetness, spreadability, tackiness, gloss, and residue were the greatest compared with the correlation of other rheological parameters. G', G'' and G^* influenced the pick up attributes to about the same extent. G'' had more effect on the rub on (wetness and spreadability) and after feel (tackiness) attributes than G'. However, tan δ was not correlated to all perceptual attributes since the tan δ values of all preparations were comparable. Furthermore, correlations between absorbency, gloss, amount of residue, liking and any viscoelastic parameters could not be found.

References

Adams, I., and Davis, S. S. The formulation and sterilization of a surgical lubricant gel based on carboxypolymethylene. J. Pharm. Pharmacol. 25 (1973): 640-648.

Aust, B., Oddo, L. P., Wild, J. E., Mills, O. H., and Deupree, J. S. The descriptive analysis of skin care products by a trained panel of judges. J. Soc. Cosmet. Chem. 38 (1987): 443-449.

Barnes, H. A., Hutton, J. F., and Walters, K. An introduction to rheology. 1st ed. Amsterdam: Elsevier science, 1989.

Barry, B. W., and Grace, A. J. Rheological and sensory evaluation of work softening and recovery of pharmaceutical white soft paraffins. J. Pharm. Sci. 60 (1971): 1198-1203.

Barry, B. W., and Meyer, M. C. Sensory assessment of spreadability of hydrophilic topical preparations. J. Pharm. Sci. 62 (1973):1349-1354.

Barry, B. W., and Meyer, M. C. The rheological properties of carbopol gels I. Contiuous shear and creep properties of carbopol gels. Int. J. Pharm. 2 (1979): 1-25.

Barry, B. W., ed. Dermatological formulation. New York: Mercel Dekker, 1983.

Bimczok, R., Ansmann, A., Bielfeldt, S., Billek, D., Driller, H., Feistkorn, G., et al. A multicenter comparison of different test methods for the assessment of the efficacy of skin care products with 368 human volunteers. J. Soc. Cosmet. Chem. 45 (1994): 1-19.

Bonferoni, M. C., Rossi, S., Ferrari, F., Bertoni, M., and Caramella, C. Influence of medium on dissolution-erosion behaviour of Na carboxymethylcellulose and on viscoelastic properties of gels. Int. J. Pharm. 117 (1995): 41-48.

Chu, J. S., Yu, D. M., Amidon, G. L., Weiner, N. D., and Goldberg, A. H. Viscoelastic properties of polyacrylic acid gels in mixed solvents. Pharm. Res. 9 (1992): 1659-1663.

Clark, A. H., and Ross-Murphy, S. B. Structure and mechanical properties of biopolymer gels. Adv. Polym. Sci. 83 (1987): 57-192.

Close, J. The concept of sensory quality. J. Soc. Cosmet. Chem. 45 (1994): 95-107.

Colo, D., Carelli, V., Giannaccini, B., Serafini, M.F., and Bottari, R. Vehicle effects in percutaneous absorption: *in vitro* study of influence of solvent power and microscopic viscosity of vehicle on benzocaine release from suspension hydrogel. J. Pharm. Sci. 69 (1980): 367-391.

Davis, S. S. Viscoelastic properites of pharmaceutical semisolids III. Nondestructive oscillatory testing. J. Pharm. Sci. 58 (1971): 1351-1356.

Dean, A., and Voss, D. Design and analysis of experiments. New York: Hamilton, 1999.

De Man, J. M., Voisey, P. W., Rasper, V. F., and Stanley, D. W. Rheology and texture in food quality. Conneticut: AVI, 1976.

Dumortier, G., Grossiord, J. L., Zuber, M., Couarraze, G., and Chaumeil, J.C. Rheological study of a thermoreversible morphine gel. Drug Dev. Ind. Pharm. 17 (1991): 1255-1265.

Edsman, K., Carlfors, J., and Harju, K. Rheological evaluation and ocular contact time of some carbomer gels for ophthalmic use. Int. J. Pharm. 137 (1996): 233-241.

Edsman, K., Carlfors, J., and Petersson, R. Rheological evaluation of poloxamer as an in situ gel for ophthalmic use. Eur. J. Pharm. Sci. 6 (1998): 105-112.

Higuchi, T. Rate of release of medicaments from ointment bases containing drugs in suspension. J. Pharm. Sci. 50 (1961): 874-875.

Higuchi, W. I. Analysis of data on the medicament release from ointments. J. Pharm. Sci. 51 (1962): 802-804.

Ho, H. O., Huang, F. C., Sokoloski, T. D., and Sheu, M. T. The influence of cosolvents on the in vitro percutaneous penetration of diclofenac sodium from a gel system. J. Pharm. Pharmacol. 46 (1994): 636-642.

Jittida Shoosanglertvijit. Flux comparisons of certain NSAIDs through synthetic membranes, human placenta and amnion, and newborn pig skin. Master' s Thesis, Department of Pharmacy, Graduate School, Chulalongkorn University, 1994.

Jones, D. S., Woolfson, A. D., and Brown, A. F. Textural, viscoelastic and mucoadhesive properties of pharmaceutical gel composed of cellulose polymers. Int. J. Pharm. 151 (1997): 223-233.

Jones, D. S., Woolfson, A. D., and Brown, A. F. Viscoelastic properties of bioadhesive, chlorhexidine-containing semisolids for topical application to the oropharynx. Pharm. Res. 15 (1998): 1131-1136.

Kantaria, S., Rees, G. D., and Lawrence, M. J. Gelatin-stabilised microemulsion-based organogels: rheology and application in iontophoretic transdermal drug delivery. J. Control. Release 60 (1999): 355-365.

Korhonen, M., Niskanen, H., Kiesvaara, J., and Yliruusi, J. Determination of optimal combiantion of surfactants in creams using rheology measuremeants. Int. J. Pharm. 197 (2000): 143-151.

Laba, D., ed. Rheological properties of cosmetics and toiletries. New York: Marcel Dekker, 1993.

Lieberman, H. A., Rieger, M. M., and Banker, G. S., eds. Pharmaceutical dasage forms. Vol. 3. New York: Marcel Dekker, 1998.

Lin, S. Y., Amidon, G. L., Weiner, N. D., and Goldberg, A. H. Viscoelasticity of cellulose polymers and mucociliary transport on frog palates. Int. J. Pharm. 95 (1993): 57-65.

Lorenzo, C. A., Amoza, J. L. G., Pacheco, R. M., Souto, C., and Concheiro, A. Microviscosity of hydroxypropylcellulose gels as a basis for prediction of drug diffusion rates. Int. J. Pharm. 180 (1999): 91-103.

Macedo, T., Block, L. H., and Shukla, A. J. Release of tolmetin from carbomer gel systems. Drug Dev. Ind. Pharm. 19 (1993): 887-902.

Martin, A. N. Physical pharmacy. 4th ed. Philadelphia: Lea & Febiger, 1993.

Meilgaard, M., Civille, G. V., and Carr, B. T. Sensory evaluation techniques. 2nd ed. Florida: CRC, 1991.

Morimoto, K., and Suzuki, S. Ultraviolet irradiation of poly(alkyl acrylates) and poly(alkyl Methacrylates). J. Appl. Polymer Sci. 16(1972): 2947-2961.

Morosawa, K., Ohtake, C., Takahashi, M., Mitsui, T., and Ishikawa, S. A study on the differential thresholds of sensory firmness and viscousness of cream base substances. J. Soc. Cosmet. Chem. 25 (1974): 481-494.

Nacht, S., Close, J., Yeung, D., and Gans, E. H. Skin friction coefficient: changes induced by skin hydration and emollient application and correlation with perceived skin feel. J. Soc. Cosmet. Chem. 32 (1981): 55-65.

Nielsen, L. E. Polymer rheology. New York: Marcel Dekker, 1977.

Osborne, D. W., and Amann, A. H., eds. Topical drug delivery formulations. New York: Marcel Dekker, 1990.

Peppas, N. A., Bures, P., Leobandung, W., and Ichikawa, H. Hydrogels in pharmaceutical formulations. Eur. J. Pharm. Biopharm. 50 (2000): 27-46.

Radebaugh, G. W., and Simonelli, A. P. Phenomenological viscoelasticity of a heterogeneous pharmaceutical semisolid. J. Pharm. Sci. 72 (1983): 415-422.

Radebaugh, G. W., and Simonelli, A. P. Relationship between powder surface characteristics and viscoelastic properties of powder-filled semisolids. J. Pharm. Sci. 74 (1985): 3-10.

Realdon, N., Ragazzi, E., Zotto, M. D., and Fini, G. D. Possibilities of conveying a cationic drug in carbomer hydrogels. Drug Dev. Ind. Pharm. 24 (1998): 337-343.

Reynolds, J.E.F., ed. Martindale. 13th ed. London: The pharmaceutical press, 1933.

Rosen, S. L. Fundamental principles of polymeric materials. 2nd ed. New York: John Wiley & Sons, 1993.

Segers, J. D., Zatz, J. L., and Shah, V. P. In vitro release of phenol from ointment formulations. Pharm. Technol. 21 (1997): 70, 72, 74, 76, 80-81.

Semenzato, A., Bau, A., Dallaglio, C., Nicolini, M., and Bettero, A. Stability of vitamin A palmitate in cosmetic emulsions: influence of physical parameters. Int. J. Cosmet. Sci. 169 (1994): 139-147.

Shin, S. C., Cho, C. W., and Choi, H. K. Permeation of piroxicam from the poloxamer gels. Drug Dev. Ind. Pharm. 25 (1999): 273-278.

Swarbrick, J., and Boylan, J. Encyclopedia of pharmaceutical technology. Vol. 6. New York: Marcel Dekker, 1996.

Tamburic, S., and Craig, D. Q. An investigation into the rheological, dielectric and mucoadhesive properties of poly(acrylic acid) gelsystems. J. Control. Release 37 (1995): 59-68.

Walkow, J. C., and McGinity, J. W. The effect of physicochemical properties on the in vitro diffusion of drug through synthetic membranes and pigskin. I. Methyl salicylate. Int. J. Pharm. 35 (1987): 91-102.

Wang, S., Kislalioglu, M. S., and Breuer, M. The effect of rheological properties of experimental moisturizing creams/lotions on their efficacy and perceptual atrributes. Int. J.Cosmet. Sci. 21(1999): 167-188.

APPENDICES

APPENDIX I

Details of Piroxicam and pH 7.4 Isotonic Phosphate Buffer

Piroxicam (4-hydroxy-2-methyl-N-(2-pyridyl)-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide) (Reynolds, 1993)

Piroxicam, an oxicam derivative, is a nonsteroidal anti-inflammatory agent. The drug is acidic because of the presence of a 4-hydroxy enolic acid substituent. Its molecular formula is $C_{15}H_{13}N_3O_4S$ with a molecular weight of 331.35.

Piroxicam is an off-white to light tan or light yellow, odourless powder. It forms a monohydrate that is yellow. Piroxicam is very slightly soluble in water, dilute acids and most organic solvent; slightly soluble in alcohol and aqueous alkaline solutions. The sample of piroxicam kept in the dark at 20 °C and 40 °C for two years had not been changed in its appearance.

Piroxicam has analgesic, anti-inflammatory and antipyretic properties. It is used in musculoskeletal and joint disorders such as an akylosing spondylitis, osteoarthritis and rheumatoid arthritis in a usual dose by mouth of 20 mg daily as a single dose. Some patients may respond to doses of 10 mg daily and others may require daily dose of 30 mg in single or divided doses; long term administration of 30 mg or more daily is associated with an increased risk of gastro-intestinal adverse effects. Piroxicam is also used in acute gout, the usual dose being 40 mg daily for 5 to 7 days. Piroxicam is given in similar doses as a rectal suppository. A dose of 20 to 40 mg daily has been given by intramuscular injection. Piroxicam is also used topically; 1 g of a 0.5 % gel is applied three or four times daily for a variety of painful or inflammatory condition. The most frequent adverse effects associated with piroxicam are gastro-intestinal disturbances including acute nephropathy and acute hepatocellular injury.

The composition of pH 7.4 isotonic phosphate buffer (Martin, 1993)

Monobasic potassium phosphate	0.190 g
Disodium hydrogen phosphate	0.810 g
Sodium chloride	0.411 g
Distilled water qs ad	100 ml

APPENDIX II

Effect of Light and Aging Time on Rheological Parameters at 27 °C

Strain sweep test data of light protected formula C.6 at frequency of 1.0 rad/s

%Strain	**G'(dyn/cm^2)**			
	1st day	**4th day**	**7th day**	**14th day**
0.05	2287.91 ± 1.52	2243.86 ± 2.12	2169.82 ± 3.21	2243.86 ± 1.65
0.08	2224.20 ± 1.29	2199.21 ± 2.22	2181.11 ± 3.12	2169.99 ± 2.12
0.12	2198.49 ± 3.21	2355.03 ± 2.13	2195.65 ± 3.12	2275.48 ± 3.79
0.20	2194.47 ± 1.23	2283.70 ± 1.99	2250.59 ± 3.22	2254.16 ± 8.72
0.31	2227.93 ± 1.25	2341.42 ± 1.23	2249.76 ± 4.32	2265.22 ± 6.12
0.49	2247.06 ± 3.23	2331.07 ± 2.21	2281.58 ± 4.12	2250.71 ± 3.15
0.78	2246.81 ± 3.72	2338.41 ± 2.22	2284.48 ± 5.35	2258.34 ± 4.67
1.25	2226.81 ± 1.12	2326.41 ± 2.25	2280.37 ± 2.21	2241.02 ± 5.79
1.98	2206.34 ± 1.23	2297.57 ± 2.17	2254.26 ± 1.22	2227.75 ± 2.69
3.14	2168.91 ± 1.45	2266.96 ± 1.21	2219.89 ± 1.57	2195.62 ± 3.12
4.98	2117.04 ± 1.12	2211.38 ± 2.21	2163.41 ± 1.47	2151.17 ± 4.12
7.89	2031.94 ± 1.57	2134.41 ± 2.54	2080.89 ± 1.59	2067.10 ± 2.15
12.50	1906.43 ± 1.69	2016.26 ± 2.44	1964.91 ± 1.42	1947.51 ± 1.07
19.84	1652.70 ± 1.12	1818.81 ± 1.12	1767.27 ± 2.72	1748.35 ± 3.99
31.43	1285.36 ± 2.99	1492.04 ± 2.97	1447.67 ± 2.99	1434.26 ± 1.27
49.83	884.06 ± 1.24	1058.18 ± 1.87	1036.58 ± 1.01	1030.59 ± 0.83
78.90	552.83 ± 2.12	673.08 ± 1.13	665.74 ± 0.93	659.86 ± 0.99
124.88	327.36 ± 1.15	396.42 ± 0.22	393.86 ± 1.23	388.16 ± 1.12
198.13	183.08 ± 1.67	218.55 ± 0.69	216.81 ± 1.07	213.57 ± 1.67
313.87	98.07 ± 0.77	115.26 ± 0.87	113.90 ± 0.05	112.56 ± 0.09
497.56	50.86 ± 0.16	59.25 ± 0.12	58.37 ± 0.25	57.84 ± 0.78

(mean ± SD, n = 3)

Frequency sweep test data of light protected formula C.4.

Frequency	**G′(dyn/cm^2)**			
(rad/s)	**1st day**	**4th day**	**7th day**	**14th day**
100.00	809.90 ± 76.90	811.92 ± 49.56	818.20 ± 73.90	816.65 ± 22.18
63.10	779.38 ± 74.09	786.21 ± 47.84	791.50 ± 71.26	789.42 ± 18.02
39.81	753.25 ± 73.87	764.81 ± 45.54	769.76 ± 67.26	766.36 ± 17.10
25.12	712.33 ± 69.84	750.97 ± 47.74	757.15 ± 67.87	754.46 ± 14.29
15.85	703.24 ± 71.86	737.68 ± 45.96	744.39 ± 65.11	740.63 ± 16.51
10.00	697.30 ± 69.60	727.53 ± 45.21	730.96 ± 67.68	728.61 ± 14.28
6.31	688.62 ± 69.80	718.12 ± 42.82	720.14 ± 68.53	720.23 ± 10.62
3.98	681.12 ± 67.89	711.90 ± 48.61	713.59 ± 60.81	710.93 ± 21.66
2.51	670.91 ± 65.91	699.76 ± 49.93	704.00 ± 68.83	702.94 ± 10.84
1.58	665.72 ± 68.71	695.53 ± 36.80	697.06 ± 65.45	698.47 ± 14.45
1.00	657.40 ± 63.44	688.45 ± 40.60	690.72 ± 62.43	692.93 ± 16.48
0.63	646.85 ± 65.54	681.45 ± 38.15	681.97 ± 63.24	682.89 ± 10.64
0.40	640.97 ± 65.51	675.48 ± 40.41	670.28 ± 67.68	677.46 ± 15.88
0.25	631.98 ± 66.87	665.53 ± 33.87	661.89 ± 71.94	665.03 ± 13.24
0.16	624.58 ± 61.87	658.67 ± 43.21	658.32 ± 66.53	662.39 ± 15.66
0.10	607.99 ± 62.92	648.31 ± 52.44	641.07± 65.46	650.65± 16.84

(mean ± SD, n = 3)

Frequency sweep test data of light protected formula C.4 (continued).

Frequency (rad/s)	**tan δ**			
	1st day	**4th day**	**7th day**	**14th day**
100.00	0.2006 ± 0.0111	0.1965 ± 0.0015	0.1904 ± 0.0072	0.1860 ± 0.0025
63.10	0.1696 ± 0.0088	0.1613 ± 0.0037	0.1604 ± 0.0045	0.1564 ± 0.0067
39.81	0.1319 ± 0.0091	0.1273 ± 0.0021	0.1262 ± 0.0022	0.1191 ± 0.0079
25.12	0.1079 ± 0.0045	0.1070 ± 0.0019	0.1078 ± 0.0009	0.1075 ± 0.0020
15.85	0.0926 ± 0.0041	0.0915 ± 0.0008	0.0926 ± 0.0021	0.0878 ± 0.0043
10.00	0.0803 ± 0.0039	0.0822 ± 0.0028	0.0800 ± 0.0026	0.0759 ± 0.0032
6.31	0.0747 ± 0.0021	0.0716 ± 0.0024	0.0744 ± 0.0016	0.0746 ± 0.0022
3.98	0.0753 ± 0.0060	0.0697 ± 0.0010	0.0698 ± 0.0139	0.0653 ± 0.0002
2.51	0.0674 ± 0.0068	0.0664 ± 0.0048	0.0686 ± 0.0032	0.0680 ± 0.0050
1.58	0.0666 ± 0.0026	0.0636 ± 0.0090	0.0645 ± 0.0040	0.0599 ± 0.0032
1.00	0.0667 ± 0.0076	0.0646 ± 0.0010	0.0718 ± 0.0050	0.0629 ± 0.0106
0.63	0.0694 ± 0.0055	0.0676 ± 0.0052	0.0706 ± 0.0054	0.0671 ± 0.0093
0.40	0.0673 ± 0.0041	0.0696 ± 0.0041	0.0743 ± 0.0106	0.0719 ± 0.0090
0.25	0.0700 ± 0.0040	0.0798 ± 0.0010	0.0775 ± 0.0047	0.0677 ± 0.0166
0.16	0.0723 ± 0.0017	0.0829 ± 0.0107	0.0791 ± 0.0117	0.0811 ± 0.0090
0.10	0.0745 ± 0.0049	0.0978 ± 0.0160	0.0802 ± 0.0103	0.0782 ± 0.0118

(mean ± SD, n = 3)

Steady rate sweep test data of light protected formula C.4.

Shear rate	**Viscosity** (P)			
(s^{-1})	**1st day**	**4th day**	**7th day**	**14th day**
0.05	1976.61 ± 156.09	1988.30 ± 402.55	1959.28 ± 115.74	2012.26 ± 138.28
0.08	1347.63 ± 122.03	1345.38 ± 242.66	1327.71 ± 92.34	1366.72 ± 135.14
0.13	879.90 ± 81.97	875.24 ± 156.61	865.02 ± 57.24	892.89 ± 86.17
0.20	569.59 ± 55.13	568.20 ± 103.50	562.09 ± 34.79	581.17 ± 56.08
0.32	370.00 ± 36.97	369.75 ± 66.78	365.91 ± 21.49	378.69 ± 37.43
0.50	247.76 ± 24.71	241.41 ± 42.90	239.20 ± 13.47	247.96 ± 25.48
0.79	157.83 ± 16.29	158.99 ± 27.99	157.41 ± 8.87	163.38 ± 17.44
1.26	109.71 ± 10.64	105.28 ± 17.97	104.06 ± 5.58	107.80 ± 11.17
1.99	70.99 ± 7.27	70.08 ± 11.67	69.42 ± 3.63	71.84 ± 7.80
3.15	48.42 ± 4.55	47.12 ± 7.61	46.70 ± 2.21	48.45 ± 4.86
5.00	33.37 ± 3.18	32.19 ± 4.91	31.89 ± 1.49	33.01 ± 3.45
7.92	25.41 ± 2.16	22.29 ± 3.21	22.08 ± 0.98	22.85 ± 2.34
12.56	15.93 ± 1.51	15.64 ± 2.10	15.51 ± 0.64	16.04 ± 1.61
19.91	11.87 ± 1.07	11.13 ± 1.37	11.04 ± 0.43	11.41 ± 1.14
31.55	8.58 ± 0.79	8.03 ± 0.91	7.97 ± 0.29	8.23 ± 0.82
50.00	5.79 ± 0.59	5.86 ± 0.60	5.81 ± 0.20	5.99 ± 0.60
79.24	4.98 ± 0.46	4.32 ± 0.41	4.29 ± 0.15	4.42 ± 0.45

(mean ± SD, n = 3)

Frequency sweep test data of light protected formula C.6.

Frequency (rad/s)	**G′(dyn/cm^2)**			
	1st day	**4th day**	**7th day**	**14th day**
100.00	2869.99 ± 156.93	2886.71 ± 115.01	2942.67 ± 56.15	2905.93 ± 38.30
63.10	2701.99 ± 145.94	2808.13 ± 113.68	2859.39 ± 54.50	2822.71 ± 37.87
39.81	2574.44 ± 142.65	2747.71 ± 113.17	2798.25 ± 58.89	2757.43 ± 34.71
25.12	2528.29 ± 137.84	2700.46 ± 115.87	2746.20 ± 53.35	2708.00 ± 32.58
15.85	2489.38 ± 139.39	2652.99 ± 114.35	2700.18 ± 56.69	2659.11 ± 34.10
10.00	2450.95 ± 139.57	2608.48 ± 111.74	2650.98 ± 48.50	2613.17 ± 34.61
6.31	2414.74 ± 141.17	2568.34 ± 110.79	2619.88 ± 47.42	2579.96 ± 35.40
3.98	2377.22 ± 141.27	2521.95 ± 96.99	2572.13 ± 45.56	2537.22 ± 23.12
2.51	2343.55 ± 123.37	2494.14 ± 114.43	2536.26 ± 49.76	2498.02 ± 25.77
1.58	2309.09 ± 142.95	2469.39 ± 118.03	2496.02 ± 57.61	2454.27 ± 38.56
1.00	2275.48 ± 133.80	2431.42 ± 113.52	2470.16 ± 52.09	2426.79 ± 25.44
0.63	2254.10 ± 125.30	2403.98 ± 115.04	2431.62 ± 46.94	2397.10 ± 43.17
0.40	2233.32 ± 112.47	2373.37 ± 107.21	2403.68 ± 53.97	2364.44 ± 31.20
0.25	2208.31 ± 119.43	2344.72 ± 94.83	2382.68 ± 47.34	2343.84 ± 28.88
0.16	2190.74 ± 120.08	2318.52 ± 96.56	2349.71 ± 52.01	2311.18 ± 27.00
0.10	2172.22 ± 120.07	2304.32 ± 98.26	2329.84 ± 53.66	2289.01 ± 26.64

(mean ± SD, n = 3)

Frequency sweep test data of light protected formula C.6 (continued).

Frequency (rad/s)	**tan δ**			
	1st day	**4th day**	**7th day**	**14th day**
100.00	0.1485 ± 0.0112	0.1490 ± 0.0092	0.1455 ± 0.0056	0.1430 ± 0.0016
63.10	0.1247 ± 0.0132	0.1309 ± 0.0072	0.1265 ± 0.0027	0.1259 ± 0.0017
39.81	0.1099 ± 0.0087	0.1092 ± 0.0061	0.1056 ± 0.0023	0.1051 ± 0.0019
25.12	0.0923 ± 0.0062	0.0912 ± 0.0071	0.0923 ± 0.0016	0.0907 ± 0.0012
15.85	0.0803 ± 0.0056	0.0812 ± 0.0053	0.0803 ± 0.0022	0.0795 ± 0.0029
10.00	0.0729 ± 0.0082	0.0755 ± 0.0033	0.0745 ± 0.0020	0.0737 ± 0.0007
6.31	0.0677 ± 0.0046	0.0690 ± 0.0033	0.0675 ± 0.0041	0.0652 ± 0.0021
3.98	0.0667 ± 0.0019	0.0668 ± 0.0042	0.0628 ± 0.0065	0.0605 ± 0.0040
2.51	0.0642 ± 0.0042	0.0659 ± 0.0079	0.0670 ± 0.0058	0.0629 ± 0.0028
1.58	0.0649 ± 0.0057	0.0653 ± 0.0051	0.0602 ± 0.0055	0.0567 ± 0.0012
1.00	0.0661 ± 0.0057	0.0627 ± 0.0056	0.0655 ± 0.0080	0.0612 ± 0.0020
0.63	0.0639 ± 0.0019	0.0670 ± 0.0069	0.0634 ± 0.0067	0.0595 ± 0.0016
0.40	0.0648 ± 0.0040	0.0659 ± 0.0055	0.0689 ± 0.0062	0.0649 ± 0.0037
0.25	0.0686 ± 0.0061	0.0701 ± 0.0068	0.0723 ± 0.0098	0.0667 ± 0.0047
0.16	0.0706 ± 0.0045	0.0712 ± 0.0054	0.0794 ± 0.0061	0.0738 ± 0.0066
0.10	0.0730 ± 0.0070	0.0770 ± 0.0069	0.0779 ± 0.0095	0.0727 ± 0.0072

(mean ± SD, n = 3)

Steady rate sweep test data of light protected formula C.6.

Shear rate	**Viscosity** (P)			
(s^{-1})	**1st day**	**4th day**	**7th day**	**14th day**
0.05	9691.19 ± 299.91	9622.18 ± 353.56	9476.33 ± 105.25	9881.56 ± 625.49
0.08	6673.42 ± 128.25	6595.69 ± 158.53	6574.82 ± 122.95	6838.70 ± 386.68
0.13	4390.44 ± 104.56	4379.65 ± 104.00	4352.26 ± 65.13	4488.63 ± 261.35
0.20	2886.84 ± 81.67	2905.06 ± 90.16	2882.17 ± 75.21	2941.38 ± 167.97
0.32	1900.68 ± 63.81	1925.43 ± 81.47	1909.25 ± 76.11	1930.13 ± 108.76
0.50	1251.37 ± 46.10	1273.65 ± 63.60	1261.62 ± 61.22	1268.25 ± 71.64
0.79	824.14 ± 29.68	841.20 ± 44.31	833.43 ± 43.62	835.24 ± 46.51
1.26	542.65 ± 20.12	554.68 ± 31.80	550.50 ± 31.58	549.79 ± 30.47
1.99	358.14 ± 14.46	367.94 ± 24.77	365.23 ± 24.85	363.34 ± 21.88
3.15	237.68 ± 9.36	243.77 ± 15.63	241.97 ± 15.63	241.08 ± 14.23
5.00	160.17 ± 6.15	164.35 ± 10.31	162.97 ± 10.34	162.47 ± 9.55
7.92	108.40 ± 4.02	111.25 ± 6.97	110.41 ± 7.02	110.11 ± 6.54
12.56	74.09 ± 2.70	76.10 ± 4.82	75.53 ± 4.87	75.28 ± 4.46
19.91	51.15 ± 1.79	52.55 ± 3.30	52.19 ± 3.34	52.03 ± 3.08
31.55	35.72 ± 1.19	36.68 ± 2.24	36.44 ± 2.27	36.34 ± 2.12
50.00	25.16 ± 0.79	25.84 ± 1.55	25.68 ± 1.58	25.61 ± 1.47
79.24	17.920 ± 0.535	18.407 ± 1.083	18.292 ± 1.104	18.252 ± 1.038

(mean ± SD, n = 3)

Frequency sweep test data of light protected formula C1.

Frequency (rad/s)	**G'(dyn/cm^2)**			
	1st day	**4th day**	**7th day**	**14th day**
100.00	4359.41 ± 268.64	4371.04 ± 112.25	4399.83 ± 188.77	4355.49 ± 258.21
63.10	4231.15 ± 253.78	4282.70 ± 108.09	4268.71 ± 181.29	4221.82 ± 249.06
39.81	4130.36 ± 251.51	4205.92 ± 103.06	4162.80 ± 179.04	4117.02 ± 243.44
25.12	4044.11 ± 241.12	4085.31 ± 101.25	4076.51 ± 172.52	4026.66 ± 243.11
15.85	3955.32 ± 244.29	3967.93 ± 102.59	3989.90 ± 170.13	3944.92 ± 229.09
10.00	3883.21 ± 249.54	3905.53 ± 105.86	3919.31 ± 167.39	3876.28 ± 222.67
6.31	3814.45 ± 229.76	3859.71 ± 103.67	3843.53 ± 167.82	3804.64 ± 217.88
3.98	3742.70 ± 226.30	3801.26 ± 92.51	3783.80 ± 159.27	3735.59 ± 223.45
2.51	3696.21 ± 240.25	3731.12 ± 98.07	3716.68 ± 149.85	3675.02 ± 213.18
1.58	3637.62 ± 223.30	3666.96 ± 90.20	3660.85 ± 155.71	3619.19 ± 218.66
1.00	3591.77 ± 234.35	3602.92 ± 100.19	3608.70 ± 157.90	3582.02 ± 204.71
0.63	3541.42 ± 220.36	3556.63 ± 92.66	3552.24 ± 156.35	3515.57 ± 206.59
0.40	3498.86 ± 222.47	3516.55 ± 85.76	3513.55 ± 148.26	3479.68 ± 206.63
0.25	3462.96 ± 207.11	3469.84 ± 98.37	3473.61 ± 144.38	3445.14 ± 200.63
0.16	3427.15 ± 203.14	3423.18 ± 103.61	3434.29 ± 134.78	3391.86 ± 179.18
0.10	3399.96 ± 197.83	3381.87 ± 114.13	3399.40 ± 123.99	3358.94 ± 171.98

(mean ± SD, n = 3)

Frequency sweep test data of light protected formula C1 (continued).

Frequency (rad/s)	**tan δ**			
	1st day	**4th day**	**7th day**	**14th day**
100.00	0.1499 ± 0.0132	0.1568 ± 0.0041	0.1560 ± 0.0047	0.1527 ± 0.0127
63.10	0.1366 ± 0.0123	0.1393 ± 0.0041	0.1406 ± 0.0053	0.1365 ± 0.0120
39.81	0.1155 ± 0.0097	0.1189 ± 0.0042	0.1190 ± 0.0034	0.1153 ± 0.0074
25.12	0.0999 ± 0.0087	0.1037 ± 0.0050	0.1052 ± 0.0022	0.1027 ± 0.0093
15.85	0.0880 ± 0.0090	0.0937 ± 0.0010	0.0943 ± 0.0014	0.0898 ± 0.0065
10.00	0.0815 ± 0.0094	0.0858 ± 0.0021	0.0858 ± 0.0020	0.0833 ± 0.0077
6.31	0.0732 ± 0.0086	0.0804 ± 0.0014	0.0815 ± 0.0018	0.0791 ± 0.0020
3.98	0.0776 ± 0.0058	0.0764 ± 0.0009	0.0752 ± 0.0018	0.0735 ± 0.0072
2.51	0.0650 ± 0.0133	0.0731 ± 0.0042	0.0751 ± 0.0030	0.0705 ± 0.0083
1.58	0.0659 ± 0.0076	0.0743 ± 0.0013	0.0742 ± 0.0013	0.0694 ± 0.0065
1.00	0.0660 ± 0.0081	0.0743 ± 0.0025	0.0768 ± 0.0005	0.0681 ± 0.0091
0.63	0.0698 ± 0.0068	0.0766 ± 0.0072	0.0774 ± 0.0036	0.0718 ± 0.0088
0.40	0.0698 ± 0.0078	0.0782 ± 0.0040	0.0762 ± 0.0062	0.0726 ± 0.0028
0.25	0.0693 ± 0.0070	0.0811 ± 0.0039	0.0804 ± 0.0082	0.0695 ± 0.0079
0.16	0.0706 ± 0.0053	0.0861 ± 0.0089	0.0812 ± 0.0077	0.0734 ± 0.0040
0.10	0.0752 ± 0.0014	0.0903 ± 0.0073	0.0830 ± 0.0041	0.0815 ± 0.0013

(mean ± SD, n = 3)

Steady rate sweep test data of light protected formula C1.

Shear rate	**Viscosity** (P)			
(s^{-1})	**1st day**	**4th day**	**7th day**	**14th day**
0.05	20442.43 ± 710.36	20559.33 ± 909.45	19290.73 ± 523.16	20160.60 ± 734.60
0.08	14198.97 ± 383.23	14608.27 ± 1028.65	13665.50 ± 574.06	14501.10 ± 287.48
0.13	9407.80 ± 259.09	9553.42 ± 474.56	9142.27 ± 365.70	9610.60 ± 132.70
0.20	6209.44 ± 190.79	6260.54 ± 263.57	6062.49 ± 254.55	6312.46 ± 56.24
0.32	4071.88 ± 128.82	4094.78 ± 159.60	3997.97 ± 182.62	4130.60 ± 21.82
0.50	2665.39 ± 83.09	2677.85 ± 99.35	2624.01 ± 124.04	2700.81 ± 9.63
0.79	1744.25 ± 55.52	1751.62 ± 65.41	1721.37 ± 73.12	1765.66 ± 6.53
1.26	1138.65 ± 34.41	1146.30 ± 45.95	1127.94 ± 37.95	1153.35 ± 10.27
1.99	748.52 ± 20.56	755.91 ± 33.22	744.59 ± 18.90	758.07 ± 14.98
3.15	493.22 ± 11.57	500.00 ± 23.03	496.34 ± 11.84	500.98 ± 9.24
5.00	332.03 ± 8.44	335.68 ± 13.82	334.55 ± 8.29	337.04 ± 2.88
7.92	223.98 ± 5.68	226.96 ± 10.09	226.43 ± 4.48	227.43 ± 1.91
12.56	152.92 ± 4.12	155.12 ± 7.40	155.02 ± 2.54	154.92 ± 0.95
19.91	105.40 ± 2.87	106.90 ± 5.24	106.92 ± 1.43	106.16 ± 0.54
31.55	73.20 ± 1.66	74.52 ± 3.84	74.34 ± 1.14	73.41 ± 0.34
50.00	51.39 ± 1.05	52.46 ± 2.87	52.25 ± 0.94	51.35 ± 0.17
79.24	36.42 ± 0.69	37.25 ± 2.11	37.10 ± 0.73	36.33 ± 0.06

(mean ± SD, n = 3)

Frequency sweep test data of light exposed formula C.6.

Frequency (rad/s)	**G′(dyn/cm^2)**		
	2nd day	**8th day**	**15th day**
100.00	2409.55 ± 94.24	217.86 ± 0.80	224.46 ± 6.55
63.10	2346.93 ± 92.20	210.74 ± 1.03	217.99 ± 5.80
39.81	2292.07 ± 92.35	205.84 ± 1.07	211.96 ± 5.58
25.12	2241.46 ± 91.79	201.46 ± 1.63	207.12 ± 5.06
15.85	2197.65 ± 90.71	198.19 ± 1.25	202.59 ± 6.42
10.00	2155.64 ± 91.65	194.08 ± 1.80	198.96 ± 6.64
6.31	2124.11 ± 95.28	191.35 ± 2.11	195.33 ± 5.65
3.98	2084.61 ± 93.87	188.51 ± 1.30	192.31 ± 6.26
2.51	2043.06 ± 87.68	186.05 ± 1.41	189.39 ± 5.53
1.58	2019.97 ± 76.57	184.59 ± 1.10	186.59 ± 5.18
1.00	1987.75 ± 94.26	182.77 ± 2.78	183.67 ± 6.22
0.63	1965.65 ± 99.77	179.57 ± 1.70	182.16 ± 5.25
0.40	1939.22 ± 103.71	178.31 ± 1.92	178.62 ± 4.68
0.25	1909.36 ± 110.89	175.95 ± 1.46	176.90 ± 3.85
0.16	1879.26 ± 111.45	173.55 ± 0.89	175.49 ± 3.45
0.10	1838.79 ± 119.83	173.34 ± 0.19	173.57 ± 3.57

(mean ± SD, n = 3)

Frequency sweep test data of light exposed formula C.6 (continued).

Frequency (rad/s)	**tan δ**		
	2nd day	**8th day**	**15th day**
100.00	0.1529 ± 0.0024	0.1560 ± 0.0038	0.1808 ± 0.0120
63.10	0.1285 ± 0.0012	0.1333 ± 0.0025	0.1533 ± 0.0074
39.81	0.1087 ± 0.0011	0.1093 ± 0.0004	0.1284 ± 0.0052
25.12	0.0936 ± 0.0007	0.0933 ± 0.0005	0.1087 ± 0.0043
15.85	0.0826 ± 0.0009	0.0814 ± 0.0005	0.0945 ± 0.0018
10.00	0.0779 ± 0.0021	0.0768 ± 0.0033	0.0868 ± 0.0049
6.31	0.0672 ± 0.0009	0.0689 ± 0.0054	0.0827 ± 0.0076
3.98	0.0569 ± 0.0025	0.0608 ± 0.0018	0.0722 ± 0.0029
2.51	0.0577 ± 0.0052	0.0585 ± 0.0009	0.0692 ± 0.0056
1.58	0.0572 ± 0.0055	0.0575 ± 0.0001	0.0627 ± 0.0042
1.00	0.0617 ± 0.0041	0.0500 ± 0.0019	0.0628 ± 0.0050
0.63	0.0589 ± 0.0074	0.0540 ± 0.0013	0.0613 ± 0.0068
0.40	0.0566 ± 0.0114	0.0488 ± 0.0048	0.0604 ± 0.0036
0.25	0.0643 ± 0.0112	0.0543 ± 0.0019	0.0656 ± 0.0027
0.16	0.0499 ± 0.0153	0.0501 ± 0.0042	0.0632 ± 0.0055
0.10	0.0499 ± 0.0133	0.0497 ± 0.0000	0.0624 ± 0.0040

(mean ± SD, n = 3)

Steady rate sweep test data of light exposed formula C.6.

Shear rate (s^{-1})	**Viscosity** (P) 2nd day	**Viscosity** (P) 8th day	**Viscosity** (P) 15th day
0.05	3915.81 ± 40.44	659.08 ± 49.45	565.28 ± 63.57
0.08	2359.78 ± 50.30	448.31 ± 16.70	399.57 ± 51.04
0.13	1618.83 ± 25.60	295.49 ± 3.96	267.33 ± 40.86
0.20	1099.92 ± 87.95	196.27 ± 0.04	178.24 ± 31.30
0.32	807.53 ± 15.84	130.26 ± 1.03	118.77 ± 21.97
0.50	535.18 ± 67.70	85.93 ± 1.18	78.84 ± 14.64
0.79	384.60 ± 27.33	56.78 ± 1.03	52.55 ± 9.39
1.26	275.22 ± 6.42	37.63 ± 0.88	35.14 ± 6.07
1.99	195.54 ± 2.74	25.28 ± 0.76	23.84 ± 4.02
3.15	134.95 ± 6.72	16.93 ± 0.50	16.08 ± 2.48
5.00	94.93 ± 4.96	11.50 ± 0.41	11.08 ± 1.56
7.92	67.48 ± 2.66	7.88 ± 0.32	7.68 ± 0.98
12.56	48.06 ± 1.36	5.45 ± 0.24	5.37 ± 0.61
19.91	34.53 ± 0.60	3.81 ± 0.19	3.80 ± 0.38
31.55	25.02 ± 0.13	2.70 ± 0.04	2.73 ± 0.24
50.00	18.24 ± 0.10	1.93 ± 0.11	1.97 ± 0.15
79.24	13.46 ± 0.21	1.40 ± 0.09	1.44 ± 0.09

(mean ± SD, n = 3)

Frequency sweep test data of light exposed 0.6 %w/w carbopol 940 gel base.

Frequency (rad/s)	**G′ (dyn/cm^2)**				
	0 day	1st day	3rd day	7th day	14th day
100.00	4769.02 ± 21.71	4659.73 ± 31.74	4362.49 ± 128.99	1510.42 ± 56.98	896.49 ± 90.01
63.10	4637.35 ± 20.07	4519.84 ± 28.15	4228.99 ± 134.28	1435.26 ± 56.49	838.56 ± 88.47
39.81	4534.26 ± 23.27	4417.11 ± 34.08	4136.66 ± 133.74	1370.97 ± 52.20	790.15 ± 85.74
25.12	4439.20 ± 24.51	4326.87 ± 31.12	4051.17 ± 130.80	1318.08 ± 53.30	749.56 ± 79.42
15.85	4353.56 ± 28.68	4238.03 ± 29.07	3973.29 ± 121.21	1274.69 ± 50.67	719.89 ± 78.97
10.00	4275.02 ± 27.11	4164.12 ± 27.52	3905.16 ± 113.03	1238.69 ± 52.39	689.91 ± 77.42
6.31	4192.41 ± 34.37	4090.11 ± 16.70	3819.42 ± 125.41	1203.59 ± 50.50	663.78 ± 75.16
3.98	4116.55 ± 33.11	4023.68 ± 37.35	3751.61 ± 124.89	1175.50 ± 55.00	646.38 ± 75.61
2.51	4056.99 ± 38.35	3962.41 ± 39.40	3701.04 ± 120.08	1143.50 ± 45.06	624.62 ± 68.97
1.58	3990.80 ± 35.30	3897.60 ± 14.64	3627.40 ± 115.84	1117.30 ± 46.28	615.37 ± 73.14
1.00	3944.05 ± 24.46	3838.37 ± 14.39	3583.30 ± 79.40	1095.67 ± 51.79	596.61 ± 72.02
0.63	3890.76 ± 31.46	3785.63 ± 20.93	3518.42 ± 102.81	1073.39 ± 52.11	576.76 ± 65.38
0.40	3834.59 ± 32.23	3735.02 ± 29.93	3466.30 ± 97.12	1051.70 ± 53.71	572.91 ± 76.26
0.25	3794.84 ± 24.29	3701.36 ± 27.91	3425.71 ± 99.35	1030.57 ± 53..17	553.22 ± 72.76
0.16	3742.03 ± 24.97	3658.92 ± 31.48	3390.99 ± 123.29	1007.01 ± 59.22	546.82 ± 76.41
0.10	3717.76 ± 10.47	3628.15 ± 35.89	3343.93 ± 141.90	990.41 ± 80.19	538.19 ± 76.44

(mean ± SD, n = 3)

Frequency sweep test data of light exposed 0.6 %w/w carbopol 940 gel base (continued).

Frequency	**tan δ**				
(rad/s)	**0 day**	**1st day**	**3rd day**	**7th day**	**14th day**
100.00	0.1304 ± 0.0025	0.1318 ± 0.0000	0.1411 ± 0.0017	0.2427 ± 0.0114	0.3075 ± 0.0143
63.10	0.1207 ± 0.0023	0.1201 ± 0.0003	0.1274 ± 0.0031	0.2159 ± 0.0104	0.2769 ± 0.0133
39.81	0.1026 ± 0.0026	0.1019 ± 0.0001	0.1078 ± 0.0029	0.1848 ± 0.0094	0.2338 ± 0.0089
25.12	0.0899 ± 0.0012	0.0910 ± 0.0017	0.0956 ± 0.0034	0.1614 ± 0.0110	0.2065 ± 0..0104
15.85	0.0831 ± 0.0021	0.0816 ± 0.0017	0.0869 ± 0.0044	0.1447 ± 0.0112	0.1775 ± 0.0053
10.00	0.0792 ± 0.0023	0.0760 ± 0.0009	0.0791 ± 0.0048	0.1279 ± 0.0082	0.1599 ± 0.0067
6.31	0.0722 ± 0.0013	0.0697 ± 0.0023	0.0740 ± 0.0062	0.1160 ± 0.0068	0.1384 ± 0.0026
3.98	0.0695 ± 0.0012	0.0695 ± 0.0001	0.0722 ± 0.0041	0.0999 ± 0.0066	0.1158 ± 0.0131
2.51	0.0666 ± 0.0020	0.0672 ± 0.0043	0.0710 ± 0.0074	0.0992 ± 0.0087	0.1262 ± 0.0112
1.58	0.0647 ± 0.0043	0.0636 ± 0.0006	0.0690 ± 0.0088	0.0948 ± 0.0091	0.1147 ± 0.0079
1.00	0.0642 ± 0.0033	0.0658 ± 0.0003	0.0743 ± 0.0043	0.0905 ± 0.0084	0.1103 ± 0.0152
0.63	0.0655 ± 0.0094	0.0636 ± 0.0018	0.0705 ± 0.0111	0.0955 ± 0.0146	0.1051 ± 0.0184
0.40	0.0659 ± 0.0047	0.0669 ± 0.0021	0.0769 ± 0.0086	0.1020 ± 0.0137	0.1119 ± 0.0118
0.25	0.0691 ± 0.0048	0.0667 ± 0.0035	0.0818 ± 0.0112	0.1036 ± 0.0127	0.1151 ± 0.0127
0.16	0.0705 ± 0.0032	0.0686 ± 0.0003	0.0839 ± 0.0025	0.1126 ± 0.0255	0.1222 ± 0.0256
0.10	0.0709 ± 0.0010	0.0694 ± 0.0035	0.0802 ± 0.0016	0.1171 ± 0.0390	0.1217 ± 0.0269

(mean ± SD, n = 3)

Steady rate sweep test data of light exposed 0.6 %w/w carbopol 940 gel base.

Shear rate	Viscosity (P)				
(s^{-1})	**0 day**	**1st day**	**3rd day**	**7th day**	**14th day**
0.05	16342.93 ± 51.15	16331.30 ± 272.80	15809.33 ± 358.48	5852.88 ± 82.20	3498.21 ± 84.15
0.08	11966.93 ± 113.85	11572.20 ± 130.77	11353.77 ± 116.80	4164.57 ± 154.60	2451.77 ± 45.52
0.13	8091.33 ± 54.93	7744.65 ± 79.59	7646.32 ± 11.14	2796.50 ± 108.84	1641.35 ± 27.67
0.20	5391.84 ± 19.03	5140.68 ± 60.54	5091.11 ± 35.23	1865.59 ± 68.46	1095.46 ± 17.22
0.32	3568.94 ± 4.13	3398.62 ± 46.40	3370.48 ± 44.06	1246.43 ± 43.84	731.59 ± 11.74
0.50	2360.32 ± 0.20	2246.99 ± 32.71	2229.64 ± 35.37	834.12 ± 27.44	490.03 ± 7.77
0.79	1564.67 ± 0.33	1488.28 ± 20.66	1476.98 ± 21.74	560.55 ± 15.96	330.33 ± 5.27
1.26	1038.55 ± 0.02	988.77 ± 13.27	978.91 ± 9.47	378.65 ± 8.60	224.71 ± 3.57
1.99	695.62 ± 0.57	661.80 ± 12.92	652.19 ± 9.20	258.78 ± 6.95	154.30 ± 1.50
3.15	465.58 ± 0.13	444.25 ± 7.69	439.91 ± 7.85	177.24 ± 3.81	107.90 ± 1.39
5.00	315.01 ± 0.08	300.45 ± 5.57	297.12 ± 5.37	123.66 ± 2.83	76.23 ± 0.74
7.92	214.67 ± 0.05	204.92 ± 3.85	202.46 ± 3.44	87.06 ± 1.95	54.63 ± 0.47
12.56	147.26 ± 0.21	140.58 ± 2.60	138.93 ± 2.33	61.81 ± 1.35	39.54 ± 0.32
19.91	101.88 ± 0.18	97.26 ± 1.83	96.09 ± 1.64	44.26 ± 0.92	28.89 ± 0.20
31.55	71.12 ± 0.15	67.84 ± 1.31	67.00 ± 1.18	32.02 ± 0.64	21.33 ± 0.15
50.00	50.01 ± 0.13	47.69 ± 0.92	47.11 ± 0.83	23.35 ± 0.44	15.91 ± 0.10
79.24	35.49 ± 0.08	33.82 ± 0.66	33.40 ± 0.58	17.19 ± 0.31	11.99 ± 0.07

(mean ± SD, n = 3)

Frequency sweep test data of light protected 0.6 %w/w carbopol 940 gel base.

Frequency	G' (dyn/cm^2)				
(rad/s)	**0 day**	**1st day**	**3rd day**	7th day	**14th day**
100.00	4781.55 ± 21.71	4775.84 ± 18.83	4713.43 ± 44.60	4710.90 ± 48.98	4736.09 ± 70.79
63.10	4648.93 ± 20.07	4641.08 ± 17.74	4570.09 ± 41.30	4568.63 ± 43.83	4597.31 ± 68.66
39.81	4547.69 ± 23.27	4538.17 ± 20.73	4468.54 ± 42.87	4465.71 ± 47.77	4491.90 ± 70.45
25.12	4453.36 ± 24.51	4447.67 ± 21.37	4379.76 ± 38.68	4377.06 ± 43.35	4409.31 ± 71.28
15.85	4370.12 ± 28.68	4358.75 ± 25.41	4301.39 ± 42.75	4299.94 ± 45.26	4317.60 ± 60.56
10.00	4290.67 ± 27.11	4286.10 ± 24.14	4216.23 ± 31.74	4209.71 ± 43.04	4248.42 ± 76.56
6.31	4212.26 ± 34.37	4202.77 ± 29.77	4143.54 ± 33.46	4138.46 ± 42.26	4165.65 ± 65.81
3.98	4135.67 ± 33.11	4128.13 ± 28.88	4066.69 ± 33.92	4063.69 ± 39.11	4094.29 ± 65.61
2.51	4079.13 ± 38.35	4071.45 ± 33.73	4008.69 ± 32.01	3997.32 ± 51.70	4031.36 ± 81.18
1.58	4011.18 ± 35.30	4001.43 ± 30.58	3939.92 ± 28.53	3931.69 ± 42.78	3962.31 ± 69.29
1.00	3958.17 ± 24.46	3949.85 ± 21.29	3894.39 ± 32.97	3886.76 ± 46.20	3909.36 ± 65.77
0.63	3908.93 ± 31.46	3895.29 ± 28.37	3815.72 ± 12.88	3808.55 ± 25.31	3850.55 ± 61.69
0.40	3853.19 ± 32.23	3841.73 ± 28.16	3763.25 ± 18.79	3762.50 ± 20.09	3804.70 ± 56.63
0.25	3808.87 ± 24.29	3798.61 ± 21.77	3729.74 ± 18.04	3719.90 ± 35.07	3754.55 ± 65.07
0.16	3756.44 ± 24.97	3750.36 ± 21.71	3670.17 ± 14.68	3671.51 ± 12.36	3720.83 ± 55.07
0.10	3723.80 ± 10.47	3722.85 ± 9.76	3629.64 ± 7.86	3623.87 ± 17.86	3685.75 ± 71.45

(mean ± SD, n = 3)

Frequency sweep test data of light protected 0.6 %w/w carbopol 940 gel base (continued).

Frequency (rad/s)	**tan δ**				
	0 day	**1st day**	**3rd day**	**7th day**	**14th day**
100.00	0.1289 ± 0.0025	0.1291 ± 0.0024	0.1320 ± 0.0004	0.1323 ± 0.0001	0.1295 ± 0.0025
63.10	0.1194 ± 0.0023	0.1188 ± 0.0028	0.1193 ± 0.0002	0.1192 ± 0.0000	0.1174 ± 0.0016
39.81	0.1011 ± 0.0026	0.1011 ± 0.0026	0.1032 ± 0.0007	0.1033 ± 0.0006	0.1006 ± 0.0017
25.12	0.0892 ± 0.0012	0.0890 ± 0.0014	0.0911 ± 0.0001	0.0902 ± 0.0017	0.0880 ± 0.0002
15.85	0.0819 ± 0.0021	0.0821 ± 0.0020	0.0827 ± 0.0020	0.0828 ± 0.0018	0.0811 ± 0.0004
10.00	0.0779 ± 0.0023	0.0757 ± 0.0052	0.0760 ± 0.0013	0.0766 ± 0.0003	0.0722 ± 0.0036
6.31	0.0714 ± 0.0013	0.0720 ± 0.0012	0.0722 ± 0.0012	0.0719 ± 0.0018	0.0716 ± 0.0015
3.98	0.0688 ± 0.0012	0.0683 ± 0.0018	0.0671 ± 0.0005	0.0677 ± 0.0003	0.0670 ± 0.0009
2.51	0.0655 ± 0.0020	0.0646 ± 0.0031	0.0668 ± 0.0037	0.0670 ± 0.0033	0.0621 ± 0.0009
1.58	0.0623 ± 0.0043	0.0634 ± 0.0037	0.0659 ± 0.0025	0.0648 ± 0.0045	0.0621 ± 0.0022
1.00	0.0623 ± 0.0033	0.0619 ± 0.0037	0.0663 ± 0.0028	0.0678 ± 0.0003	0.0620 ± 0.0048
0.63	0.0601 ± 0.0094	0.0632 ± 0.0081	0.0698 ± 0.0055	0.0703 ± 0.0047	0.0644 ± 0.0003
0.40	0.0632 ± 0.0047	0.0650 ± 0.0042	0.0738 ± 0.0053	0.0734 ± 0.0059	0.0662 ± 0.0003
0.25	0.0663 ± 0.0048	0.0664 ± 0.0047	00.737 ± 0.0060	0.0737 ± 0.0060	0.0649 ± 0.0016
0.16	0.0687 ± 0.0032	0.0679 ± 0.0040	0.0808 ± 0.0073	0.0802 ± 0.0083	0.0666 ± 0.0035
0.10	0.0703 ± 0.0010	0.0700 ± 0.0014	0.0792 ± 0.0079	0.0773 ± 0.0012	0.0673 ± 0.0025

(mean ± SD, n = 3)

Steady rate sweep test data of light protected 0.6 %w/w carbopol 940 gel base.

Shear rate	Viscosity (P)				
(s^{-1})	**0 day**	**1st day**	**3rd day**	**7th day**	**14th day**
0.05	16372.17 ± 51.15	16290.47 ± 96.59	16264.37 ± 906.56	16564.27 ± 537.92	16557.93 ± 543.49
0.08	12032.67 ± 113.85	11397.87 ± 606.68	11508.73 ± 832.01	11711.33 ± 656.33	11616.40 ± 752.15
0.13	8123.05 ± 54.93	7690.43 ± 402.12	7689.00 ± 505.78	7816.54 ± 391.84	7772.52 ± 435.00
0.20	5402.82 ± 19.03	5148.66 ± 229.63	5100.96 ± 292.02	5162.51 ± 228.20	5157.62 ± 232.56
0.32	3571.33 ± 4.13	3427.30 ± 126.79	3376.26 ± 176.40	3403.00 ± 138.30	3413.32 ± 130.29
0.50	2360.20 ± 0.20	2277.50 ± 71.53	2233.35 ± 114.00	2246.54 ± 86.05	2259.65 ± 77.24
0.79	1564.48 ± 0.33	1514.00 ± 43.55	1480.12 ± 74.29	1485.33 ± 55.70	1497.23 ± 48.78
1.26	1038.56 ± 0.02	1008.03 ± 26.45	984.81 ± 45.55	985.56 ± 34.90	994.67 ± 30.27
1.99	695.30 ± 0.57	675.25 ± 17.08	661.38 ± 24.27	659.15 ± 21.01	665.27 ± 18.19
3.15	465.50 ± 0.13	453.05 ± 10.72	443.65 ± 15.41	441.13 ± 13.92	445.72 ± 12.10
5.00	315.05 ± 0.08	306.81 ± 7.18	300.27 ± 9.69	298.29 ± 8.87	301.45 ± 7.75
7.92	214.70 ± 0.05	209.21 ± 4.78	204.65 ± 6.48	203.17 ± 5.94	205.41 ± 5.23
12.56	147.38 ± 0.21	143.58 ± 3.40	140.37 ± 4.22	139.44 ± 3.80	140.89 ± 3.35
19.91	101.98 ± 0.18	99.35 ± 2.37	97.05 ± 2.86	96.45 ± 2.48	97.44 ± 2.20
31.55	71.20 ± 0.15	69.35 ± 1.68	67.70 ± 1.94	67.27 ± 1.67	67.96 ± 1.49
50.00	50.08 ± 0.13	48.77 ± 1.20	47.59 ± 1.30	47.30 ± 1.10	47.77 ± 0.99
79.24	35.53 ± 0.08	34.58 ± 0.87	33.73 ± 0.88	33.54 ± 0.73	33.86 ± 0.66

(mean ± SD, n = 3)

APPENDIX III

Effect of Formula Compositions on Rheological Parameters at 27 °C

Frequency sweep test data of formula C.4.

Frequency **(rad/s)**	**G′** **(dyn/cm^2)**	**G″** **(dyn/cm^2)**	**tan δ**
100.00	776.30 ± 9.82	164.97 ± 11.95	0.2126 ± 0.0172
63.10	754.38 ± 7.99	132.21 ± 6.51	0.1753 ± 0.0099
39.81	733.25 ± 7.61	96.96 ± 5.78	0.1322 ± 0.0079
25.12	722.33 ± 9.30	76.99 ± 1.98	0.1066 ± 0.0040
15.85	709.24 ± 10.09	64.65 ± 0.91	0.0912 ± 0.0026
10.00	697.40 ± 5.25	49.69 ± 4.91	0.0712 ± 0.0065
6.31	688.67 ± 3.59	50.93 ± 4.20	0.0739 ± 0.0059
3.98	683.15 ± 4.04	46.76 ± 4.33	0.0684 ± 0.0061
2.51	671.41 ± 6.62	43.65 ± 9.24	0.0650 ± 0.0133
1.58	664.40 ± 4.41	42.34 ± 11.23	0.0638 ± 0.0170
1.00	659.00 ± 6.72	39.41 ± 7.74	0.0598 ± 0.0115
0.63	647.95 ± 2.19	42.53 ± 4.68	0.0656 ± 0.0073
0.40	641.07 ± 11.13	47.55 ± 6.96	0.0743 ± 0.0122
0.25	630.88 ± 5.92	42.91 ± 12.66	0.0681 ± 0.0208
0.16	623.79 ± 6.77	51.27 ± 11.09	0.0823 ± 0.0185
0.10	612.08 ± 14.99	59.86 ± 13.02	0.0978 ± 0.0239

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6.

Frequency (rad/s)	**G' (dyn/cm^2)**	**G'' (dyn/cm^2)**	**tan δ**
100.00	2937.48 ± 85.42	418.72 ± 4.53	0.1427 ± 0.0056
63.10	2861.15 ± 77.60	354.34 ± 4.25	0.1239 ± 0.0048
39.81	2807.78 ± 72.98	287.84 ± 9.47	0.1026 ± 0.0060
25.12	2760.91 ± 67.67	244.90 ± 7.66	0.0888 ± 0.0049
15.85	2711.70 ± 63.52	218.63 ± 7.86	0.0807 ± 0.0047
10.00	2672.63 ± 63.17	200.11 ± 2.52	0.0749 ± 0.0027
6.31	2635.02 ± 65.11	180.64 ± 4.45	0.0686 ± 0.0033
3.98	2592.09 ± 82.31	178.83 ± 29.10	0.0693 ± 0.0132
2.51	2554.01 ± 68.95	161.62 ± 10.39	0.0634 ± 0.0057
1.58	2521.08 ± 58.87	154.34 ± 0.35	0.0612 ± 0.0015
1.00	2489.35 ± 70.13	151.58 ± 2.04	0.0609 ± 0.0025
0.63	2476.31 ± 53.62	167.95 ± 16.17	0.0679 ± 0.0079
0.40	2428.89 ± 61.36	165.90 ± 0.45	0.0683 ± 0.0019
0.25	2412.27 ± 45.91	165.58 ± 4.92	0.0686 ± 0.0007
0.16	2390.52 ± 54.12	174.97 ± 7.35	0.0733 ± 0.0047
0.10	2370.01 ± 46.52	182.03 ± 12.57	0.0768 ± 0.0067

(mean ± SD, n = 3)

Frequency sweep test data of formula C1.

Frequency (rad/s)	**G' (dyn/cm^2)**	**G'' (dyn/cm^2)**	**tan δ**
100.00	4873.39 ± 35.97	637.56 ± 12.54	0.1308 ± 0.0016
63.10	4732.51 ± 37.45	555.27 ± 0.68	0.1173 ± 0.0011
39.81	4624.74 ± 42.17	474.71 ± 5.00	0.1027 ± 0.0020
25.12	4566.86 ± 6.14	423.38 ± 31.75	0.0927 ± 0.0068
15.85	4446.54 ± 39.16	352.13 ± 5.74	0.0792 ± 0.0006
10.00	4365.43 ± 42.22	327.12 ± 4.93	0.0749 ± 0.0004
6.31	4284.05 ± 35.15	300.58 ± 0.64	0.0702 ± 0.0007
3.98	4214.02 ± 31.12	276.73 ± 13.92	0.0657 ± 0.0028
2.51	4156.96 ± 45.73	264.75 ± 7.35	0.0637 ± 0.0011
1.58	4094.74 ± 41.30	247.83 ± 3.12	0.0605 ± 0.0014
1.00	4034.49 ± 52.06	252.82 ± 3.46	0.0627 ± 0.0000
0.63	3991.68 ± 42.97	253.35 ± 0.74	0.0635 ± 0.0005
0.40	3935.00 ± 34.87	255.01 ± 8.12	0.0648 ± 0.0015
0.25	3879.43 ± 43.47	262.60 ± 2.69	0.0677 ± 0.0001
0.16	3837.53 ± 37.64	276.91 ± 3.70	0.0722 ± 0.0003
0.10	3810.11 ± 49.40	282.96 ± 0.81	0.0743 ± 0.0012

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6/G5.

Frequency (rad/s)	$\mathbf{G'}$ **(dyn/cm^2)**	$\mathbf{G''}$ **(dyn/cm^2)**	**tan δ**
100.00	2975.09 ± 30.62	426.52 ± 6.47	0.1434 ± 0.0007
63.10	2890.44 ± 26.68	356.25 ± 6.85	0.1232 ± 0.0012
39.81	2827.20 ± 24.84	289.40 ± 12.48	0.1023 ± 0.0035
25.12	2775.56 ± 19.27	249.06 ± 7.07	0.0897 ± 0.0019
15.85	2726.62 ± 22.07	211.26 ± 9.30	0.0775 ± 0.0028
10.00	2682.79 ± 18.55	194.12 ± 9.31	0.0723 ± 0.0030
6.31	2626.98 ± 22.89	170.95 ± 15.07	0.0651 ± 0.0051
3.98	2596.46 ± 24.34	169.48 ± 7.80	0.0653 ± 0.0036
2.51	2554.97 ± 26.66	157.39 ± 2.67	0.0616 ± 0.0004
1.58	2531.05 ± 18.35	152.04 ± 10.85	0.0601 ± 0.0038
1.00	2494.59 ± 19.87	149.69 ± 2.82	0.0600 ± 0.0016
0.63	2465.75 ± 22.83	143.74 ± 0.95	0.0583 ± 0.0009
0.40	2438.22 ± 11.88	151.58 ± 3.13	0.0622 ± 0.0010
0.25	2402.03 ± 31.64	153.83 ± 0.07	0.0641 ± 0.0008
0.16	2371.38 ± 15.96	162.70 ± 12.70	0.0686 ± 0.0049
0.10	2348.25 ± 14.21	170.62 ± 7.16	0.0727 ± 0.0026

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6/G10.

Frequency (rad/s)	G' (dyn/cm^2)	G'' (dyn/cm^2)	**tan** δ
100.00	3002.42 ± 12.82	466.79 ± 1.98	0.1555 ± 0.0000
63.10	2905.08 ± 19.17	390.33 ± 3.89	0.1344 ± 0.0005
39.81	2835.99 ± 14.08	316.48 ± 1.56	0.1116 ± 0.0011
25.12	2777.40 ± 17.15	266.94 ± 1.58	0.0961 ± 0.0000
15.85	2725.90 ± 19.99	223.85 ± 6.37	0.0821 ± 0.0017
10.00	2678.40 ± 17.98	204.26 ± 3.73	0.0763 ± 0.0009
6.31	2646.02 ± 13.24	172.90 ± 3.29	0.0653 ± 0.0009
3.98	2571.93 ± 28.21	172.05 ± 0.63	0.0669 ± 0.0005
2.51	2554.92 ± 14.51	168.59 ± 6.73	0.0660 ± 0.0023
1.58	2518.88 ± 12.18	155.15 ± 5.59	0.0616 ± 0.0025
1.00	2483.59 ± 12.33	148.83 ± 7.51	0.0599 ± 0.0033
0.63	2454.01 ± 18.74	150.91 ± 10.15	0.0615 ± 0.0046
0.40	2424.70 ± 20.69	145.08 ± 2.89	0.0598 ± 0.0007
0.25	2400.52 ± 14.50	152.15 ± 7.77	0.0634 ± 0.0036
0.16	2368.90 ± 16.59	145.38 ± 7.42	0.0614 ± 0.0027
0.10	2343.01 ± 26.82	172.31 ± 7.62	0.0735 ± 0.0041

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6/G15.

Frequency (rad/s)	**G' (dyn/cm^2)**	**G'' (dyn/cm^2)**	**tan δ**
100.00	2334.34 ± 28.68	458.95 ± 13.65	0.1967 ± 0.0082
63.10	2249.42 ± 22.90	373.69 ± 11.36	0.1662 ± 0.0067
39.81	2185.86 ± 29.72	293.97 ± 1.03	0.1345 ± 0.0014
25.12	2129.30 ± 27.10	248.97 ± 3.29	0.1170 ± 0.0030
15.85	2078.76 ± 25.29	214.49 ± 8.14	0.1032 ± 0.0051
10.00	2039.50 ± 18.50	191.05 ± 6.60	0.0937 ± 0.0041
6.31	1996.13 ± 16.11	173.31 ± 11.21	0.0869 ± 0.0063
3.98	1966.21 ± 19.17	156.44 ± 5.66	0.0796 ± 0.0036
2.51	1928.87 ± 14.90	144.37 ± 12.92	0.0749 ± 0.0072
1.58	1910.48 ± 18.13	134.40 ± 0.18	0.0704 ± 0.0006
1.00	1869.82 ± 30.64	137.59 ± 6.02	0.0736 ± 0.0044
0.63	1849.07 ± 20.22	145.74 ± 16.05	0.0789 ± 0.0095
0.40	1828.78 ± 26.40	144.72 ± 17.68	0.0792 ± 0.0107
0.25	1814.74 ± 8.46	136.11 ± 9.16	0.0750 ± 0.0054
0.16	1788.80 ± 15.86	160.06 ± 24.29	0.0896 ± 0.0143
0.10	1786.21 ± 16.22	148.70 ± 23.53	0.0832 ± 0.0139

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6/S.09.

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	2616.03 ± 19.72	359.71 ± 3.24	0.1375 ± 0.0002
63.10	2542.42 ± 24.40	297.74 ± 0.03	0.1171 ± 0.0011
39.81	2492.96 ± 24.42	246.55 ± 2.01	0.0989 ± 0.0018
25.12	2454.70 ± 21.89	205.97 ± 2.80	0.0839 ± 0.0019
15.85	2412.01 ± 27.25	177.46 ± 3.71	0.0736 ± 0.0024
10.00	2379.32 ± 19.58	159.78 ± 0.76	0.0672 ± 0.0002
6.31	2344.41 ± 24.82	138.33 ± 10.19	0.0590 ± 0.0037
3.98	2302.77 ± 23.97	122.40 ± 15.85	0.0531 ± 0.0063
2.51	2289.13 ± 23.33	130.87 ± 3.87	0.0572 ± 0.0023
1.58	2247.06 ± 38.74	120.37 ± 2.58	0.0536 ± 0.0020
1.00	2224.88 ± 21.48	125.40 ± 5.39	0.0564 ± 0.0019
0.63	2191.29 ± 22.95	133.37 ± 10.61	0.0609 ± 0.0055
0.40	2168.92 ± 25.49	138.50 ± 2.90	0.0639 ± 0.0021
0.25	2151.69 ± 24.35	151.26 ± 1.79	0.0703 ± 0.0016
0.16	2138.17 ± 25.42	160.10 ± 4.57	0.0749 ± 0.0030
0.10	2130.24 ± 11.37	194.70 ± 6.45	0.0914 ± 0.0025

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6/S.9.

Frequency (rad/s)	**G'** (dyn/cm^2)	**G''** (dyn/cm^2)	**tan δ**
100.00	349.63 ± 20.07	107.49 ± 0.70	0.3082 ± 0.0191
63.10	337.96 ± 15.09	79.40 ± 4.71	0.2356 ± 0.0238
39.81	325.75 ± 18.96	56.00 ± 1.43	0.1724 ± 0.0139
25.12	323.10 ± 14.50	41.98 ± 1.43	0.1302 ± 0.0100
15.85	314.86 ± 13.61	32.88 ± 2.61	0.1043 ± 0.0037
10.00	314.62 ± 20.74	26.22 ± 3.50	0.0831 ± 0.0055
6.31	308.15 ± 17.38	23.08 ± 2.68	0.0748 ± 0.0043
3.98	305.25 ± 21.53	18.46 ± 4.61	0.0600 ± 0.0104
2.51	300.12 ± 13.65	20.99 ± 3.08	0.0697 ± 0.0069
1.58	293.30 ± 12.62	21.43 ± 2.71	0.0734 ± 0.0121
1.00	294.44 ± 17.87	13.92 ± 0.71	0.0473 ± 0.0005
0.63	294.03 ± 11.15	19.49 ± 0.33	0.0663 ± 0.0014
0.40	286.39 ± 12.70	19.31 ± 3.13	0.0672 ± 0.0077
0.25	280.00 ± 11.21	26.21 ± 1.11	0.0938 ± 0.0076
0.16	281.48 ± 9.56	30.31 ± 3.14	0.1080 ± 0.0145
0.10	283.12 ± 8.03	31.64 ± 0.97	0.1118 ± 0.0064

(mean ± SD, n = 3)

Frequency sweep test data of formula C1/S.09.

Frequency (rad/s)	G' (dyn/cm^2)	G'' (dyn/cm^2)	tan δ
100.00	4257.87 ± 205.36	580.22 ± 18.82	0.1366 ± 0.0107
63.10	4143.68 ± 191.24	507.02 ± 18.17	0.1227 ± 0.0098
39.81	4059.14 ± 192.38	425.56 ± 16.11	0.1051 ± 0.0087
25.12	3988.18 ± 190.41	363.20 ± 5.63	0.0913 ± 0.0056
15.85	3912.13 ± 186.98	319.69 ± 11.59	0.0819 ± 0.0067
10.00	3844.04 ± 185.95	292.19 ± 10.96	0.0762 ± 0.0064
6.31	3792.23 ± 180.79	270.91 ± 14.09	0.0717 ± 0.0069
3.98	3730.98 ± 175.92	259.94 ± 7.13	0.0698 ± 0.0051
2.51	3659.24 ± 182.83	241.47 ± 5.49	0.0661 ± 0.0047
1.58	3616.35 ± 188.31	226.06 ± 0.23	0.0626 ± 0.0032
1.00	3588.60 ± 167.54	238.68 ± 17.82	0.0668 ± 0.0079
0.63	3535.28 ± 161.01	255.39 ± 6.86	0.0639 ± 0.0047
0.40	3484.48 ± 173.59	231.28 ± 8.17	0.0666 ± 0.0055
0.25	3448.63 ± 165.43	237.12 ± 8.88	0.0689 ± 0.0057
0.16	3421.45 ± 150.52	247.83 ± 0.59	0.0725 ± 0.0033
0.10	3382.34 ± 138.88	261.24 ± 1.66	0.0773 ± 0.0026

(mean ± SD, n = 3)

Frequency sweep test data of formula C1/S.9.

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	2255.20 ± 77.43	325.02 ± 1.51	0.1442 ± 0.0055
63.10	2214.39 ± 71.03	266.75 ± 2.91	0.1205 ± 0.0025
39.81	2174.44 ± 69.61	230.71 ± 3.66	0.1061 ± 0.0047
25.12	2144.09 ± 66.57	197.90 ± 0.40	0.0923 ± 0.0027
15.85	2111.85 ± 59.40	173.38 ± 2.34	0.0821 ± 0.0030
10.00	2083.80 ± 53.68	166.91 ± 10.51	0.0801 ± 0.0066
6.31	2057.59 ± 56.87	152.47 ± 2.42	0.0741 ± 0.0005
3.98	2038.09 ± 55.75	142.87 ± 8.61	0.0701 ± 0.0058
2.51	2009.75 ± 56.41	134.65 ± 16.98	0.0670 ± 0.0097
1.58	1994.18 ± 53.03	125.63 ± 7.75	0.0630 ± 0.0053
1.00	1960.30 ± 67.01	130.95 ± 3.35	0.0668 ± 0.0035
0.63	1953.33 ± 40.95	126.97 ± 2.98	0.0650 ± 0.0027
0.40	1948.94 ± 52.77	130.58 ± 5.91	0.0670 ± 0.0046
0.25	1931.14 ± 50.36	130.52 ± 14.55	0.0677 ± 0.0092
0.16	1915.23 ± 59.51	147.09 ± 10.79	0.0770 ± 0.0079
0.10	1903.67 ± 45.60	138.64 ± 8.15	0.0728 ± 0.0059

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.4.

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	1994.06 ± 45.95	99.33 ± 2.30
0.08	1346.60 ± 33.84	106.71 ± 2.68
0.13	877.72 ± 24.42	110.24 ± 3.07
0.20	570.49 ± 16.88	113.56 ± 3.36
0.32	371.45 ± 11.36	117.18 ± 3.58
0.50	242.86 ± 7.89	121.43 ± 3.95
0.79	159.93 ± 5.35	126.73 ± 4.24
1.26	105.71 ± 3.31	132.77 ± 4.15
1.99	70.45 ± 2.17	140.23 ± 4.31
3.15	47.42 ± 1.58	149.61 ± 4.99
5.00	32.37 ± 1.00	161.83 ± 5.02
7.92	22.41 ± 0.68	177.56 ± 5.41
12.56	15.73 ± 0.48	197.55 ± 6.00
19.91	11.19 ± 0.33	222.83 ± 6.62
31.55	8.08 ± 0.23	254.77 ± 7.30
50.00	5.89 ± 0.16	294.42 ± 8.19
79.24	4.34 ± 0.12	344.27 ± 9.13

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6.

Shear rate (s^{-1})	**Viscosity** (P)	**Stress** (dyn/cm^2)
0.05	10211.67 ± 386.97	505.40 ± 19.35
0.08	6950.19 ± 347.97	550.77 ± 27.57
0.13	4567.96 ± 217.26	573.71 ± 27.29
0.20	2983.05 ± 135.72	593.79 ± 27.02
0.32	1945.11 ± 85.61	613.64 ± 27.01
0.50	1269.48 ± 55.23	634.74 ± 27.61
0.79	829.14 ± 35.61	657.05 ± 28.22
1.26	542.89 ± 22.99	681.84 ± 28.87
1.99	360.10 ± 14.34	716.78 ± 28.55
3.15	238.99 ± 9.28	753.95 ± 29.27
5.00	160.03 ± 5.75	800.15 ± 28.77
7.92	107.86 ± 3.46	854.70 ± 27.45
12.56	73.55 ± 2.21	923.81 ± 27.74
19.91	50.72 ± 1.36	1009.64 ± 27.08
31.55	35.33 ± 0.85	1114.46 ± 26.79
50.00	24.82 ± 0.51	1241.09 ± 25.75
79.24	17.67 ± 0.31	1400.13 ± 24.41

(mean ± SD, n = 3)

Steady rate sweep test data of formula C1.

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	20611.02 ± 337.23	1012.88 ± 16.86
0.08	14734.33 ± 359.69	1151.16 ± 28.50
0.13	9799.68 ± 218.50	1214.94 ± 27.44
0.20	6452.32 ± 131.54	1269.24 ± 26.18
0.32	4223.09 ± 82.16	1317.33 ± 25.92
0.50	2757.15 ± 53.47	1363.14 ± 26.73
0.79	1797.26 ± 27.10	1411.83 ± 21.48
1.26	1168.25 ± 11.09	1459.21 ± 13.93
1.99	768.71 ± 9.71	1518.98 ± 19.33
3.15	513.21 ± 4.83	1610.25 ± 15.25
5.00	340.90 ± 2.95	1695.99 ± 14.74
7.92	229.13 ± 2.78	1803.03 ± 22.04
12.56	155.54 ± 1.54	1942.35 ± 19.38
19.91	106.72 ± 0.83	2114.88 ± 16.47
31.55	74.19 ± 0.00	2340.66 ± 0.00
50.00	51.99 ± 0.00	2599.47 ± 0.00
79.24	36.79 ± 0.00	2915.80 ± 0.00

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6/G5.

Shear rate (s^{-1})	**Viscosity** (P)	**Stress** (dyn/cm^2)
0.05	10018.18 ± 292.18	510.14 ± 14.61
0.08	6906.60 ± 326.23	574.50 ± 25.85
0.13	4531.23 ± 203.57	600.96 ± 25.57
0.20	2951.39 ± 125.95	618.20 ± 25.07
0.32	1923.25 ± 80.52	635.88 ± 25.40
0.50	1256.39 ± 53.23	656.57 ± 26.61
0.79	821.58 ± 34.14	681.39 ± 27.06
1.26	538.75 ± 21.97	708.37 ± 27.59
1.99	357.87 ± 13.68	744.14 ± 27.22
3.15	237.65 ± 9.01	783.59 ± 28.42
5.00	159.42 ± 5.61	827.11 ± 28.05
7.92	107.64 ± 3.41	887.99 ± 26.99
12.56	73.53 ± 2.20	963.50 ± 27.65
19.91	50.80 ± 1.39	1071.25 ± 27.62
31.55	35.45 ± 0.89	1198.36 ± 28.21
50.00	24.96 ± 0.58	1348.11 ± 28.76
79.24	17.81 ± 0.38	1538.47 ± 29.89

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6/G10.

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	10293.69 ± 145.49	500.91 ± 7.27
0.08	7249.65 ± 164.72	547.31 ± 13.05
0.13	4784.96 ± 109.93	569.10 ± 13.81
0.20	3105.69 ± 64.04	587.48 ± 12.75
0.32	2015.59 ± 40.66	606.74 ± 12.83
0.50	1313.14 ± 24.96	628.20 ± 12.48
0.79	859.86 ± 15.71	651.06 ± 12.45
1.26	564.02 ± 10.19	676.63 ± 12.80
1.99	373.84 ± 6.68	712.35 ± 13.31
3.15	248.38 ± 4.53	749.73 ± 14.28
5.00	167.14 ± 3.09	835.69 ± 15.46
7.92	113.50 ± 2.29	899.43 ± 18.11
12.56	77.93 ± 1.56	978.72 ± 19.65
19.91	54.14 ± 1.07	1077.60 ± 21.30
31.55	38.05 ± 0.76	1200.42 ± 24.12
50.00	27.03 ± 0.54	1351.38 ± 26.99
79.24	19.44 ± 0.39	1540.40 ± 30.92

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6/G15.

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	8011.63 ± 175.01	399.85 ± 8.75
0.08	5690.54 ± 13.61	450.94 ± 1.08
0.13	3753.72 ± 19.45	471.45 ± 2.44
0.20	2448.69 ± 16.04	487.42 ± 3.19
0.32	1598.12 ± 14.21	504.17 ± 4.48
0.50	1046.53 ± 11.37	523.27 ± 5.69
0.79	686.89 ± 5.68	544.32 ± 4.50
1.26	453.58 ± 2.07	569.67 ± 2.60
1.99	302.72 ± 1.15	602.58 ± 2.28
3.15	203.51 ± 1.59	642.02 ± 5.02
5.00	138.34 ± 0.96	691.68 ± 4.80
7.92	95.01 ± 0.75	752.88 ± 5.92
12.56	66.00 ± 0.51	828.88 ± 6.43
19.91	46.52 ± 0.41	926.09 ± 8.15
31.55	33.21 ± 0.26	1047.58 ± 8.30
50.00	23.93 ± 0.19	1196.69 ± 9.36
79.24	17.46 ± 0.13	1383.61 ± 9.91

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6/S.09.

Shear rate (s^{-1})	**Viscosity** (P)	**Stress** (dyn/cm^2)
0.05	9231.67 ± 126.09	458.98 ± 6.30
0.08	6214.29 ± 220.98	492.45 ± 17.51
0.13	4058.76 ± 148.34	509.76 ± 18.63
0.20	2628.68 ± 89.56	523.25 ± 17.83
0.32	1699.22 ± 56.87	536.07 ± 17.94
0.50	1099.52 ± 37.61	549.76 ± 18.81
0.79	714.79 ± 24.78	566.43 ± 19.64
1.26	467.48 ± 15.32	587.13 ± 19.24
1.99	307.87 ± 10.23	612.83 ± 20.36
3.15	204.06 ± 6.12	643.76 ± 19.31
5.00	136.27 ± 4.06	681.36 ± 20.32
7.92	91.85 ± 2.62	727.88 ± 20.75
12.56	62.39 ± 1.68	783.52 ± 21.14
19.91	42.78 ± 1.11	851.56 ± 22.12
31.55	29.67 ± 0.66	935.97 ± 20.90
50.00	20.77 ± 0.35	1038.33 ± 17.71
79.24	14.72 ± 0.23	1166.81 ± 17.88

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6/S.9.

Shear rate (s^{-1})	**Viscosity** (P)			**Stress** (dyn/cm^2)		
0.05	1109.60	±	96.27	53.04	±	4.81
0.08	735.61	±	65.59	58.29	±	5.20
0.13	478.20	±	30.56	60.06	±	3.84
0.20	305.29	±	20.01	60.77	±	3.98
0.32	195.36	±	13.22	61.63	±	4.17
0.50	127.06	±	9.06	63.53	±	4.53
0.79	83.08	±	6.25	65.83	±	4.95
1.26	53.73	±	3.20	67.49	±	4.02
1.99	35.56	±	2.34	70.79	±	4.66
3.15	23.57	±	1.56	74.37	±	4.92
5.00	15.81	±	1.04	79.06	±	5.20
7.92	10.76	±	0.63	85.26	±	4.98
12.56	7.50	±	0.41	94.16	±	5.13
19.91	5.29	±	0.28	105.30	±	5.65
31.55	3.78	±	0.20	119.33	±	6.17
50.00	2.84	±	0.13	142.16	±	6.28
79.24	2.16	±	0.07	171.51	±	5.66

(mean ± SD, n = 3)

Steady rate sweep test data of formula C1/S.09.

Shear rate (s^{-1})	**Viscosity** (P)	**Stress** (dyn/cm^2)
0.05	19209.60 ± 77.25	960.48 ± 3.86
0.08	13786.77 ± 77.48	1092.53 ± 6.14
0.13	9084.69 ± 68.11	1140.98 ± 8.55
0.20	5922.98 ± 51.82	1178.99 ± 10.32
0.32	3853.26 ± 34.08	1215.62 ± 10.75
0.50	2510.11 ± 26.30	1255.05 ± 13.15
0.79	1636.56 ± 14.45	1296.89 ± 11.45
1.26	1069.14 ± 8.97	1342.79 ± 11.26
1.99	705.32 ± 4.70	1403.96 ± 9.36
3.15	467.06 ± 5.94	1473.48 ± 18.74
5.00	310.95 ± 2.28	1554.76 ± 11.38
7.92	209.49 ± 1.44	1660.08 ± 11.38
12.56	142.10 ± 1.00	1784.66 ± 12.53
19.91	96.93 ± 0.46	1929.35 ± 9.12
31.55	66.48 ± 0.35	2097.16 ± 11.09
50.00	46.32 ± 0.31	2315.78 ± 15.71
79.24	32.67 ± 0.25	2588.56 ± 19.80

(mean ± SD, n = 3)

Steady rate sweep test data of formula C1/S.9.

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	8170.90 ± 198.77	407.94 ± 9.94
0.08	5656.38 ± 153.95	448.24 ± 12.20
0.13	3676.44 ± 103.30	461.74 ± 12.97
0.20	2365.43 ± 65.77	407.85 ± 13.09
0.32	1522.78 ± 41.99	480.40 ± 13.25
0.50	978.04 ± 27.11	489.02 ± 13.56
0.79	626.72 ± 18.61	496.64 ± 14.75
1.26	402.70 ± 13.53	505.77 ± 17.00
1.99	261.52 ± 8.84	520.57 ± 17.60
3.15	171.80 ± 5.68	541.99 ± 17.62
5.00	113.83 ± 3.75	569.15 ± 18.73
7.92	76.45 ± 2.49	605.86 ± 19.71
12.56	51.87 ± 1.69	651.40 ± 21.17
19.91	35.56 ± 1.16	707.90 ± 23.10
31.55	24.67 ± 0.79	778.24 ± 25.05
50.00	17.30 ± 0.57	865.08 ± 28.61
79.24	12.32 ± 0.41	976.47 ± 32.13

(mean ± SD, n = 3)

APPENDIX IV

Rheological Data of Piroxicam Gels at 33 °C for Release Studies

Frequency sweep test data of formula C.4.

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	763.36 ± 9.99	160.46 ± 7.95	0.2102 ± 0.0572
63.10	744.39 ± 8.95	144.58 ± 6.42	0.1942 ± 0.0089
39.81	729.25 ± 5.71	95.69 ± 5.57	0.1312 ± 0.0069
25.12	720.36 ± 8.60	80.89 ± 1.98	0.1123 ± 0.0045
15.85	706.16 ± 10.59	70.55 ± 0.91	0.0999 ± 0.0026
10.00	686.00 ± 6.52	49.78 ± 5.97	0.0726 ± 0.0065
6.31	684.77 ± 8.56	49.93 ± 6.56	0.0729 ± 0.0077
3.98	682.89 ± 6.25	45.89 ± 5.66	0.0672 ± 0.0061
2.51	675.89 ± 7.00	45.70 ± 6.12	0.0676 ± 0.0133
1.58	660.40 ± 6.94	43.34 ± 5.23	0.0656 ± 0.0570
1.00	659.00 ± 8.72	40.41 ± 8.00	0.0613 ± 0.0215
0.63	657.97 ± 6.25	42.57 ± 6.68	0.0647 ± 0.0033
0.40	643.57 ± 7.13	46.69 ± 6.66	0.0726 ± 0.022
0.25	635.86 ± 6.92	42.00 ± 12.66	0.0661 ± 0.0258
0.16	625.89 ± 6.86	49.34 ± 11.09	0.0788 ± 0.0285
0.10	608.78 ± 5.26	58.55 ± 6.02	0.0965 ± 0.0339

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6.

Frequency **(rad/s)**	**G′** **(dyn/cm^2)**	**G″** **(dyn/cm^2)**	**tan δ**
100.00	3005.58 ± 85.42	402.23 ± 6.85	0.1338 ± 0.0066
63.10	2961.15 ± 77.60	344.13 ± 5.69	0.1162 ± 0.0058
39.81	2857.56 ± 72.98	280.13 ± 7.47	0.0980 ± 0.0070
25.12	2768.56 ± 67.67	243.90 ± 7.88	0.0881 ± 0.0079
15.85	2752.17 ± 63.52	218.88 ± 8.19	0.0795 ± 0.0087
10.00	2642.86 ± 63.17	201.56 ± 5.65	0.0763 ± 0.0089
6.31	2630.12 ± 65.11	170.26 ± 9.45	0.0647 ± 0.0037
3.98	2632.09 ± 82.31	169.43 ± 17.10	0.0644 ± 0.0532
2.51	2565.15 ± 68.95	152.24 ± 12.39	0.0593 ± 0.0077
1.58	2531.51 ± 58.87	144.84 ± 10.35	0.0572 ± 0.0085
1.00	2478.36 ± 70.13	141.38 ± 12.52	0.0570 ± 0.0064
0.63	2476.60 ± 53.62	157.87 ± 16.17	0.0637 ± 0.0098
0.40	2433.13 ± 61.36	164.81 ± 3.45	0.0677 ± 0.0067
0.25	2422.66 ± 45.91	165.12 ± 4.92	0.0682 ± 0.0087
0.16	2399.55 ± 54.12	178.12 ± 5.35	0.0742 ± 0.0068
0.10	2365.59 ± 36.58	180.14 ± 9.57	0.762 ± 0.0088

(mean ± SD, n = 3)

Frequency sweep test data of formula C1.

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	4883.36 ± 24.27	620.11 ± 3.54	0.1270 ± 0.0026
63.10	4769.22 ± 27.11	541.22 ± 5.68	0.1135 ± 0.0051
39.81	4504.23 ± 32.12	431.21 ± 5.10	0.0957 ± 0.0020
25.12	4501.11 ± 12.13	422.22 ± 25.75	0.0938 ± 0.0069
15.85	4411.54 ± 29.16	342.66 ± 3.57	0.0777 ± 0.0013
10.00	4345.11 ± 32.21	337.68 ± 3.93	0.0777 ± 0.0051
6.31	4264.05 ± 33.22	302.48 ± 0.94	0.0709 ± 0.0037
3.98	4232.00 ± 35.12	272.75 ± 2.92	0.0644 ± 0.0038
2.51	4132.12 ± 40.71	263.55 ± 3.35	0.0638 ± 0.0051
1.58	4094.74 ± 40.11	247.12 ± 4.52	0.0604 ± 0.0034
1.00	4034.49 ± 12.06	256.22 ± 2.36	0.0635 ± 0.0050
0.63	3991.68 ± 22.97	253.55 ± 1.74	0.0635 ± 0.0025
0.40	3935.00 ± 14.23	255.69 ± 6.37	0.0650 ± 0.0015
0.25	3879.43 ± 23.23	258.23 ± 1.24	0.0666 ± 0.0001
0.16	3811.60 ± 31.21	266.91 ± 2.14	0.0700 ± 0.0003
0.10	3799.99 ± 29.38	280.72 ± 0.57	0.0739 ± 0.0014

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6/G10.

Frequency **(rad/s)**	**G′** **(dyn/cm^2)**	**G″** **(dyn/cm^2)**	**tan δ**
100.00	3052.85 ± 12.52	460.79 ± 1.12	0.1509 ± 0.0006
63.10	2969.18 ± 11.17	390.00 ± 2.89	0.1313 ± 0.0007
39.81	2820.99 ± 14.08	320.48 ± 1.59	0.1136 ± 0.0011
25.12	2765.45 ± 12.15	267.94 ± 1.58	0.0969 ± 0.0001
15.85	2705.92 ± 13.99	253.85 ± 2.37	0.0938 ± 0.0027
10.00	2673.45 ± 17.23	214.26 ± 3.62	0.0801 ± 0.0019
6.31	2666.58 ± 13.55	178.23 ± 3.29	0.0668 ± 0.0019
3.98	2561.13 ± 18.21	162.05 ± 1.63	0.0633 ± 0.0005
2.51	2552.23 ± 13.22	162.12 ± 6.73	0.0635 ± 0.0033
1.58	2511.28 ± 16.20	154.11 ± 5.59	0.0614 ± 0.0065
1.00	2463.00 ± 16.33	145.12 ± 2.12	0.0589 ± 0.0083
0.63	2452.61 ± 12.74	149.12 ± 2.20	0.0608 ± 0.0036
0.40	2428.13 ± 12.69	144.28 ± 2.34	0.0594 ± 0.0009
0.25	2395.15 ± 14.73	153.16 ± 4.12	0.0639 ± 0.0036
0.16	2358.90 ± 14.59	143.22 ± 6.12	0.0607 ± 0.0097
0.10	2332.92 ± 12.18	169.39 ± 5.13	0.0726 ± 0.0081

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6/G15.

Frequency **(rad/s)**	**G′** **(dyn/cm^2)**	**G″** **(dyn/cm^2)**	**tan δ**
100.00	2324.34 ± 24.23	448.19 ± 13.65	0.1928 ± 0.0012
63.10	2239.62 ± 22.12	370.37 ± 11.36	0.1654 ± 0.0067
39.81	2184.57 ± 29.72	290.20 ± 1.03	0.1328 ± 0.0014
25.12	2120.12 ± 27.10	240.23 ± 10.29	0.1133 ± 0.0020
15.85	2062.23 ± 15.29	224.40 ± 12.14	0.1088 ± 0.0051
10.00	2011.26 ± 13.25	192.02 ± 11.60	0.0955 ± 0.0021
6.31	1990.01 ± 13.11	183.22 ± 11.30	0.0921 ± 0.0013
3.98	1963.22 ± 14.22	166.55 ± 12.66	0.0848 ± 0.0016
2.51	1922.12 ± 13.19	148.24 ± 12.92	0.0771 ± 0.0012
1.58	1902.11 ± 15.19	134.40 ± 5.18	0.0707 ± 0.0002
1.00	1860.02 ± 29.64	139.86 ± 6.82	0.0752 ± 0.0024
0.63	1840.11 ± 11.21	145.74 ± 16.05	0.0792 ± 0.0095
0.40	1823.13 ± 16.20	143.27 ± 12.68	0.0786 ± 0.0097
0.25	1804.37 ± 11.46	136.13 ± 15.16	0.0754 ± 0.0014
0.16	1780.88 ± 11.29	161.06 ± 14.29	0.0904 ± 0.0430
0.10	1773.69 ± 14.12	144.60 ± 13.53	0.0816 ± 0.0394

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6/S.09.

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	2603.99 ± 22.17	349.51 ± 3.89	0.1342 ± 0.0004
63.10	2540.55 ± 20.24	295.23 ± 1.09	0.1162 ± 0.0021
39.81	2490.12 ± 23.14	245.23 ± 2.81	0.0985 ± 0.0038
25.12	2450.13 ± 20.89	225.45 ± 2.88	0.0920 ± 0.0029
15.85	2422.10 ± 27.25	197.66 ± 3.71	0.0816 ± 0.0030
10.00	2382.11 ± 19.26	169.88 ± 1.76	0.0713 ± 0.0005
6.31	2340.36 ± 23.18	137.73 ± 10.04	0.0589 ± 0.0007
3.98	2312.12 ± 25.34	128.40 ± 15.33	0.0555 ± 0.0053
2.51	2289.13 ± 23.98	135.87 ± 13.87	0.0594 ± 0.0023
1.58	2247.06 ± 37.12	126.22 ± 12.58	0.0562 ± 0.0020
1.00	2224.88 ± 11.48	129.24 ± 15.39	0.0581 ± 0.0059
0.63	2191.29 ± 22.95	138.37 ± 10.61	0.0631 ± 0.0085
0.40	2168.92 ± 28.49	139.48 ± 2.89	0.0643 ± 0.0021
0.25	2151.69 ± 24.93	189.76 ± 11.79	0.0882 ± 0.0046
0.16	2138.17 ± 19.12	152.30 ± 14.57	0.0712 ± 0.0023
0.10	2120.43 ± 18.34	192.61 ± 4.95	0.0908 ± 0.0016

(mean ± SD, n = 3)

Frequency sweep test data of formula C.6/S.9.

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	340.12 ± 19.51	99.48 ± 5.70	0.2925 ± 0.0906
63.10	331.13 ± 16.90	74.54 ± 4.71	0.2251 ± 0.0108
39.81	323.26 ± 18.96	55.00 ± 5.43	0.1701 ± 0.0039
25.12	320.00 ± 14.87	42.30 ± 7.43	0.1322 ± 0.0050
15.85	313.56 ± 11.61	34.59 ± 2.61	0.1103 ± 0.0037
10.00	312.02 ± 19.17	27.62 ± 3.50	0.0885 ± 0.0058
6.31	307.02 ± 18.44	24.58 ± 2.68	0.0801 ± 0.0093
3.98	301.22 ± 11.65	19.25 ± 4.69	0.0639 ± 0.0004
2.51	299.22 ± 13.45	21.96 ± 3.08	0.0734 ± 0.0019
1.58	293.13 ± 17.62	21.55 ± 2.71	0.0735 ± 0.0121
1.00	294.58 ± 17.87	14.92 ± 2.79	0.0507 ± 0.0015
0.63	293.06 ± 17.22	19.59 ± 5.33	0.0668 ± 0.0044
0.40	289.11 ± 18.70	19.76 ± 5.18	0.0684 ± 0.0087
0.25	280.90 ± 17.28	26.71 ± 1.51	0.0951 ± 0.0086
0.16	282.55 ± 14.56	29.41 ± 4.18	0.1041 ± 0.0145
0.10	279.81 ± 11.03	29.83 ± 1.45	0.1067 ± 0.0085

(mean ± SD, n = 3)

Frequency sweep test data of formula C1/S.9.

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	2241.55 ± 67.04	310.92 ± 0.51	0.1387 ± 0.0059
63.10	2204.28 ± 21.83	256.97 ± 1.96	0.1166 ± 0.0055
39.81	2162.77 ± 59.56	221.47 ± 2.56	0.1024 ± 0.0077
25.12	2138.11 ± 26.86	174.87 ± 2.30	0.0818 ± 0.0057
15.85	2110.23 ± 29.24	147.78 ± 2.34	0.0700 ± 0.0080
10.00	2084.88 ± 13.27	135.08 ± 7.51	0.0648 ± 0.0076
6.31	2040.26 ± 26.29	127.04 ± 5.52	0.0623 ± 0.0015
3.98	2031.99 ± 45.57	121.30 ± 8.61	0.0597 ± 0.0024
2.51	2000.47 ± 16.41	109.94 ± 6.89	0.0550 ± 0.0088
1.58	1984.22 ± 23.53	109.52 ± 5.75	0.0552 ± 0.0053
1.00	1965.83 ± 12.01	108.49 ± 7.35	0.0552 ± 0.0028
0.63	1957.83 ± 32.19	115.87 ± 5.98	0.0592 ± 0.0027
0.40	1946.29 ± 42.28	114.66 ± 5.99	0.0589 ± 0.0045
0.25	1941.66 ± 20.14	128.55 ± 2.55	0.0662 ± 0.0068
0.16	1925.99 ± 49.41	141.22 ± 8.79	0.0733 ± 0.0081
0.10	1897.29 ± 35.20	135.08 ± 7.19	0.0713 ± 0.0051

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.4.

Shear rate **(s^{-1})**	**Viscosity** **(P)**
0.05	1989.61 ± 5.96
0.08	1340.75 ± 3.82
0.13	870.60 ± 4.43
0.20	570.58 ± 6.87
0.32	369.55 ± 1.38
0.50	243.96 ± 7.82
0.79	152.73 ± 5.36
1.26	115.72 ± 3.32
1.99	75.45 ± 2.13
3.15	48.43 ± 2.58
5.00	34.33 ± 2.00
7.92	20.52 ± 3.68
12.56	16.73 ± 2.48
19.91	10.19 ± 2.33
31.55	9.09 ± 0.23
50.00	6.79 ± 0.16
79.24	3.99 ± 0.12

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6.

Shear rate (s^{-1})	**Viscosity** (P)
0.05	10108.05 ± 297.68
0.08	6962.39 ± 247.79
0.13	4668.36 ± 317.26
0.20	2986.65 ± 195.82
0.32	1847.11 ± 95.61
0.50	1288.47 ± 65.26
0.79	828.64 ± 25.62
1.26	544.89 ± 22.99
1.99	366.00 ± 16.37
3.15	268.02 ± 19.20
5.00	150.06 ± 2.75
7.92	97.86 ± 2.46
12.56	63.77 ± 3.21
19.91	49.72 ± 2.36
31.55	36.22 ± 0.75
50.00	23.83 ± 0.21
79.24	18.67 ± 0.21

(mean ± SD, n = 3)

Steady rate sweep test data of formula C1.

Shear rate **(s^{-1})**	**Viscosity** **(P)**
0.05	20452.20 ± 217.21
0.08	13734.22 ± 256.69
0.13	9888.66 ± 228.50
0.20	6458.33 ± 130.54
0.32	4183.09 ± 82.16
0.50	2656.16 ± 22.47
0.79	1787.36 ± 26.10
1.26	1068.35 ± 10.09
1.99	758.72 ± 6.72
3.15	506.21 ± 3.87
5.00	330.91 ± 3.95
7.92	212.17 ± 3.78
12.56	153.34 ± 1.54
19.91	100.72 ± 1.83
31.55	69.29 ± 0.02
50.00	52.99 ± 0.06
79.24	38.79 ± 0.06

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6/G10.

Shear rate **(s^{-1})**	**Viscosity** **(P)**
0.05	10202.70 ± 145.49
0.08	7246.95 ± 164.72
0.13	4580.96 ± 99.33
0.20	3206.89 ± 54.04
0.32	2006.69 ± 30.66
0.50	1312.24 ± 21.96
0.79	848.89 ± 5.71
1.26	556.02 ± 0.19
1.99	353.64 ± 8.68
3.15	238.08 ± 4.96
5.00	148.04 ± 3.09
7.92	103.56 ± 3.39
12.56	67.93 ± 1.76
19.91	54.24 ± 2.08
31.55	36.26 ± 0.76
50.00	26.03 ± 0.64
79.24	12.24 ± 0.69

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6/G15

Shear rate (s^{-1})	**Viscosity** (P)
0.05	7997.01 ± 75.62
0.08	5820.52 ± 12.62
0.13	3623.73 ± 12.45
0.20	2242.69 ± 12.04
0.32	1392.12 ± 17.21
0.50	996.52 ± 11.38
0.79	666.89 ± 2.68
1.26	452.28 ± 3.08
1.99	292.72 ± 2.15
3.15	212.52 ± 1.69
5.00	128.34 ± 0.96
7.92	89.01 ± 1.72
12.56	60.00 ± 1.62
19.91	49.53 ± 0.21
31.55	36.21 ± 0.26
50.00	22.93 ± 0.39
79.24	18.46 ± 0.33

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6/S.09.

Shear rate **(s^{-1})**	**Viscosity** **(P)**
0.05	9179.54 ± 108.09
0.08	6200.28 ± 122.97
0.13	4048.78 ± 128.34
0.20	2328.88 ± 87.66
0.32	1599.32 ± 55.87
0.50	999.62 ± 57.62
0.79	704.79 ± 34.78
1.26	462.28 ± 10.32
1.99	297.87 ± 10.33
3.15	199.78 ± 6.12
5.00	126.37 ± 5.06
7.92	92.65 ± 3.62
12.56	63.99 ± 2.68
19.91	43.28 ± 3.11
31.55	22.67 ± 1.66
50.00	20.78 ± 1.25
79.24	14.73 ± 2.23

(mean ± SD, n = 3)

Steady rate sweep test data of formula C.6/S.9.

Shear rate (s^{-1})	**Viscosity** (P)
0.05	1060.90 ± 66.37
0.08	726.63 ± 65.67
0.13	438.29 ± 20.56
0.20	295.99 ± 20.11
0.32	192.00 ± 10.02
0.50	123.96 ± 0.06
0.79	82.98 ± 7.25
1.26	50.23 ± 2.20
1.99	36.59 ± 2.39
3.15	22.07 ± 2.56
5.00	13.82 ± 2.64
7.92	10.99 ± 1.63
12.56	8.51 ± 0.41
19.91	5.32 ± 2.28
31.55	3.80 ± 0.35
50.00	2.80 ± 0.23
79.24	2.27 ± 0.07

(mean ± SD, n = 3)

Steady rate sweep test data of formula C1/S.9.

Shear rate (s^{-1})	**Viscosity** (P)
0.05	8158.80 ± 108.77
0.08	4952.38 ± 103.25
0.13	3636.22 ± 102.29
0.20	2300.21 ± 37.81
0.32	1503.76 ± 43.99
0.50	969.02 ± 26.11
0.79	606.82 ± 19.61
1.26	412.70 ± 12.53
1.99	260.82 ± 9.84
3.15	161.60 ± 5.88
5.00	102.80 ± 2.75
7.92	78.45 ± 3.49
12.56	53.87 ± 1.69
19.91	30.22 ± 0.10
31.55	26.68 ± 0.89
50.00	16.00 ± 0.58
79.24	10.38 ± 0.42

(mean ± SD, n = 3)

APPENDIX V

Rheological Data of Carbopol 940 Gel Bases at 33 °C for Sensory Evaluations

Frequency sweep test data of gel base T1.

Frequency (rad/s)	**G' (dyn/cm^2)**	**G'' (dyn/cm^2)**	**tan δ**
100.00	4358.56 ± 21.91	529.51 ± 18.72	0.1215 ± 0.0037
63.10	4250.18 ± 30.17	460.10 ± 11.40	0.1083 ± 0.0019
39.81	4176.07 ± 30.84	383.07 ± 13.65	0.0917 ± 0.0026
25.12	4097.15 ± 37.22	338.20 ± 12.20	0.0825 ± 0.0022
15.85	4028.29 ± 36.67	295.17 ± 9.48	0.0733 ± 0.0017
10.00	3969.47 ± 40.19	276.61 ± 15.65	0.0697 ± 0.0032
6.31	3900.99 ± 47.57	257.97 ± 10.11	0.0661 ± 0.0018
3.98	3857.94 ± 35.80	250.01 ± 14.25	0.0648 ± 0.0031
2.51	3790.65 ± 50.09	242.80 ± 10.82	0.0640 ± 0.0020
1.58	3733.61 ± 36.94	238.28 ± 8.35	0.0638 ± 0.0016
1.00	3691.57 ± 39.76	237.89 ± 22.57	0.0644 ± 0.0054
0.63	3616.75 ± 62.15	260.47 ± 9.10	0.0721 ± 0.0037
0.40	3584.00 ± 36.58	247.84 ± 17.97	0.0691 ± 0.0043
0.25	3547.16 ± 48.21	259.63 ± 1.56	0.0732 ± 0.0005
0.16	3534.39 ± 32.53	251.16 ± 14.01	0.0710 ± 0.0033
0.10	3497.62 ± 43.35	249.25 ± 15.19	0.0713 ± 0.0035

(mean ± SD, n = 3)

Frequency sweep test data of gel base T2.

Frequency (rad/s)	**G' (dyn/cm^2)**	**G'' (dyn/cm^2)**	**tan δ**
100.00	4903.67 ± 3.72	558.98 ± 0.55	0.1140 ± 0.0001
63.10	4773.93 ± 4.86	493.97 ± 1.88	0.1035 ± 0.0003
39.81	4680.29 ± 4.46	417.29 ± 0.46	0.0892 ± 0.0002
25.12	4592.02 ± 6.83	368.72 ± 6.25	0.0803 ± 0.0012
15.85	4512.74 ± 5.72	337.26 ± 5.37	0.0747 ± 0.0011
10.00	4438.33 ± 2.47	305.55 ± 5.39	0.0688 ± 0.0012
6.31	4367.54 ± 11.74	281.23 ± 3.99	0.0644 ± 0.0011
3.98	4300.13 ± 8.89	279.58 ± 15.72	0.0650 ± 0.0038
2.51	4239.48 ± 7.74	264.04 ± 1.91	0.0623 ± 0.0006
1.58	4181.34 ± 11.04	254.83 ± 6.49	0.0609 ± 0.0014
1.00	4113.37 ± 10.53	254.67 ± 7.73	0.0619 ± 0.0017
0.63	4062.60 ± 18.78	270.33 ± 0.57	0.0665 ± 0.0002
0.40	4007.89 ± 10.46	272.17 ± 16.33	0.0679 ± 0.0039
0.25	3943.75 ± 5.40	298.52 ± 28.16	0.0757 ± 0.0072
0.16	3912.91 ± 9.28	292.51 ± 5.72	0.0748 ± 0.0013
0.10	386098 ± 4.35	296.58 ± 1.71	0.0768 ± 0.0004

(mean ± SD, n = 3)

Frequency sweep test data of gel base T3.

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	5253.76 ± 41.77	609.70 ± 0.41	0.1161 ± 0.0010
63.10	5109.52 ± 43.58	540.44 ± 7.22	0.1058 ± 0.0023
39.81	5009.52 ± 38.72	459.43 ± 1.22	0.0917 ± 0.0010
25.12	4923.74 ± 42.74	404.72 ± 3.82	0.0822 ± 0.0001
15.85	4836.21 ± 46.14	349.93 ± 5.29	0.0724 ± 0.0004
10.00	4756.21 ± 46.19	325.58 ± 2.49	0.0683 ± 0.0012
6.31	4685.96 ± 40.58	310.34 ± 7.39	0.0662 ± 0.0022
3.98	4609.32 ± 40.54	286.47 ± 2.86	0.0622 ± 0.0012
2.51	4544.48 ± 48.40	273.63 ± 7.76	0.0602 ± 0.0011
1.58	4476.89 ± 44.48	267.62 ± 2.39	0.0598 ± 0.0011
1.00	4419.07 ± 30.55	271.22 ± 8.00	0.0614 ± 0.0022
0.63	4352.33 ± 39.23	290.87 ± 20.05	0.0668 ± 0.0040
0.40	4307.76 ± 34.36	259.37 ± 5.16	0.0602 ± 0.0007
0.25	4251.30 ± 48.23	271.74 ± 9.22	0.0639 ± 0.0015
0.16	4213.78 ± 47.79	252.48 ± 5.64	0.0599 ± 0.0007
0.10	4150.38 ± 61.49	295.91 ± 2.32	0.0713 ± 0.0016

(mean ± SD, n = 3)

Frequency sweep test data of gel base T4.

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	264.06 ± 4.42	60.11 ± 7.27	0.2280 ± 0.0317
63.10	257.74 ± 6.35	42.51 ± 0.12	0.1650 ± 0.0046
39.81	253.34 ± 6.42	29.82 ± 0.59	0.1177 ± 0.0007
25.12	250.67 ± 4.24	22.07 ± 0.84	0.0880 ± 0.0019
15.85	248.02 ± 5.38	16.06 ± 0.45	0.0648 ± 0.0033
10.00	244.61 ± 5.26	12.59 ± 0.69	0.0515 ± 0.0040
6.31	243.11 ± 6.13	12.38 ± 0.32	0.0509 ± 0.0001
3.98	241.63 ± 2.06	7.79 ± 1.75	0.0322 ± 0.0070
2.51	238.11 ± 6.51	8.87 ± 1.46	0.0374 ± 0.0073
1.58	236.89 ± 5.91	9.51 ± 0.28	0.0402 ± 0.0022
1.00	235.10 ± 4.58	11.75 ± 0.01	0.0500 ± 0.0009
0.63	233.87 ± 8.61	11.71 ± 0.15	0.0502 ± 0.0025
0.40	226.69 ± 3.28	9.32 ± 2.64	0.0412 ± 0.0123
0.25	227.67 ± 5.89	11.52 ± 1.16	0.0507 ± 0.0065
0.16	224.26 ± 8.22	13.20 ± 5.92	0.0582 ± 0.0248
0.10	219.82 ± 5.49	16.74 ± 3.51	0.0759 ± 0.0143

(mean ± SD, n = 3)

Frequency sweep test data of gel base T5 .

Frequency (rad/s)	**G′ (dyn/cm^2)**	**G″ (dyn/cm^2)**	**tan δ**
100.00	5788.52 ± 50.58	779.84 ± 5.10	0.1347 ± 0.0004
63.10	5345.01 ± 43.69	703.90 ± 2.18	0.1317 ± 0.0007
39.81	5199.75 ± 50.28	609.56 ± 0.75	0.1172 ± 0.0013
25.12	5072.24 ± 48.61	523.48 ± 1.99	0.1032 ± 0.0006
15.85	4959.25 ± 36.49	464.91 ± 1.97	0.0938 ± 0.0003
10.00	4861.22 ± 41.99	410.63 ± 1.20	0.0845 ± 0.0010
6.31	4756.07 ± 38.45	385.58 ± 2.01	0.0811 ± 0.0011
3.98	4671.36 ± 44.13	339.72 ± 0.06	0.0727 ± 0.0007
2.51	4588.72 ± 36.12	325.26 ± 1.46	0.0709 ± 0.0002
1.58	4518.59 ± 40.22	303.95 ± 12.54	0.0673 ± 0.0022
1.00	4452.06 ± 44.47	302.88 ± 5.60	0.0680 ± 0.0019
0.63	4382.71 ± 42.82	302.96 ± 5.61	0.0691 ± 0.0006
0.40	4326.96 ± 33.15	297.39 ± 0.59	0.0687 ± 0.0007
0.25	4268.40 ± 46.16	290.40 ± 0.94	0.0680 ± 0.0010
0.16	4215.40 ± 16.33	302.74 ± 23.39	0.0718 ± 0.0053
0.10	4152.68 ± 23.30	323.81 ± 7.18	0.0780 ± 0.0022

(mean ± SD, n = 3)

Frequency sweep test data of gel baseT6.

Frequency **(rad/s)**	**G'** **(dyn/cm^2)**	**G''** **(dyn/cm^2)**	**tan δ**
100.00	5961.66 ± 3.74	673.93 ± 2.12	0.1130 ± 0.0004
63.10	5808.28 ± 11.90	605.16 ± 13.69	0.1042 ± 0.0026
39.81	5693.21 ± 0.16	510.39 ± 5.50	0.0897 ± 0.0010
25.12	5597.98 ± 8.38	439.78 ± 11.92	0.0786 ± 0.0022
15.85	5502.07 ± 15.69	395.95 ± 8.19	0.0720 ± 0.0017
10.00	5411.05 ± 12.56	355.12 ± 4.90	0.0656 ± 0.0011
6.31	5335.02 ± 29.01	326.75 ± 8.49	0.0613 ± 0.0019
3.98	5253.39 ± 5.44	326.62 ± 10.9	0.0622 ± 0.0020
2.51	5166.96 ± 20.32	308.25 ± 3.95	0.0597 ± 0.0010
1.58	5102.77 ± 5.83	314.84 ± 5.06	0.0617 ± 0.0009
1.00	5036.99 ± 3.36	307.56 ± 13.83	0.0611 ± 0.0028
0.63	4994.53 ± 3.40	299.94 ± 5.09	0.0601 ± 0.0010
0.40	4918.70 ± 3.83	287.40 ± 5.73	0.0584 ± 0.0012
0.25	4864.04 ± 6.33	293.60 ± 27.55	0.0604 ± 0.0056
0.16	4808.00 ± 24.88	318.56 ± 7.99	0.0663 ± 0.0013
0.10	4762.55 ± 28.30	344.94 ± 12.94	0.0724 ± 0.0031

(mean ± SD, n = 3)

Steady rate sweep test data of gel base T1.

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	6123.13 ± 322.08	306.16 ± 16.10
0.08	4172.20 ± 212.26	330.62 ± 16.82
0.13	2900.44 ± 140.22	364.28 ± 17.61
0.20	2047.79 ± 92.89	407.62 ± 18.49
0.32	1470.91 ± 58.94	464.04 ± 18.59
0.50	1075.66 ± 33.03	537.83 ± 16.51
0.79	794.82 ± 13.02	629.85 ± 10.32
1.26	585.45 ± 2.36	735.30 ± 2.96
1.99	423.44 ± 6.04	842.87 ± 12.02
3.15	298.29 ± 9.59	941.03 ± 30.25
5.00	207.54 ± 4.42	1037.71 ± 22.10
7.92	143.06 ± 2.19	1133.70 ± 17.39
12.56	98.40 ± 1.36	1235.82 ± 17.03
19.91	67.69 ± 0.79	1347.37 ± 15.65
31.55	46.67 ± 0.42	1472.46 ± 13.10
50.00	32.36 ± 0.20	1617.91 ± 9.98
79.24	22.47 ± 0.06	1780.97 ± 4.47
125.59	15.70 ± 0.04	1971.92 ± 5.37
199.05	11.08 ± 0.01	2206.26 ± 2.93
315.48	7.88 ± 0.02	2485.05 ± 5.60
500.00	5.65 ± 0.02	2826.91 ± 7.62

(mean ± SD, n = 3)

Steady rate sweep test data of gel baseT2 .

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	9305.26 ± 178.52	465.26 ± 8.93
0.08	6291.89 ± 154.93	498.60 ± 12.28
0.13	4282.86 ± 107.68	537.90 ± 13.53
0.20	2957.59 ± 83.88	588.72 ± 16.70
0.32	2069.27 ± 54.68	652.81 ± 17.25
0.50	1468.47 ± 39.64	734.23 ± 19.82
0.79	1047.90 ± 33.77	830.40 ± 26.76
1.26	744.06 ± 27.09	934.49 ± 34.03
1.99	528.03 ± 10.99	1051.06 ± 21.88
3.15	357.11 ± 9.78	1126.60 ± 30.85
5.00	244.92 ± 5.83	1224.62 ± 29.15
7.92	164.57 ± 3.47	1327.92 ± 27.47
12.56	114.47 ± 2.54	1437.62 ± 31.90
19.91	78.65 ± 1.37	1565.52 ± 27.19
31.55	54.26 ± 0.75	1711.73 ± 23.66
50.00	37.70 ± 0.41	1885.07 ± 20.62
79.24	26.29 ± 0.16	2083.72 ± 13.05
125.59	18.40 ± 0.02	2311.05 ± 3.05
199.05	12.99 ± 0.04	2586.00 ± 8.08
315.48	9.27 ± 0.07	2925.08 ± 22.59
500.00	6.66 ± 0.06	3332.26 ± 30.14

(mean ± SD, n = 3)

Steady rate sweep test data of gel base T3 .

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	14471.47 ± 940.45	723.57 ± 47.02
0.08	10059.31 ± 668.65	797.15 ± 52.99
0.13	6947.23 ± 426.98	872.53 ± 53.63
0.20	4807.91 ± 270.79	957.03 ± 53.90
0.32	3312.89 ± 172.56	1045.15 ± 54.44
0.50	2261.82 ± 111.45	1130.91 ± 55.73
0.79	1518.33 ± 79.09	1203.19 ± 62.67
1.26	1010.58 ± 52.15	1269.24 ± 65.50
1.99	681.61 ± 25.97	1356.77 ± 51.68
3.15	464.07 ± 8.92	1464.05 ± 28.13
5.00	311.59 ± 3.30	1557.94 ± 16.51
7.92	210.42 ± 1.50	1667.47 ± 11.90
12.56	143.06 ± 1.05	1796.73 ± 13.15
19.91	97.94 ± 0.60	1949.49 ± 12.01
31.55	67.47 ± 0.07	2128.52 ± 2.23
50.00	46.83 ± 0.17	2341.45 ± 8.72
79.24	32.69 ± 0.19	2590.42 ± 15.08
125.59	22.97 ± 0.17	2885.45 ± 20.93
199.05	16.26 ± 0.14	3236.97 ± 28.83
315.48	11.61 ± 0.11	3664.26 ± 33.45
500.00	8.35 ± 0.08	4175.59 ± 41.96

(mean ± SD, n = 3)

Steady rate sweep test data of gel base T4.

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	796.72 ± 27.79	39.84 ± 1.39
0.08	493.35 ± 23.75	39.10 ± 1.88
0.13	292.91 ± 16.97	36.79 ± 2.13
0.20	178.57 ± 4.93	35.55 ± 0.98
0.32	113.80 ± 2.43	35.90 ± 0.77
0.50	72.93 ± 2.94	36.46 ± 1.47
0.79	45.92 ± 2.21	36.39 ± 1.75
1.26	29.15 ± 0.94	36.61 ± 1.18
1.99	19.41 ± 0.28	38.64 ± 0.57
3.15	13.72 ± 0.15	43.28 ± 0.48
5.00	9.20 ± 0.24	45.98 ± 1.22
7.92	6.02 ± 0.14	47.71 ± 1.11
12.56	4.05 ± 0.08	50.88 ± 0.95
19.91	2.81 ± 0.05	55.96 ± 0.92
31.55	2.02 ± 0.03	63.61 ± 0.80
50.00	1.49 ± 0.01	74.58 ± 0.61
79.24	1.13 ± 0.01	89.36 ± 0.58
125.59	0.87 ± 0.00	108.66 ± 0.13
199.05	0.67 ± 0.00	133.91 ± 0.16
315.48	0.52 ± 0.00	164.65 ± 0.15
500.00	0.40 ± 0.00	202.49 ± 0.70

(mean ± SD, n = 3)

Steady rate sweep test data of gel base T5.

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	17066.47 ± 800.78	853.32 ± 40.04
0.08	12430.07 ± 502.32	985.02 ± 39.81
0.13	8569.82 ± 226.49	1076.32 ± 28.45
0.20	5831.89 ± 73.10	1160.86 ± 14.55
0.32	3937.47 ± 13.38	1242.19 ± 4.23
0.50	2641.58 ± 10.06	1320.78 ± 5.03
0.79	1765.85 ± 16.56	1399.35 ± 13.12
1.26	1175.53 ± 14.54	1476.40 ± 18.26
1.99	786.33 ± 7.40	1565.23 ± 14.73
3.15	530.15 ± 5.10	1672.49 ± 15.82
5.00	358.51 ± 3.15	1792.56 ± 15.77
7.92	244.77 ± 2.41	1939.67 ± 19.13
12.56	169.25 ± 1.23	2125.73 ± 15.43
19.91	118.06 ± 0.32	2350.08 ± 6.41
31.55	82.89 ± 0.01	2614.90 ± 0.30
50.00	58.46 ± 0.02	2923.17 ± 1.00
79.24	41.52 ± 0.05	3290.17 ± 3.82
125.59	29.74 ± 0.03	2734.99 ± 3.83
199.05	21.47 ± 0.02	4272.69 ± 4.12
315.48	15.61 ± 0.00	4923.51 ± 1.25
500.00	11.45 ± 0.01	5722.75 ± 7.26

(mean ± SD, n = 3)

Steady rate sweep test data of gel base T6 .

Shear rate **(s^{-1})**	**Viscosity** **(P)**	**Stress** **(dyn/cm^2)**
0.05	26244.80 ± 184.46	1312.24 ± 9.23
0.08	18727.20 ± 257.90	1484.03 ± 20.44
0.13	12433.77 ± 212.41	1561.61 ± 26.68
0.20	8177.42 ± 170.71	1627.74 ± 33.98
0.32	5334.92 ± 129.47	1683.05 ± 40.84
0.50	3465.10 ± 96.48	1732.55 ± 48.24
0.79	2247.49 ± 57.00	1781.01 ± 45.17
1.26	1449.78 ± 43.08	1820.85 ± 54.10
1.99	944.77 ± 32.36	1880.61 ± 64.42
3.15	619.68 ± 14.96	1954.96 ± 47.19
5.00	407.74 ± 9.39	2038.68 ± 46.93
7.92	270.88 ± 6.94	2146.58 ± 54.97
12.56	182.21 ± 4.43	2288.42 ± 55.64
19.91	123.94 ± 3.02	2467.16 ± 60.18
31.55	85.12 ± 1.84	2685.43 ± 57.99
50.00	58.94 ± 1.08	2946.80 ± 53.83
79.24	41.08 ± 0.62	3255.50 ± 49.42
125.59	28.95 ± 0.36	3636.36 ± 45.47
199.05	20.58 ± 0.23	4095.80 ± 46.41
315.48	14.72 ± 0.14	4642.60 ± 44.76
500.00	11.66 ± 0.11	5328.50 ± 53.35

(mean ± SD, n = 3)

APPENDIX VI

Piroxicam Release Data

Formula : C.4

Time (min)	Square root of time ($min^{1/2}$)	Run I		Run II		Run III	
		Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.8730	0.3180	0.3180	0.3369	0.3369	0.3521	0.3521
30	5.4772	0.3331	0.6511	0.3242	0.6611	0.3213	0.6733
60	7.7460	0.6632	1.3144	0.6240	1.2851	0.5967	1.2700
90	9.4868	0.3502	1.6646	0.3654	1.6505	0.3947	1.6648
120	10.9545	0.4285	2.0930	0.3957	2.0461	0.6799	2.3447
150	12.2474	0.4061	2.4992	0.4066	2.4527	0.2092	2.5538
180	13.4164	0.3464	2.8456	0.3348	2.7876	0.3567	2.9106
Slope of cumulative amount against square root of time plot		0.2647		0.2567		0.2747	
R^2		0.9966		0.9968		0.991	
Diffusion coefficient x 10^4 (cm^2 min^{-1})		1.1667		1.0972		1.2565	
mean of D$\times10^4$		1.1735					
SD$\times10^6$		7.9852					
%CV		6.8048					

Formula : C.6

Time (min)	Square root of time ($min^{1/2}$)	Run I		Run II		Run III	
		Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)
15	3.8730	0.2170	0.2170	0.2164	0.2164	0.2104	0.2104
30	5.4772	0.3337	0.5508	0.3449	0.5613	0.3367	0.5472
60	7.7460	0.4792	1.0300	0.4770	1.0383	0.4792	1.0264
90	9.4868	0.4376	1.4675	0.4144	1.4527	0.4160	1.4423
120	10.9545	0.3926	1.8602	0.3925	1.8451	0.3943	1.8367
150	12.2474	0.3188	2.1789	0.3057	2.1508	0.3085	2.1452
180	13.4164	0.3266	2.5056	0.3110	2.4617	0.3210	2.4662
Slope of cumulative amount against square root of time plot		0.2402		0.2353		0.2364	
R^2		0.9973		0.9981		0.9977	
Diffusion coefficient x 10^5 (cm^2 min^{-1})		9.2910		8.9158		8.9994	
Mean of D x 10^5		9.0687					
SD x 10^6		1.9698					
%CV		2.1721					

Formula : C1

Time (min)	Square root of time (min$^{1/2}$)	Run I		Run II		Run III	
		Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)
15	3.8730	0.3106	0.3106	0.2885	0.2885	0.3131	0.3131
30	5.4772	0.2148	0.5253	0.2519	0.5404	0.2442	0.5573
60	7.7460	0.5311	1.0564	0.5122	1.0526	0.5882	1.1454
90	9.4868	0.3519	1.4083	0.3794	1.4320	0.3043	1.4497
120	10.9545	0.3471	1.7554	0.3412	1.7732	0.3654	1.8151
150	12.2474	0.3384	2.0938	0.3137	2.0870	0.3272	2.1423
180	13.4164	0.3304	2.4242	0.2657	2.3527	0.2829	2.4252
Slope of cumulative amount against square root of time plot		0.2229		0.2199		0.2237	
R^2		0.9937		0.9978		0.9965	
Diffusion coefficient x 10^5 (cm^2 min^{-1})		8.6398		8.4088		8.7019	
Mean of D x 10^5		8.5835					
SD x 10^6		1.5446					
%CV		1.7995					

Formula : C.6/G10

Time (min)	Square root of time (min$^{1/2}$)	Run I		Run II		Run III	
		Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)
15	3.8730	0.3106	0.3106	0.3196	0.3196	0.2395	0.2395
30	5.4772	0.2693	0.5799	0.2663	0.5859	0.2868	0.5263
60	7.7460	0.5122	1.0921	0.5225	1.1084	0.4882	1.0145
90	9.4868	0.4178	1.5099	0.3867	1.4951	0.4076	1.4221
120	10.9545	0.3792	1.8891	0.3795	1.8746	0.3329	1.7550
150	12.2474	0.2657	2.1549	0.2584	2.1330	0.3572	2.1121
180	13.4164	0.3719	2.5268	0.3377	2.4707	0.3078	2.4199
Slope of cumulative amount against square root of time plot		0.2325		0.2266		0.2291	
R^2		0.9962		0.9973		0.9965	
Diffusion coefficient x 10^5 (cm^2 min^{-1})		9.1024		8.6463		8.8382	
Mean of D x 10^5		8.8623					
SD x 10^6		2.2901					
%CV		2.5841					

Formula : C.6/G15

Time (min)	Square root of time (min$^{1/2}$)	Run I		Run II		Run III	
		Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)
15	3.8730	0.2021	0.2021	0.1918	0.1918	0.1952	0.1952
30	5.4772	0.2538	0.4559	0.2527	0.4445	0.2504	0.4456
60	7.7460	0.5781	1.0340	0.5767	1.0211	0.5685	1.0141
90	9.4868	0.3631	1.3972	0.3126	1.3338	0.3492	1.3633
120	10.9545	0.2400	1.6372	0.2383	1.5721	0.2393	1.6026
150	12.2474	0.3894	2.0266	0.3512	1.9233	0.3666	1.9692
180	13.4164	0.2242	2.2507	0.1796	2.1029	0.2288	2.1980
Slope of cumulative amount against square root of time plot		0.2179		0.2041		0.2125	
R^2		0.9966		0.9964		0.997	
Diffusion coefficient x 10^5 (cm^2 min^{-1})		7.9060		6.9363		7.5190	
Mean of D x 10^5		7.4538					
SD x 10^6		4.8813					
%CV		6.5487					

Formula : C.6/S.09

Time (min)	Square root of time (min$^{1/2}$)	Run I		Run II		Run III	
		Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)
15	3.8730	0.3106	0.3106	0.3219	0.3219	0.3546	0.3546
30	5.4772	0.3128	0.6233	0.3270	0.6489	0.3576	0.7123
60	7.7460	0.5865	1.2098	0.5754	1.2244	0.5354	0.2476
90	9.4868	0.5129	1.7228	0.5201	1.7444	0.5268	1.7745
120	10.9545	0.3734	2.0962	0.3718	2.1162	0.4663	2.2407
150	12.2474	0.4075	2.5037	0.3812	2.4974	0.3627	2.6035
180	13.4164	0.3791	2.8828	0.3641	2.8615	0.3684	2.9719
Slope of cumulative amount against square root of time plot		0.2712		0.2680		0.2768	
R^2		0.9962		0.9974		0.9961	
Diffusion coefficient x 10^4 (cm^2 min^{-1})		1.1183		1.0920		1.1649	
Mean of D x 10^4		1.1251					
SD x 10^6		3.6920					
%CV		3.2816					

Formula : C.6/S.9

Time (min)	Square root of time (min$^{1/2}$)	Run I		Run II		Run III	
		Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)
15	3.8730	0.3677	0.3677	0.3861	0.3861	0.3758	0.3758
30	5.4772	0.3550	0.7227	0.3498	0.7359	0.3559	0.7317
60	7.7460	0.6613	1.3840	0.6700	1.4059	0.6726	1.4043
90	9.4868	0.5606	1.9446	0.5907	1.9966	0.5139	1.9182
120	10.9545	0.5502	2.4948	0.5505	2.5471	0.5081	2.4263
150	12.2474	0.4262	2.9210	0.3514	2.8984	0.4929	2.9192
180	13.4164	0.4338	3.3547	0.4149	3.3134	0.4571	3.3762
Slope of cumulative amount against square root of time plot		0.3170		0.3130		0.3149	
R^2		0.995		0.9963		0.9934	
Diffusion coefficient x 10^4 (cm^2 min^{-1})		1.4994		1.4618		1.4796	
Mean of D x 10^4		1.4803					
SD x 10^6		1.8810					
%CV		1.2707					

Formula : C1/S.9

Time (min)	Square root of time ($\mathrm{min}^{1/2}$)	Run I		Run II		Run III	
		Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)	Amount (mg)	Cumulative amount (mg)
15	3.8730	0.2874	0.2874	0.2973	0.2973	0.3173	0.3173
30	5.4772	0.2673	0.5547	0.2661	0.5634	0.2833	0.6006
60	7.7460	0.5135	1.0681	0.5710	1.1344	0.5422	1.1429
90	9.4868	0.3683	1.4365	0.3239	1.4582	0.4558	1.5987
120	10.9545	0.4423	1.8788	0.4402	1.8984	0.3784	1.9771
150	12.2474	0.2774	2.1562	0.2712	2.1697	0.3398	2.3169
180	13.4164	0.3463	2.5025	0.3375	2.5072	0.3363	2.6532
Slope of cumulative amount against square root of time plot		0.2336		0.2329		0.2475	
R^2		0.995		0.9961		0.9969	
Diffusion coefficient x 10^5 ($\mathrm{cm}^2\ \mathrm{min}^{-1}$)		9.6578		9.6000		10.0841	
Mean of D x 10^4		1.0033					
SD x 10^6		7.0060					
%CV		6.9829					

One - way ANOVA table for piroxicam release studies data analysis :

Source of variations	df	SSQ	MS	Ratio
Total	23	1.1698×10^{-8}		
TMT	7	1.1367×10^{-8}	1.6239×10^{-9}	78.5706
error	16	3.3069×10^{-10}	2.0668×10^{-11}	

F_{table} = 2.66 ($p < 0.05$, df = 7, 16) ∴ Ho was rejected.

Tukey test :

MSE = 2.0668×10^{-11}

df = 16 , n = 24, $p < 0.05$, TMT = 8

Q_{α} = 4.9, HSD = 4.5472×10^{-6}

APPENDIX VII

Sensory Evaluations

แบบสอบถามเพื่อคัดเลือกอาสาสมัคร วันที่.....................................

ประวัติ

1. เพศ ☐ ชาย ☐ หญิง 2. อายุ..........................ปี

3. ชื่อ...นามสกุล..ชื่อเล่น...........................

4. ที่อยู่..

....

5. เบอร์โทรศัพท์ที่ติดต่อได้สะดวก..

6. ท่านเคยใช้ยาทาภายนอก/เครื่องสำอางทาผิวหรือไม่ ☐ เคย ☐ ไม่เคย

ช่วงเวลา

7. วันเสาร์ หรืออาทิตย์ ในเดือนพฤศจิกายน และธันวาคม พ.ศ. 2544 ท่านมีโครงการที่จะทำธุระอะไรหรือไม่

☐ ไม่มี

☐ มี (โปรดระบุวันที่ที่ท่านคาดว่าจะมีธุระ...)

8. ในเดือนพฤศจิกายน และธันวาคม พ.ศ. 2544 ท่านคาดว่าจะมีเวลาว่างในวันใด (นอกจากวันเสาร์หรืออาทิตย์)

เดือนพฤศจิกายน..

เดือนธันวาคม..... ....

สุขภาพ

9. ท่านมีอาการต่อไปนี้หรือไม่

- อาการ/โรคทางระบบประสาท (เช่น อัมพาต, ภาวะทางจิตผิดปกติ, ลมชัก และอื่น ๆ) ☐มี ☐ไม่มี
- อาการร้อน หรือเย็นที่มือ และ/หรือแขนทั้ง 2 ข้าง/ข้างใดข้างหนึ่ง อย่างผิดปกติ ☐มี ☐ไม่มี
- อาการผื่นแพ้คันที่บริเวณมือ และ/หรือแขนอยู่บ่อย ๆ ☐มี ☐ไม่มี
- มีแผลที่มือ หรือแขน ☐มี ☐ไม่มี

10. โปรดระบุชื่อยาที่ท่านใช้อยู่เป็นประจำ

....

11. โปรดระบุชื่อยา หรือสารเคมีที่ท่านแพ้

....

<u>แบบทดสอบความรู้สึกสัมผัส</u> (ให้เลือกคำตอบที่คิดว่าถูกต้องที่สุดเพียงข้อเดียว)

1. ยาเจลที่มีเนื้อแน่น, แข็ง จะมีลักษณะเป็นเช่นใด
   - ก. จะต้องใช้แรงเพื่อบีบเจลที่อยู่ระหว่างนิ้วหัวแม่มือ และนิ้วชี้มาก
   - ข. รู้สึกถึงปริมาณน้ำขณะที่ถูยาเจลกับผิวหนังมาก
   - ค. เมื่อทาไปที่ผิวแล้ว ผิวจะมีลักษณะเป็นมัน สะท้อนแสงมาก
   - ง. สามารถกระจายยาเจลบนผิวหนังได้อย่างง่ายดาย

2. เมื่อท่านทาน้ำมัน (เช่น Baby Oil ของ Johnson and Johnson) ที่แขนของท่าน แล้วใช้นิ้วถู ท่านจะรู้สึกว่าแขนบริเวณนั้นลื่นกว่าบริเวณที่ไม่ได้ทาน้ำมันหรือไม่
   - ก. ลื่นกว่า ข. ไม่แตกต่างกัน

3. ท่านจะบรรยายความรู้สึกเหนอะหนะหลังจากทายาเจลที่แขน ได้อย่างไร
   - ก. ผิวมีลักษณะเป็นมัน สะท้อนแสงมาก
   - ข. รู้สึกถึงความยากในการดึงนิ้วมือออกจากผิวหนัง หลังจากที่ยาเจลถูกดูดซึมหมด
   - ค. รู้สึกว่ากระจายยาเจลบนผิวหนังได้ค่อนข้างยาก
   - ง. รู้สึกว่ามีน้ำมาก ขณะที่ถูยาเจลกับผิวหนัง

4. เมื่อท่านทาเครื่องสำอางที่เป็นมันที่แขน แล้วท่านรู้สึกถึงความมันอยู่ที่ผิว ทั้ง ๆ ที่ท่านถูหลายครั้งแล้ว ท่านคิดว่าเครื่องสำอางนั้นหลงเหลืออยู่บนผิวหนังของท่านหรือไม่
   - ก. หลงเหลือ ข. ไม่หลงเหลือ

5. ท่านรู้สึกอย่างไรกับยาเจลที่มีเนื้อนุ่ม ถูกเพียงไม่กี่ครั้งยาเจลก็จะถูกดูดซึมหมด ไม่มีความเหนอะหนะ และไม่มียาเจลหลงเหลืออยู่บนผิวหนัง
   - ก. ชอบ ข. ไม่ชอบ

รวมคะแนน...

☐ ผ่าน ☐ ไม่ผ่าน

แบบทดสอบความสามารถในการแยกความแตกต่าง

หมายเลขประจำชุดทดสอบ หมายเลข.......................

<u>คำสั่ง</u> ให้ท่านระบุ**หมายเลขของผลิตภัณฑ์**ที่ให้ความรู้สึกสัมผัสต่างไปจากผลิตภัณฑ์อื่น ๆ (หมายเลข 1 หรือ 2 หรือ 3) เพียง 1 ผลิตภัณฑ์เท่านั้น

การทดสอบครั้งที่ 1

ผลิตภัณฑ์ที่ให้ความรู้สึกสัมผัสต่างไปจากผลิตภัณฑ์อื่น ๆ คือ **ผลิตภัณฑ์หมายเลข**......................

☐ ผ่าน ☐ ไม่ผ่าน

หมายเหตุ ☐ ผ่าน ☐ ไม่ผ่าน เกณฑ์การคัดเลือกเพื่อเป็นอาสาสมัคร

....

การทดสอบครั้งที่ 2

ผลิตภัณฑ์ที่ให้ความรู้สึกสัมผัสต่างไปจากผลิตภัณฑ์อื่น ๆ คือ **ผลิตภัณฑ์หมายเลข**......................

☐ ผ่าน ☐ ไม่ผ่าน

การทดสอบครั้งที่ 3

ผลิตภัณฑ์ที่ให้ความรู้สึกสัมผัสต่างไปจากผลิตภัณฑ์อื่น ๆ คือ **ผลิตภัณฑ์หมายเลข**......................

☐ ผ่าน ☐ ไม่ผ่าน

หมายเหตุ ☐ ผ่าน ☐ ไม่ผ่าน เกณฑ์การคัดเลือกเพื่อเป็นอาสาสมัคร

....

คุณสมบัติของผลิตภัณฑ์ที่อาสาสมัครจะต้องประเมิน

กลุ่มของคุณสมบัติ	คุณสมบัติเฉพาะ	คำจำกัดความ
- ลักษณะของเนื้อเจล	- ความแน่นของเนื้อเจล	แรงที่ใช้ในการบีบเจลด้วยนิ้วหัวแม่มือกับนิ้วชี้
	- ความเหนียวของเนื้อเจล	แรงที่ใช้ในการดึงนิ้วหัวแม่มือออกจากนิ้วชี้
	- ความสูงของเนื้อเจล	เป็นความสูงของเนื้อเจลเมื่อดึงนิ้วออกมา
- ขณะที่ทำการถู	- ความเปียก	ปริมาณของน้ำที่สัมผัสได้ขณะถู
	- การกระจายตัว	ความง่ายในการทำให้เจลกระจายบนผิวหนัง
	- การดูดซึม	จำนวนครั้งของการถูจนกว่าจะไม่รู้สึกถึงความเปียกหรือความชื้น
- ความรู้สึกหลังการใช้	- ความเหนียวเหนอะหนะ	แรงที่ใช้ในการแยกนิ้วออกจากผิวหนัง ในขณะที่พยายามยกนิ้วจากผิวหนัง
	- ความมันวาว	ระดับความรู้สึกเป็นมันวาว
	- ปริมาณของเจลที่เหลือบนผิว	ปริมาณของเจลที่รู้สึกว่ามีเหลืออยู่หลังจากเจลถูกดูดซึมไปแล้ว
	- ความพึงพอใจ	ระดับความรู้สึกต่อคุณสมบัติต่างๆ ทางกายภาพของเจลโดยรวม

ตารางแสดงค่าความรู้สึกสัมผัสของผลิตภัณฑ์อ้างอิง (ช่วงคะแนน 0-15)

คุณสมบัติ	คะแนน	ผลิตภัณฑ์	บริษัทผู้ผลิต
ความแน่นของเนื้อเจล	0	Baby Oil	Johnson and Johnson
	8.4	Petrolatum	ชื่อสามัญ
ความเหนียวของเนื้อเจล	0.1	Baby Oil	Johnson and Johnson
	8.4	Petrolatum	ชื่อสามัญ
ความสูงของเนื้อเจล	0	Baby Oil	Johnson and Johnson
	9.6	Petrolatum	ชื่อสามัญ
ความเปียก	2.2	Petrolatum	ชื่อสามัญ
	9.9	น้ำ	ชื่อสามัญ
การกระจายตัว	2.9	Petrolatum	ชื่อสามัญ
	9.7	Baby Oil	Johnson and Johnson
ปริมาณของเจลที่เหลือบนผิว	0	ผิวหนังปกติ	-
	8.5	Petrolatum	ชื่อสามัญ

<u>แบบประเมินผลิตภัณฑ์</u> วันที่......................................

ชื่อ – นามสกุล..

หมายเลขประจำชุดทดสอบ หมายเลข................................

<u>คำสั่ง</u>
1. ให้ท่านประเมินผลิตภัณฑ์ตามหัวข้อที่กำหนดให้ตามความรู้สึกของท่าน โดยให้คะแนนเป็นตัวเลข ซึ่งอาจจะเป็นเลขจำนวนเต็ม หรือเศษส่วน หรือ ทศนิยมกี่ตำแหน่งก็ได้ในช่วงคะแนน 0-15 โดยที่ 0 หมายถึง น้อยที่สุด, 15 หมายถึง มากที่สุด
2. การประเมิน ท่านต้องประเมินผลิตภัณฑ์ตามลำดับหมายเลข 1-6 ห้ามประเมินกลับไป-มา โดยท่านจะต้องประเมินผลิตภัณฑ์ทั้งหมด 3 ครั้ง แต่ละครั้งท่านจะต้องประเมินให้ครบทุกหัวข้อก่อน แล้วจึงจะประเมินครั้งต่อไปได้
3. เมื่อท่านประเมินครั้งต่อไปแล้ว <u>ห้ามแก้ไขผลการประเมินในครั้งก่อน</u>

<u>การประเมินครั้งที่ 1</u>

หมายเลขประจำชุดทดสอบ **หมายเลข**......................................

กลุ่มของคุณสมบัติ	**คุณสมบัติเฉพาะ**	**คะแนนที่ให้ (ในช่วง 0-15) ผลิตภัณฑ์ต่างๆ**					
		1	**2**	**3**	**4**	**5**	**6**
1. ลักษณะของเนื้อเจล	1.1 ความแน่นของเนื้อเจล						
	1.2 ความเหนียวของเนื้อเจล						
	1.3 ความสูงของเนื้อเจล						
2. ขณะที่ถู	2.1 ความเปียก						
	2.2 การกระจายตัว						
	2.3 การดูดซึม						
3. ความรู้สึกหลังการใช้	3.1 ความเหนียวเหนอะหนะ						
	3.2 ความมันวาว						
	3.3 ปริมาณของเจลที่เหลือบนผิว						
	3.4 ความพึงพอใจ						

การประเมินครั้งที่ 2

หมายเลขประจำชุดทดสอบ **หมายเลข**.......................................

กลุ่มของคุณสมบัติ	คุณสมบัติเฉพาะ	คะแนนที่ให้ (ในช่วง 0-15) ผลิตภัณฑ์ต่าง ๆ					
		1	2	3	4	5	6
1. ลักษณะของเนื้อเจล	1.1 ความแน่นของเนื้อเจล						
	1.2 ความเหนียวของเนื้อเจล						
	1.3 ความสูงของเนื้อเจล						
2. ขณะที่ถู	2.1 ความเปียก						
	2.2 การกระจายตัว						
	2.3 การดูดซึม						
3. ความรู้สึกหลังการใช้	3.1 ความเหนียวเหนอะหนะ						
	3.2 ความมันวาว						
	3.3 ปริมาณของเจลที่เหลือบนผิว						
	3.4 ความพึงพอใจ						

การประเมินครั้งที่ 3

หมายเลขประจำชุดทดสอบ **หมายเลข**......................................

กลุ่มของคุณสมบัติ	**คุณสมบัติเฉพาะ**	**คะแนนที่ให้ (ในช่วง 0-15) ผลิตภัณฑ์ต่าง ๆ**					
		1	**2**	**3**	**4**	**5**	**6**
1. ลักษณะของเนื้อเจล	1.1 ความแน่นของเนื้อเจล						
	1.2 ความเหนียวของเนื้อเจล						
	1.3 ความสูงของเนื้อเจล						
2. ขณะที่ถู	2.1 ความเปียก						
	2.2 การกระจายตัว						
	2.3 การดูดซึม						
3. ความรู้สึกหลังการใช้	3.1 ความเหนียวเหนอะหนะ						
	3.2 ความมัน						
	3.3 ปริมาณของเจลที่เหลือบนผิว						
	3.4 ความพึงพอใจ						

APPENDIX VIII

Latin Square ANOVA Table for Differentiating Perceptual Attributes between Gel Bases.

1. Firmness

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	1250.6580		
Row (subject)	29	98.4316		
Column (time)	5	12.4189		
TMT	5	1060.1220	212.0244	372.5076
error	140	79.6854	0.5692	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) $\therefore$ Ho was rejected.

Tukey test :

MSE = 0.5692

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_α = 4.03 , HSD = 0.5550

2. Stickiness

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	1253.7680		
Row (subject)	29	53.0530		
Column (time)	5	7.5615		
TMT	5	936.0784	187.2157	101.9555
error	140	257.0749	1.8362	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) $\therefore$ Ho was rejected.

Tukey test :

MSE = 1.8362

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_α = 4.03, HSD = 0.9970

3. Peaking

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	1244.4300		
Row (subject)	29	298.2245		
Column (time)	5	16.5003		
TMT	5	868.2507	173.6501	395.5904
error	140	61.4550	0.4390	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) $\therefore$ Ho was rejected.

Tukey test :

MSE = 0.4390

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_α = 4.03, HSD = 0.5849

4. Wetness

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	542.9135		
Row (subject)	29	63.3507		
Column (time)	5	2.5735		
TMT	5	430.5954	86.1191	259.8761
error	140	46.3939	0.3314	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) $\therefore$ Ho was rejected.

Tukey test :

MSE = 0.3314

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_α = 4.03, HSD = 0.4236

5. Spreadability

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	643.5121		
Row (subject)	29	95.1782		
Column (time)	5	2.6849		
TMT	5	468.7382	93.7476	170.6480
error	140	76.9108	0.5494	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) ∴ Ho was rejected.

Tukey test :

MSE = 0.5494

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_α = 4.03, HSD = 0.5453

6. Absorbency

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	1055.2900		
Row (subject)	29	100.1829		
Column (time)	5	97.6301		
TMT	5	460.5943	92.1189	32.4649
error	140	396.8825	2.8349	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) ∴ Ho was rejected.

Tukey test :

MSE = 2.8349

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_α = 4.03, HSD = 1.2388

7. Tackiness

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	983.8272		
Row (subject)	29	199.0914		
Column (time)	5	3.9992		
TMT	5	644.8764	128.9753	132.9053
error	140	135.8602	0.9704	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) $\therefore$ Ho was rejected.

Tukey test :

MSE = 0.9704

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_{α} = 4.03, HSD = 0.7248

8. Gloss

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	1487.5490		
Row (subject)	29	791.5128		
Column (time)	5	3.4885		
TMT	5	333.4423	66.6885	25.9990
error	140	359.1056	2.5650	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) $\therefore$ Ho was rejected.

Tukey test :

MSE = 2.5650

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_{α} = 4.03, HSD = 1.1784

9. Amount of residue

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	797.7574		
Row (subject)	29	208.6550		
Column (time)	5	2.9732		
TMT	5	439.8800	87.9760	84.2168
error	140	146.2492	1.0446	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) ∴ Ho was rejected.

Tukey test :

MSE = 1.0446

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_α = 4.03, HSD = 0.7520

10. Liking

Source of variations	df	SSQ	MS	Ratio (F_{calc})
Total	179	1990.2630		
Row (subject)	29	699.5359		
Column (time)	5	48.0890		
TMT	5	836.1315	167.2263	57.5924
error	140	406.5068	2.9036	

F_{table} = 2.278 ($p < 0.05$, df = 5, 140) ∴ Ho was rejected.

Tukey test :

MSE = 2.9036

df = 140 (infinite), n = 30, $p < 0.05$, TMT = 6

Q_α = 4.03, HSD = 1.2538

APPENDIX IX

Analysis of Correlation Coefficient (r) by Pearson's Test at $p < 0.05$.

Pearson' s test

Null hypothesis Ho: $\rho = 0$

Alternate hypothesis Ha: $\rho \neq 0$

Where ρ is popular correlation coefficient.

$t_{calc} = \left[r\,(n-2)^{1/2} / (1-r^2)^{1/2} \right]$

t_{table} = t - test at df = n-2, $p < 0.05$

Where r^2 is determination coefficient and n is number of samples.

Reject Ho: $\left| t_{calc} \right| > t_{table}$

I. Relationship between diffusion coefficient (D) and rheological parameters

at df = 6, $p < 0.05$, n = 8 thus, t_{table} = 2.447

Linear regression equations	r^2	r	t_{calc}
$D = 0.0181/G' + 8 \times 10^{-5}$	0.7722	0.8787	4.5099
$D = 0.002/G'' + 8 \times 10^{-5}$	0.7606	0.8721	4.3661
$D = 0.0182/G^* + 8 \times 10^{-5}$	0.7721	0.8787	4.5086
$D = 0.0015(\tan \delta) - 3 \times 10^{-5}$	0.7267	0.8525	3.9942
$D = 0.0659/\eta + 9 \times 10^{-5}$	0.7806	0.8835	4.6203

II. Relationship between perceptual attributes and rheological parameters

at df = 4, $p < 0.05$, n = 6 thus, $t_{table} = 2.776$

1. Firmness (represented by y).

Linear regression equations	r^2	r	t_{calc}
$\log(y) = 0.5506 \log G' - 1.855$	0.9343	0.9666	7.5421
$\log(y) = 0.5566 \log G'' - 0.5775$	0.9366	0.9678	7.6871
$\log(y) = 0.5506 \log G^* - 1.1863$	0.9342	0.9665	7.5359
$\log(y) = -3.5877 \log(\tan \delta) - 3.3667$	0.0443	-0.2105	-0.4306
$\log(y) = 0.5442 \log \eta - 1.4433$	0.9903	0.9951	20.2082

2. Stickiness (represented by y).

Linear regression equations	r^2	r	t_{calc}
$\log(y) = 0.4409 \log G' - 0.803$	0.8402	0.9166	4.5860
$\log(y) = 0.4466 \log G'' - 0.3181$	0.8457	0.9196	4.6823
$\log(y) = 0.4409 \log G^* - 0.8036$	0.8403	0.9167	4.5877
$\log(y) = -2.1138 \log(\tan \delta) - 1.6923$	0.0216	-0.1470	-0.2972
$\log(y) = 0.4598 \log \eta - 1.1033$	0.9915	0.9957	21.6007

3. Peaking (represented by y).

Linear regression equations	r^2	r	t_{calc}
$\log(y) = 0.4602 \log G' - 0.857$	0.9451	0.9722	8.2982
$\log(y) = 0.4657 \log G'' - 0.3499$	0.9494	0.9744	8.6632
$\log(y) = 0.4602 \log G^* - 0.8577$	0.9454	0.9723	8.3223
$\log(y) = -2.591 \log(\tan \delta) - 2.2197$	0.0335	-0.1830	-0.3724
$\log(y) = 0.4511 \log \eta - 1.058$	0.9855	0.9927	16.4882

4. Wetness (represented by y).

Linear regression equations	r^2	r	t_{calc}
$y = -0.0007\ G' + 9.1396$	0.7285	-0.8535	-3.2761
$y = -0.0061G'' + 9.392$	0.8082	-0.8990	-4.1055
$y = -0.0007\ G^* + 9.1457$	0.7300	-0.8544	-3.2886
$y = 23.57\ (\tan \delta) + 9.1457$	0.3895	0.6241	1.5975
$y = -0.3891\eta + 8.9863$	0.9285	-0.9636	-7.2072

5. Spreadability (represented by y).

Linear regression equations	r^2	r	t_{calc}
$y = -0.0009\ G' + 10.255$	0.7574	-0.8703	-3.5338
$y = -0.0139\ G'' + 10.211$	0.7581	-0.8707	-3.5406
$y = -0.0009\ G^* + 10.256$	0.7574	-0.8703	-3.5338
$y = -193.86\ (\tan \delta) + 18.862$	0.4388	-0.6624	-1.7685
$y = -0.0081\eta + 10.098$	0.9624	-0.9810	-10.1184
$y = -0.0026\ \sigma_y + 10.13$	0.9517	-0.9756	-8.8778

6. Absorbency (represented by y).

Linear regression equations	r^2	r	t_{calc}
$y = 0.0002\,G' + 6.2382$	0.0564	0.2375	0.4890
$y = 0.0025\,G'' + 5.7813$	0.1240	0.3521	0.7525
$y = 0.0002\,G^* + 6.2308$	0.0572	0.2392	0.4926
$y = 3.7512\,(\tan\delta) + 6.5889$	0.0092	0.0959	0.1927
$y = 0.2225\,\eta + 5.4684$	0.2838	0.5327	1.2590
$\log(y) = 0.0077\log G' + 0.8142$	0.0016	0.0400	0.0801
$\log(y) = 0.024\log G'' + 0.7782$	0.0097	0.0985	0.1979
$\log(y) = 0.008\log G^* + 0.8134$	0.0017	0.0412	0.0825
$\log(y) = 0.1461\log(\tan\delta) + 0.9693$	0.0284	0.1685	0.3419
$\log(y) = 0.0301\log\eta + 0.8201$	0.0027	0.0517	0.1035

7. Tackiness (represented by y).

Linear regression equations	r^2	r	t_{calc}
$y = 0.0008\,G' + 2.058$	0.6986	0.8358	3.0449
$y = 0.0074\,G'' + 1.7045$	0.7953	0.8918	3.9422
$y = 0.0008\,G^* + 2.05$	0.7003	0.8368	3.0572
$y = -27.481\,(\tan\delta) + 9.4631$	0.3535	0.5946	1.4789
$y = 0.4726\,\eta + 2.1952$	0.9147	0.9564	6.5493

8. Gloss (represented by y).

Linear regression equations	r^2	r	t_{calc}
$y = 0.0005\,G' + 1.6026$	0.4756	0.6896	1.9047
$y = 0.0047\,G'' + 1.244$	0.6121	0.7824	2.5124
$y = 0.0005\,G^* + 1.5957$	0.4778	0.6912	1.9131
$y = -13.474\,(\tan\delta) + 5.6058$	0.1644	-0.4055	-0.8871
$y = 0.306\,\eta + 1.495$	0.7421	0.8615	3.3926
$\log(y) = 0.2106\,\log G' + 0.1904$	0.4650	0.6819	1.8646
$\log(y) = 0.2837\,\log G'' + 0.1979$	0.5254	0.7248	2.1043
$\log(y) = 0.2121\,\log G^* + 0.1965$	0.4660	0.6826	1.8683
$\log(y) = -0.6946\,\log(\tan\delta) + 0.061$	0.2484	-0.4984	-1.1498
$\log(y) = 0.227\,\log\eta + 0.3873$	0.5876	0.7666	2.3873

9. Amount of residue (represented by y).

Linear regression equations	r^2	r	t_{calc}
$y = 0.0006\,G' + 1.0224$	0.5208	0.7217	2.0850
$y = 0.0055\,G'' + 0.6472$	0.6457	0.8036	2.7000
$y = 0.0006\,G^* + 1.0149$	0.5229	0.7231	2.0938
$y = -16.91\,(\tan\delta) + 5.9329$	0.1962	-0.4429	-0.9881
$y = 0.3644\,\eta + 0.9188$	0.7973	0.8929	3.9666
$\log(y) = 0.2852\,\log G' + 0.4824$	0.5453	0.7384	2.1902
$\log(y) = 0.3798\,\log G'' + 0.4812$	0.6022	0.7760	2.4608
$\log(y) = 0.2872\,\log G^* + 0.4906$	0.5463	0.7391	2.1946
$\log(y) = -0.9959\,\log(\tan\delta) + 0.3558$	0.3266	-0.5715	-1.3928
$\log(y) = 0.3031\,\log\eta + 0.3027$	0.6703	0.8187	2.8517

10. Liking (represented by y).

Linear regression equations	r^2	r	t_{calc}
$y = 0.0002\ G' + 8.154$	0.0342	0.1849	0.3764
$y = 0.0004\ G'' + 8.8394$	0.0020	0.0447	0.0895
$y = 0.0002\ G^* + 8.1633$	0.0334	0.1828	0.3718
$y = -26.016\ (\tan \delta) + 12.652$	0.2444	-0.4944	-1.1375
$y = -0.0651\ \eta + 9.5441$	0.0134	0.1158	0.2331
$\log(y) = 0.0628 \log G' + 0.7235$	0.0712	0.2668	0.5537
$\log(y) = 0.0596 \log G'' + 0.7869$	0.0399	0.1997	0.4077
$\log(y) = 0.0629 \log G^* + 0.7227$	0.0707	0.2659	0.5516
$\log(y) = -0.5231 \log(\tan \delta) + 0.4853$	0.2428	-0.4927	-1.1325
$\log(y) = 0.0366 \log \eta + 0.9176$	0.0264	0.1625	0.3293

VITA

Mr. Rathapon A-sasutjarit was born on 10th December 1973, in Saraburi, Thailand. He got Bachelor of Science in Pharmacy (1st Class Honours) in 1998 from Faculty of Pharmaceutical Science, Chulalongkorn University, Bangkok, Thailand. He has been working as a pharmacist in the production unit of Department of Pharmacy, Thammasart Chalermprakiat Hospital since 1999.