

## Rheological Study of Diclofenac Gel Containing Different Concentration of Carbapol 940

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### ABSTRACT

Topical gels of Diclofenac were prepared by using varying concentrations of Carbapol 940 as gelling agents. Diclofenac Sodium, a non steroidal anti-inflammatory agent is frequently prescribed for the long term treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis<sup>10</sup>. The drug undergoes substantial first pass effect and only 50% of drug is available systemically. Diclofenac sodium via skin offers the potential advantage of bypassing hepatogastrointestinal first pass metabolism associated with oral administration. Carbapol 940 is used in concentration of 0.5%, 1% and 1.5% w/v. Carbapol solution gelatinized upon addition of alkaline molecules like Triethanolamine (TEA) to nullify the acidic group, allowing the polymer chain to align closer together forming network. The viscosity of prepared gels was estimated using a Brookfield viscometer having T-bar spindles and a helipath attachment. A number of spindles of various geometry including T-bars and a cone-plate configuration are available to provide scientific rheological data for empirical measurement of viscosity on paste and other semi-solid material. The viscosity of the gels increased with increase in gelling agent concentrations. Rate of shearing is directly proportional to shearing stress, which shows that the formulation is non-newtonian in nature. When the rate of shear is increased viscosity decrease that proves that the formulation is shear thinning pseudo-plastic in nature. The Diclofenac gel formulation also exhibits thixotropic nature

**Keyword-** Diclofenac gel, Brookfield viscometer, Rheological study, Thixotropic nature, Carbapol 940

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## **INTRODUCTION**

Over recent years non-steroidal anti-inflammatory drugs (NSAIDs) have been increasingly preferred as topical preparations for Epicondylitis, Rheumatism and local treatment of musculoskeletal soft tissues. Topical NSAIDs have several advantages over their systemically administered counterparts, they are simple to apply and deliver high drug concentrations locally into affected tissues, while producing only limited side effects. Despite several disadvantages they are still preferred as analgesic agents. Topical applications of NSAIDs are preferred now a day's to overcome systemic side effects which are manifested on oral administration. Decreased dose, reduction in onset of action time, localized effects with minimum side effects are the advantages of topical applications<sup>1,2</sup>.

Examples of drug commonly prepared in topical gel form include gastrointestinal (GI)-irritating nonsteroidal antiinflammatory drugs (NSAID) and antibacterials, antifungal, local anaesthetic and antihistaminic agents. The formulation of an effective gel requires the use of an appropriate gelling agent, usually a polymer. The preferred characteristics of such polymer include the inertness, safety, and biocompatibility with other ingredients, good adhesion to mucous membrane, and permission of drug permeation while not being absorbed into the body, irritation-free and preferably biodegradable. When in the formulation, the polymer should exhibit good swelling, syneresis and rheological properties suitable for solidifying stiffening the system. A number of gelling agents have been commercially employed in the preparation of topical gels, including the synthetic carbomers and the semi-synthetic cellulose, cellulose derivatives. As the number of newly formulated topical gel products containing drugs and chemicals continue to increase in recent years and expand into products containing natural compounds or extracts, coupled with concerned over the safety of totally synthetic materials, the development of new gelling agents from natural source has regained the attention. E.g. Of biopolymer reported as gelling agent for topical preparation are carrageen, xanthan gum and chitosan. Different types of polymers may undergo gelation through different mechanisms. For e.g. CP solution gelatinized upon addition of alkaline molecules like Triethanolamine (TEA) to nullify the acidic group, allowing the polymer chain to align closer together forming network<sup>3,4,5</sup>.

Gels consist of liquids gelled by means of suitable gelling agents. Gels comprise of homogenous preparations intended to be applied to the skin or certain mucous membranes; Gels may contain auxiliary substances such as antimicrobial preservatives, antioxidant and stabilizers<sup>6</sup>. The active ingredients in gel based formulations are better precutaneously absorbed than cream or ointment bases. A gel based formulation can hold/contain more percentage of ethyl alcohol than ointment and creams<sup>7</sup>.

Polymers are used to provide the structural network for gel system. The polymers are used in the concentration range of 0.5 to 15% <sup>8,9</sup>

Diclofenac Sodium, a non steroidal anti-inflammatory agent is frequently prescribed for the long term treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis<sup>10</sup>. The drug undergoes substantial first pass effect and only 50% of drug is available systemically.

Further, the drug is known to induce ulceration and bleeding of the intestinal wall. To avoid the adverse effect, alternate routes of administration have been tried by investigators<sup>11</sup>. Delivery of Diclofenac sodium via skin offers the potential advantage of bypassing hepatogastrointestinal first pass metabolism associated with oral administration. The drug is prescribed in a dose of 75 to 150 mg daily in divided doses by oral route. The dosing frequency can be reduced if patients are instructed to use topical products along with the conventional tablets<sup>12,13</sup>

## **MATERIALS AND METHODS**

### **MATERIALS**

Diclofenac, Sodium, Carbapol-940, Triethnol Amine, Propylene Glycol, Ethanol, were obtained Form B.N. College of pharmacy, Udaipur. All other chemicals and reagents used were of analytical grade.

### **FORMULATION**

**Table no-1: Formulation of Diclofenac Gel**

<b>Name of Ingredient</b>	<b>Formulation no.1</b>	<b>Formulation no.2</b>	<b>Formulation no.3</b>
Diclofenac Sodium	1.0%	1.0%	1.0%
Carbapol-940	0.5%	1.0%	1.5%
Triethnol Amine	0.5%	0.5%	0.5%
Propylene Glycol	10.0%	10.0%	10.0%
Ethanol	2.5%	2.5%	2.5%
Water	100.0ml	100.0ml	100.0ml

### **PREPARATION<sup>14</sup>**

The polymer and purified water were taken in motar and allow soaking for 24 hrs. Solid dispersion containing required amount of the drug was dissolved in ethanol and other additives were added. The filtration was combined to get homogenous dispersion of drug in gel.

## **VISCOSITY STUDY**

### **BROOK-FIELD VISCOMETER**

The brook field viscometer is a rotation viscometer of seal-type that is popular in the quality control laboratory of pharmaceutical mfg. A number of spindles of various geometry including T-bars and a cone-plate configuration are available to provide scientific rheological data for empirical measurement of viscosity on paste and other semi-solid material

### **VISCOSITY ESTIMATION<sup>15</sup>**

The viscosity of gel has determined by using brook-field viscometer Dvil model with T-bar spindle with combination of helical path

The accessory prevents the wall slip of the sample at the spindle surface and vortexing in the gels

#### **(A) Selection of spindle**

The best method for selection of spindle has trial and error the goal is to obtain a viscometer dial or display (% Torque) reading between 10 to 100 the relative error of measurement of viscosity of all the gels

#### **(B) Sample container size**

The viscosity was measured using 500gm. of gels filled in 500ml. beaker

#### **(C) Spindle immersion-**

The T-bar spindle was lowered perpendicularly in the centre and spindle should not touch the bottom of the jar.

#### **(D) Measurement of viscosity**

The T-bar spindle was used for determining the viscosity of the gels. The factor like temperature, pressure and sample size etc. which can affect the viscosity where keep constant, during the process.

The helipath T-bar spindle was moved up and down giving viscosities at number of points along the path. The torque reading was always greater than 10%. The average of five reading taken in one minute was noted as a viscosity of gel.

## **RESULT AND DISCUSSION**

The rheological studies of the prepared diclofenac gel was carried out and as shown in graph the rate of shearing is directly proportional to shearing stress, which shows that the formulation is non-newtonian in nature.

Table no-2: Torque table for 0.5% w/v Carbapol 940 Diclofenac Gel

RPM	Torque	
	Up	Down
0.3	19.94	17.93
0.5	28.03	26.86
0.6	30.94	29.2
1	39.3	38.2
1.5	42.03	41.13
2	45.33	45.23

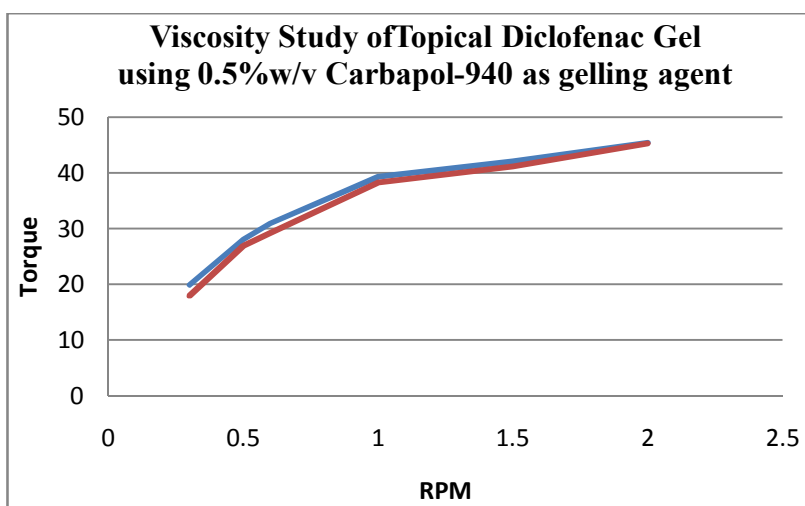


Figure 1: Graph b/w Torque Vs RPM of 0.5 % Carbapol 940

Table no-3: Torque table for 1% w/v Carbapol 940 Diclofenac Gel

RPM	Torque	
	Up	Down
0.3	31.5	26.5
0.5	41.5	35.4
0.6	46.7	41.56
1	57.8	54.1
1.5	70.1	69.2

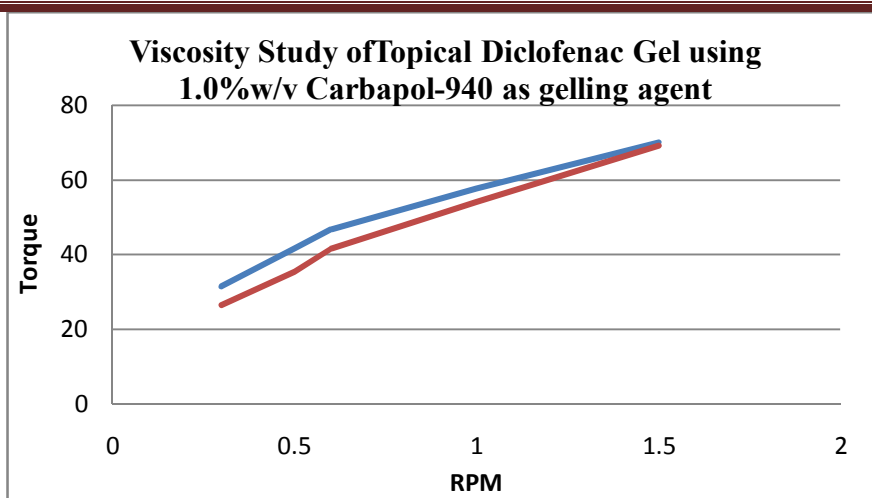


Figure 2: Graph b/w Torque Vs RPM of 1% Carbapol 940

Table no-4: Torque table for 1.5 % w/v Carbapol 940 Diclofenac Gel

RPM	Torque	
	Up	Down
0.3	43.8	41.5
0.5	56.7	54.9
0.6	61.3	60.1
1	75.7	74.7
1.5	90.1	89.7

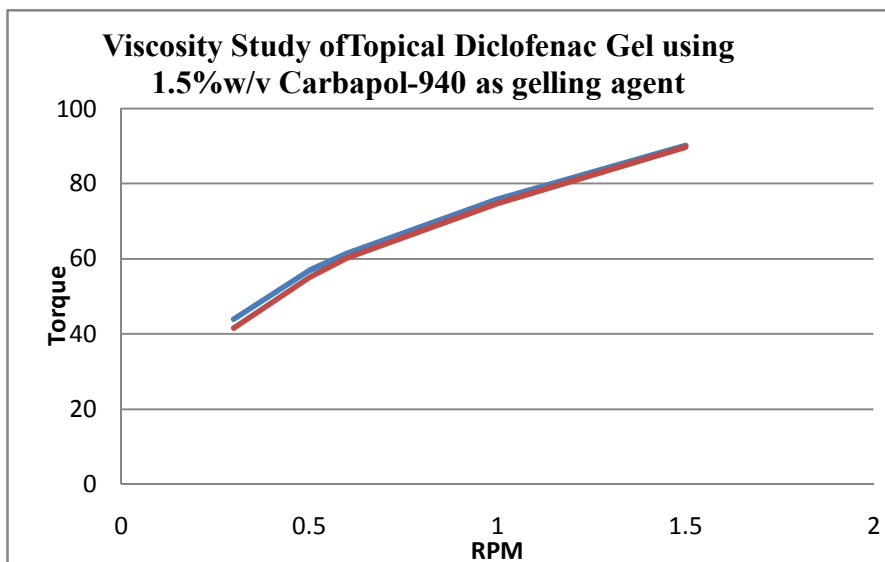


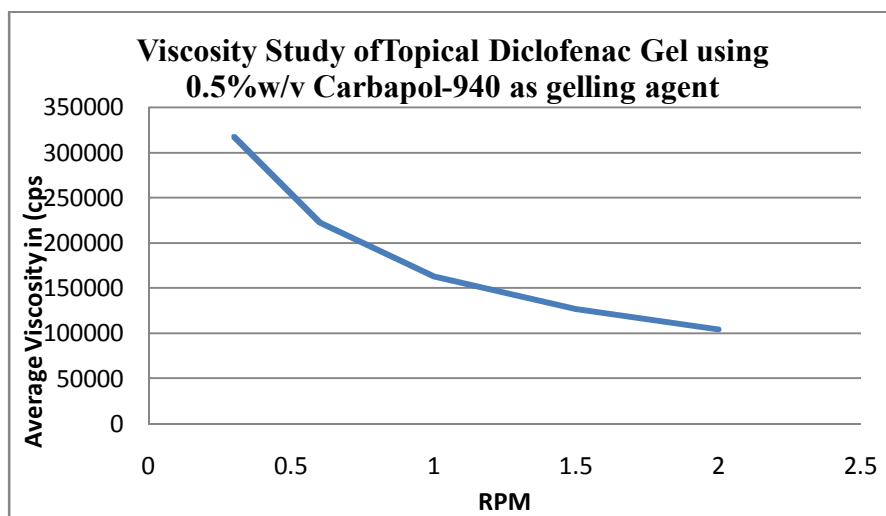
Figure 3: Graph b/w Torque Vs RPM of 1.5% Carbapol 940

As the result shows that the viscosity of the formulation changes with the time which prove that formulation are the time dependant system.

When the rate of shear is increased as shown in graph viscosity decrease that proves that the formulation is shear thinning pseudo-plastic in nature.

**Table no-5: Average Viscosity table for 0.5% w/v Carbapol 940 Diclofenac Gel**

RPM	Average Viscosity
3	317500
0.5	254733.4
0.6	222283.3
1	163166.7
1.5	127266.7
2	104316.7



**Figure 4: Graph b/w Average viscosity Vs RPM of 0.5 % Carbapol 940**

**Table no-6: Average Viscosity table for 1% w/v Carbapol 940 Diclofenac Gel**

RPM	Average viscosity
0.3	650500
0.5	511250
0.6	464200
1	349150
1.5	278450

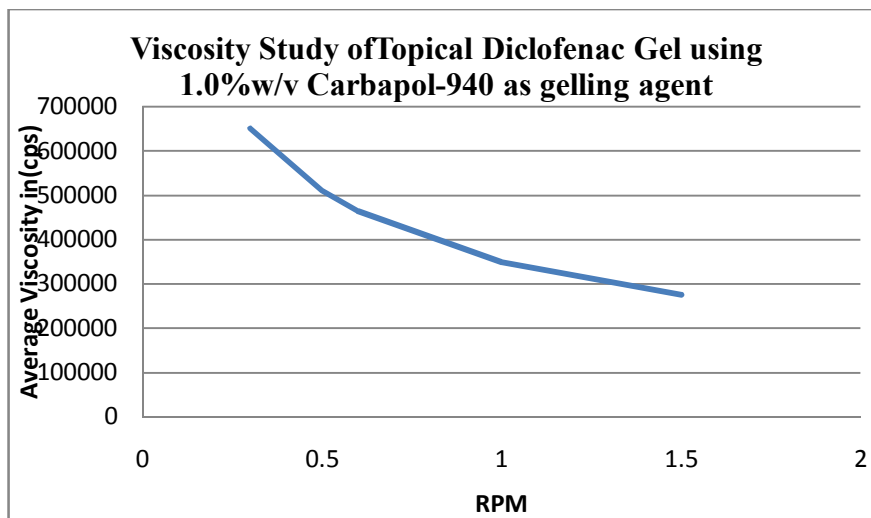


Figure 5: Graph b/w Average viscosity Vs RPM of 1% Carbapol 940

Table no-7: Average Viscosity table for 1.5% w/v Carbapol 940 Diclofenac Gel

RPM	Average Viscosity
0.3	665500
0.5	525350
0.6	474200
1	358200
1.5	280950

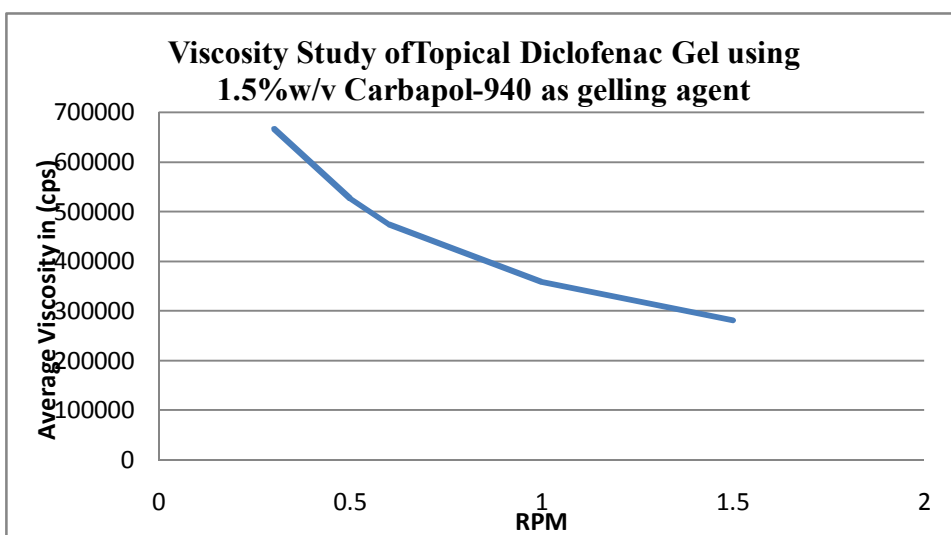


Figure 6: Graph b/w Average viscosity Vs RPM of 1.5% Carbapol 940



Table no-8: Viscosity table for 0.5% w/v Carbapol 940 Diclofenac Gel

RPM	VISCOSITY	
	UP	DOWN
0.3	321000	314000
0.5	258167	251300
0.6	224233	220333
1	165300	161033
1.5	129667	124867
2	104733	103900

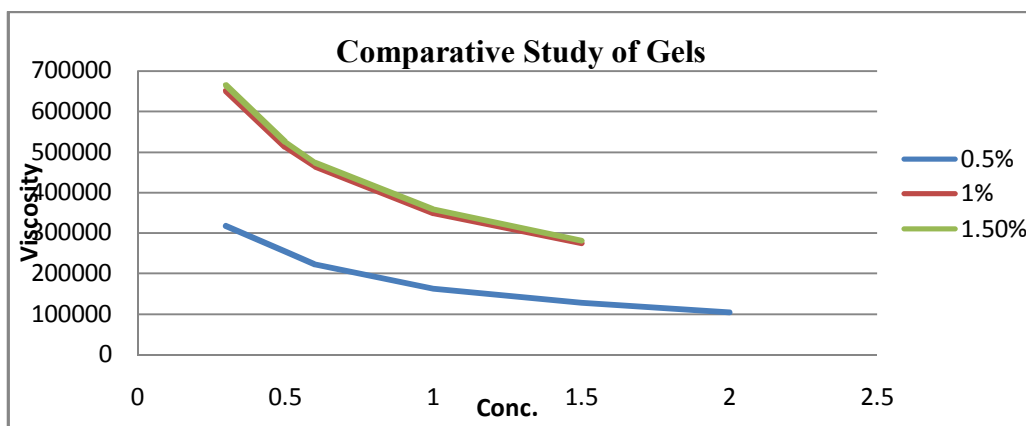


Figure 7: Graph of comparative viscosity of Diclofenac Gel Containing 0.5%, 1%, and 1.5% Carbapol 940 as gelling agent

As shown graphically when the up and down curve of viscosity (rate of shear) Vs shearing stress (RPM) were plotted down curve shift towards the left which proves that the formulation exhibits “thixotropic in nature”.

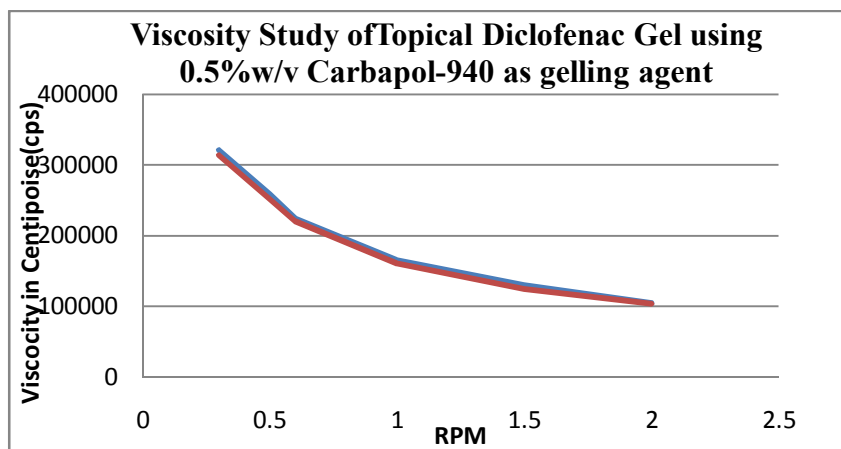


Figure 8: Graph b/w Viscosity Vs RPM of 0.5 % Carbapol 940

Table no-9: Viscosity table for 1% w/v Carbapol 940 Diclofenac Gel

RPM	VISCOSITY	
	UP	DOWN
0.3	684000	617000
0.5	536000	486500
0.6	478900	449500
1	35400	343500
1.5	282200	274700

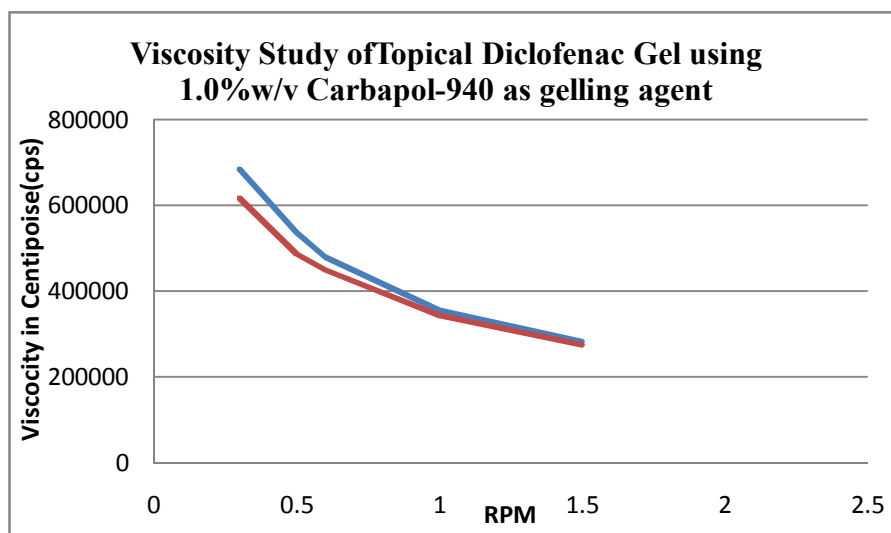


Figure 9: Graph b/w Viscosity Vs RPM of 1% Carbapol 940

Table no-10: Viscosity table for 1.5% w/v Carbapol 940 Diclofenac Gel

RPM	VISCOSITY	
	UP	DOWN
0.3	684000	647000
0.5	536000	514700
0.6	478900	469500
1	364800	351600
1.5	282200	279700

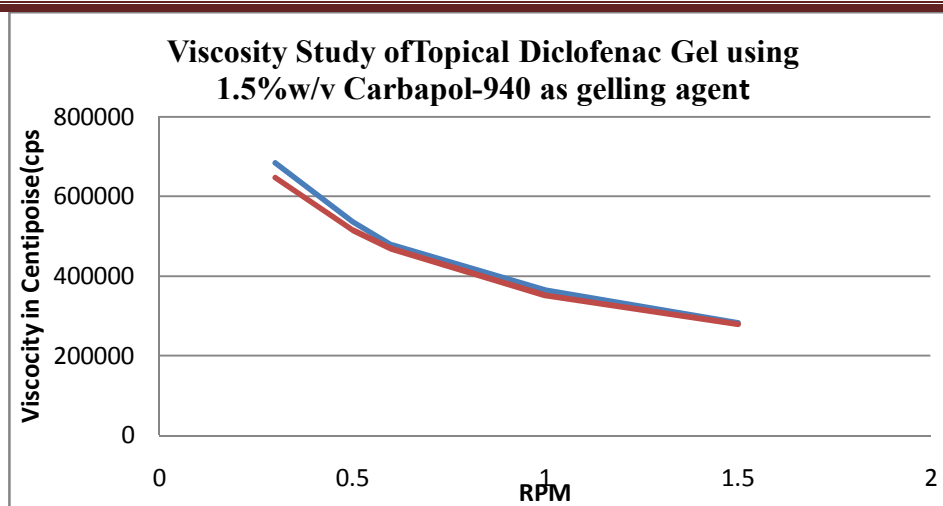


Figure 10: Graph b/w Viscosity Vs RPM of 1.5% Carbapol 940

## CONCLUSION

The present investigation suggests that the viscosity of the gels increases with the concentration of gelling agent. Viscosity plays a vital role in the dispensing and formulation of topical gels. Depending on the need gels with good rheological properties can be prepared using different gelling agent in variable concentrations

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