Int. J. Chem. Sci.: 6(2), 2008, 569-578

HYDROTROPICALLY PREPARED STARCH GELS AS TOPICAL DRUG DELIVERY-A RHEOLOGICAL STUDY

K. PURUSHOTHAM RAO*, Md. NAJMUDDIN[a] and B. SATYANATH

H.K.E.S College of Pharmacy, GULBARGA – 585105 (K. S.) INDIA
[a]Swamy Ramanand Teerth Marathwada University, NANDED (M. S.) INDIA

ABSTRACT

Rheologic behaviour of hydrotropically prepared potato starch gels using sodium salicylate in presence and absence of two added polyols ; (propylene glycol and polyethylene glycol) each at 3% concentration was studied with the help of Brookfield Synchroelectirc RVT model digital viscometer with spindle No. $SC_4$28/13R. The apparent viscosity (cp) values were found to be 116780 and 3130; 100780 and 3620; 159780 and 3955 respectively for blank gel, gel with polyethylene glycol 6000 and gel with propylene glycol at low shear rate 0.14 sec^{-1} and high shear rate 28 sec^{-1} at room temperature . The results conclusively proved that all the three types of gels exhibited shear thinning tendency. Stress-Shear rate rheograms indicated that the gel systems are pseudoplastic and exhibited thixotropy. The data further indicated when plotted as Casson and Fitch plots. Both the methods of plotting were found to generate unambiguous intercepts for calculating yield values and were found to be 18975, 20140 and 20638 dynes/cm^2 for blank gel, gel with polyethylne glycol 6000 and gel with propylene glycol, respectively form Casson plots. The added polyols were found to increase apparent viscosity of the prepared hydrotropically gelled potato starch and were found to be in order PG > PEG > Blank.

Key words: Hydrotropic, Rhealogy, Daug delivery, Starch gel

INTRODUCTION

Hydrotropic salts were reported as a class of compounds which are fairly in high concentrations, increases the solubility of variety of poorly soluble drugs in water[1-5]. Khordaqui[6] has reported that starch suspension can be gelled by using sodium salicylate as hydrotropic salt. In the present work, an attempt has been made to develop topical hydrotropic starch gels by using potato starch as vehicle with sodium salicylate[7,11] as hydrotropic salt for pharmaceutical application. The formulations were evaluated for

* Author for correspondence; Tel: +91 – 8472 – 226675, Cell: +91 – 98441 57453,
Fax: +91 – 8472 – 222039, E-mail: kprao369@rediffmail.com

rheologic behviour. A systematic study about the rheologic behaviour will be vitally important for the product development. The rheologic behaviour of hydrotropically gelled potato starch by using sodium salicylate in the presence and absence of polyoles was studied.

EXPERIMENTAL

Materials

Sodium salicylate, potato starch, propylene glycol and polyethylene glycol 6000 (S D Fine Chemicals-Mumbai).

Method

Preparation of potato starch gel

Sodium salicylate (11% w/w) was accurately weighed and dissolved in 20 mL of water. The potato starch (10% w/w) was mixed with another 20 mL of water to form a smooth suspension which was added to sodium salicylate salt solution. The mixture was stirred continuously till a translucent gel was obtained and kept under vaccum for a period of 48 hours to remove the entrapped air. The gel systems with added propylene glycol and polyethylene glycol 6000 were prepared similarly.

Determination of viscosity

The viscosity of prepared gels was determined by using Brookfield synchroelectric RVT model digital viscometer at room temperature with the following variables. Spindle No. $SC_4$28/13R was used with 12 mL volume adapter. Eight spindle speeds (rpm) 0.5, 1.0, 2.5, 5.0, 10.0, 20.0, 50.0 and 100 was used. The shear stress (dynes/cm^2) and shear rate (sec^{-1}) was calculated.

Rheogram

In the present work, the shear rate (sec^{-1}) was considered as independent variable and shear stress (dynes/cm^2) as dependent variable.

Stress-shear rate rheograms

The data was plotted for stress-shear rate in which shear stress (dynes/cm^2) was plotted against shear rate (sec^{-1}) to ascertain thixotropy. The data was further plotted as Casson plots [12] and Fitch plots [13]. In Casson plots, the square root of shear stress are plotted against the square root of shear rate. In Fitch plots, the shear stress (dynes/cm^2) was directly plotted against the square root of shear rate. The intercepts on the stress, axis in both the type can be defined more clearly as the yield value in the units of dynes/cm^2.

RESULTS AND DISCUSSION

The basic viscosity of hydrotropic starch gels systems with added propylene glycol and polyethylene glycol 6000 were determined at room temperature and it was found that the added propylene glycol and polyethylene glycol 6000 increase significantly the apparent viscosity of the blank gel at each shear rate (sec^{-1}). The apparent viscosity (cp) values were found to be 116780 and 3130; 100780 and 3620; 159780 and 3955 respectively for blank gel, gel with polyethylene glycol 6000 and gel with propylene glycol at low shear rate 0.14 (sec^{-1}) and high shear rate 28 (sec^{-1}) as shown in Tables 1, 2 and 3.

Table 1. Viscosity (cps) for hydrotropically gelled starch with out polyols

Speed (rpm)	Shear rate (sec^{-1})	Square root of shear rate	Apparent viscosity up curve (cps)	Shear stress up curve (dynes/cm^2)	Square root of shear stress up curve	Apparent viscosity down curve (cps)	Shear stress down curve (dynes/cm^2)
0.5	0.14	0.374	116780	16349	127	86780	12149
1.0	0.28	0.529	70280	19678	140	52280	14638
2.5	0.70	0.836	36580	25606	160	28380	19866
5.0	1.40	1.183	21380	29932	173	17980	25172
10.0	2.80	1.673	13180	36904	192	11530	32284
20.0	5.60	2.366	8180	45808	214	7580	42448
50.0	14.00	3.741	4640	64960	254	4510	63140
100.0	28.00	5.291	3130	87640	296	3130	87640

Stress-shear rate rheograms for all the gels with and without polyols showed that the ascending and descending rheograms are not superimposed on each other, so the gel systems are pseudoplastic and exhibited thixotropy with hysteresis loop as shown in Fig. 1, 4, and 7. It has also been observed that at low shear rate values the stress values were found to be excessively compacted and gave difficulties in deciding the existence of yield value for the systems.

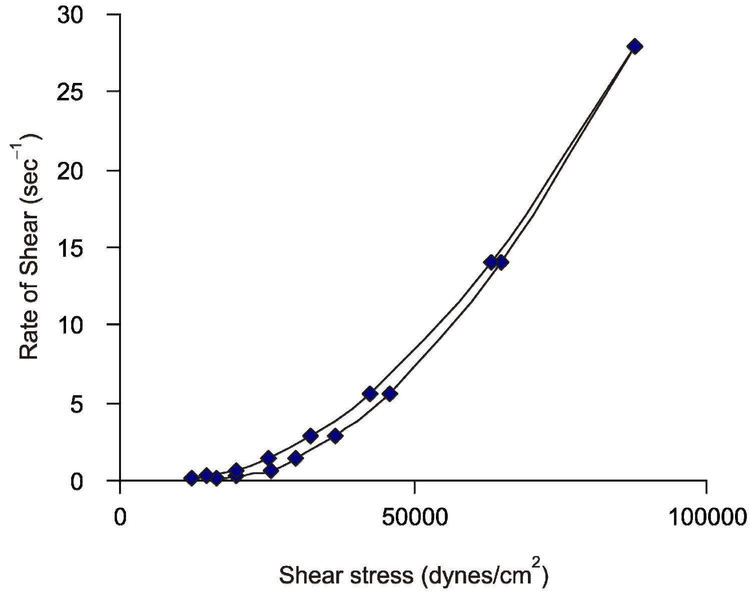

Fig. 1: Thixotropy curve for blank gel

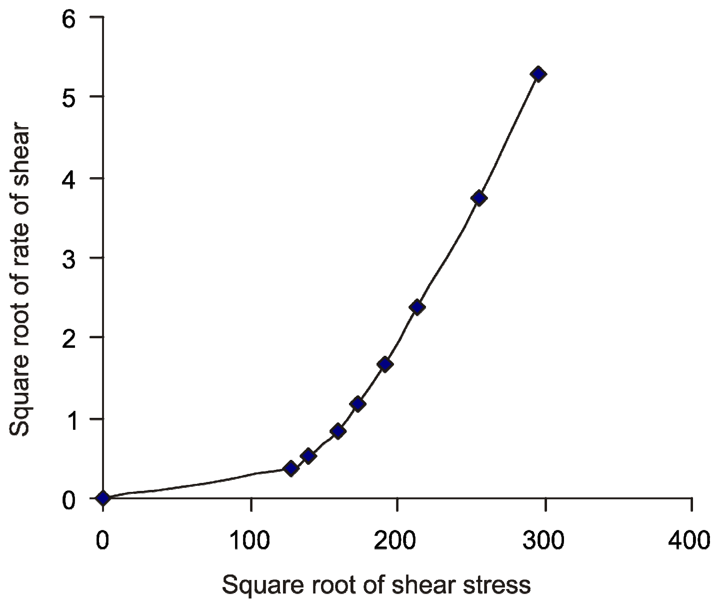

Fig. 2: Casson plots for blak gel

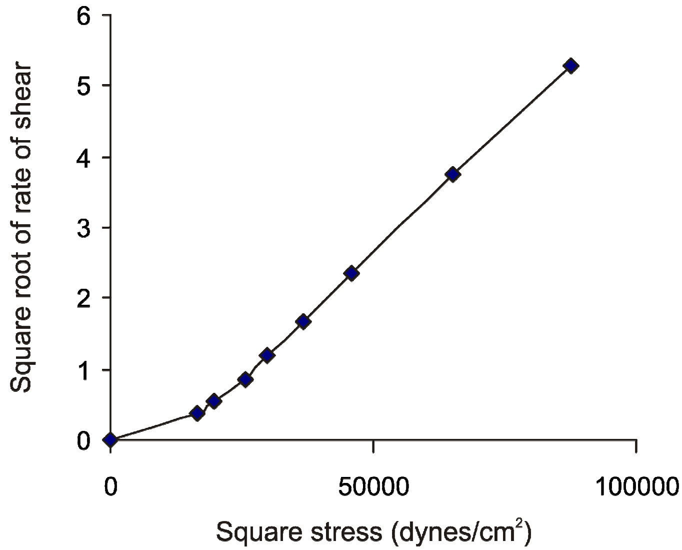

Fig. 3: Fitch plots for blank gel

Table 2. Viscosity (cps) for hydrotropically gelled starch with polyethylene glycol 6000

Speed (rpm)	Shear rate (sec^{-1})	Square root of shear rate	Apparent viscosity up curve (cps)	shear stress up curve (dynes/cm^2)	Square root of shear stress up curve	Apparent viscosity down curve (cps)	Shear stress down curve (dynes/cm^2)
0.5	0.14	0.374	100780	14109	118	82780	11589
1	0.28	0.529	63780	17858	133	53780	15058
2.5	0.7	0.836	34780	24346	156	30780	21546
5	1.4	1.183	22280	31192	176	19880	27832
10	2.8	1.673	13980	39144	197	13030	36484
20	5.6	2.366	9055	50708	225	8580	48048
50	14	3.741	5320	74480	272	5170	72380
100	28	5.291	3620	101360	318	3620	101360

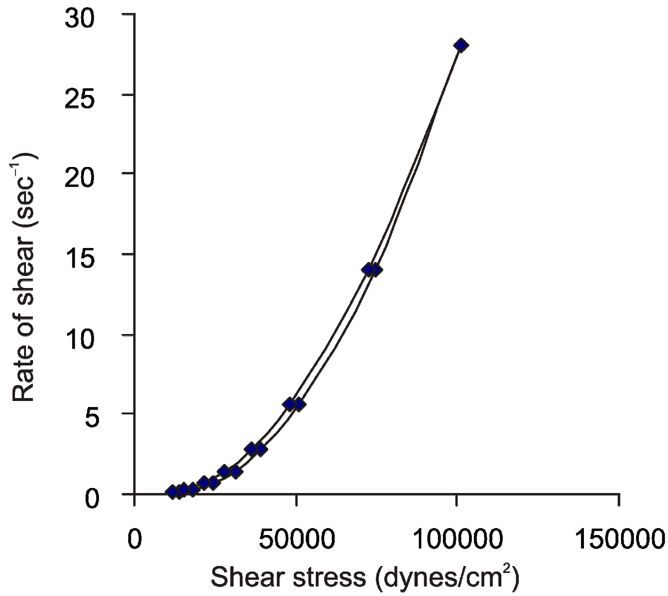

Fig. 4: Thixotropy cruve for polyethylene glycol 6000

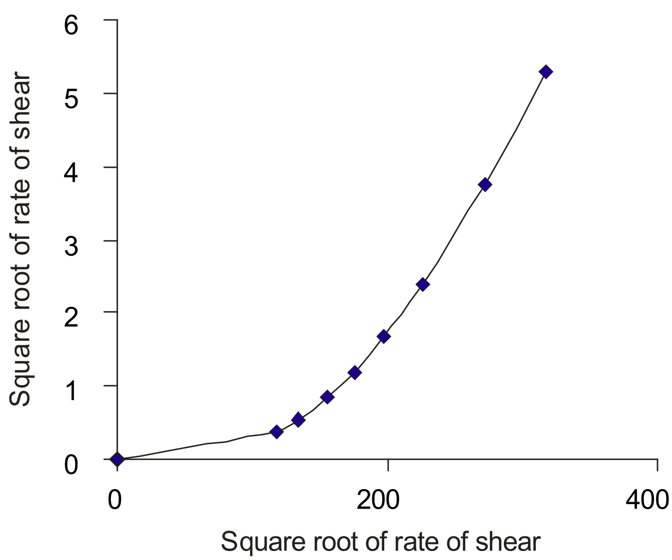

Fig. 5: Casson plots for gel with polyethylene glycol 6000

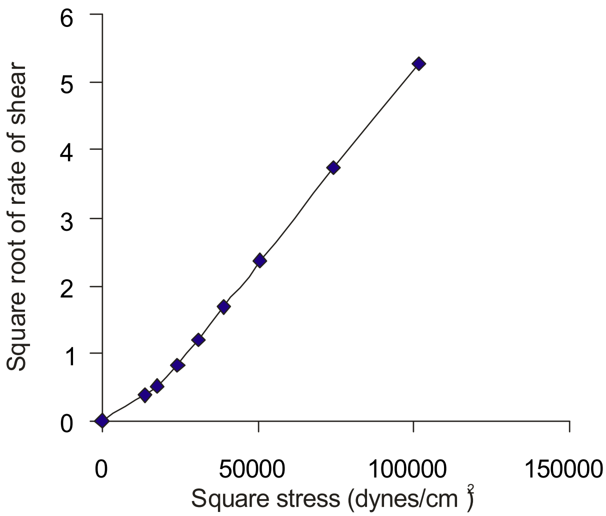

Fig. 6: Fitch plots for gel with polyethylene glycol 6000

Table 3. Viscosity (cps) for hydrotropically gelled starch with propylene glycol

Speed (rpm)	Shear rate (sec-1)	Square root of shear rate	Apparent viscosity up curve (cps)	Shear stress up curve (dynes/cm^2)	Square root of shear stress up curve	Apparent viscosity down curve (cps)	Shear stress down curve (dynes/cm^2)
0.5	0.14	0.374	159780	22369	149	128780	18029
1	0.28	0.529	90280	25278	158	76280	21358
2.5	0.7	0.836	45780	32046	179	39780	27846
5	1.4	1.183	27880	39032	197	24580	34412
10	2.8	1.673	17280	48384	219	15480	43344
20	5.6	2.366	10880	60928	246	9930	55608
50	14	3.741	6120	85680	292	5740	80360
100	28	5.291	3955	110740	332	3955	110740

For predicting clearly the existence of yield value, the data was further plotted as

Casson and Fitch plots. Both the methods of plotting were found to generate unambiguous intercepts for calculating yield values and was found to be 18975, 20140 and 20638 dynes/cm^2 respectively for blank gel, gel with polyethylene glycol 6000 and gel with propylene glycol respectively from Casson plots Fig. 2, 5 and 8.

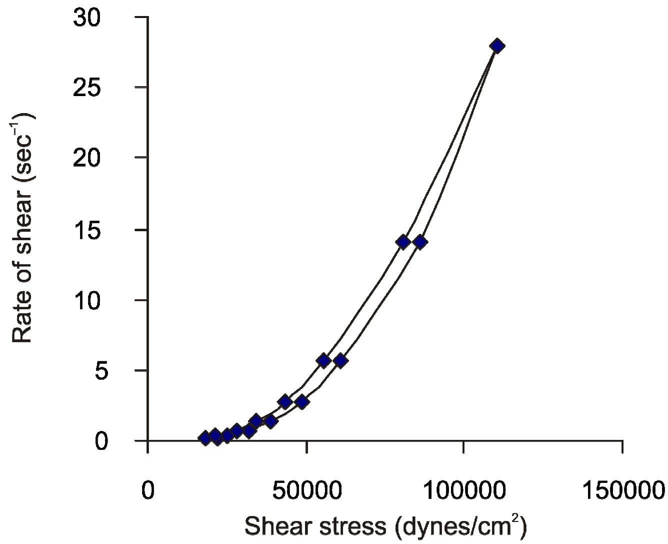

Fig. 7: Thixotropy curve for gel with propylene glycol

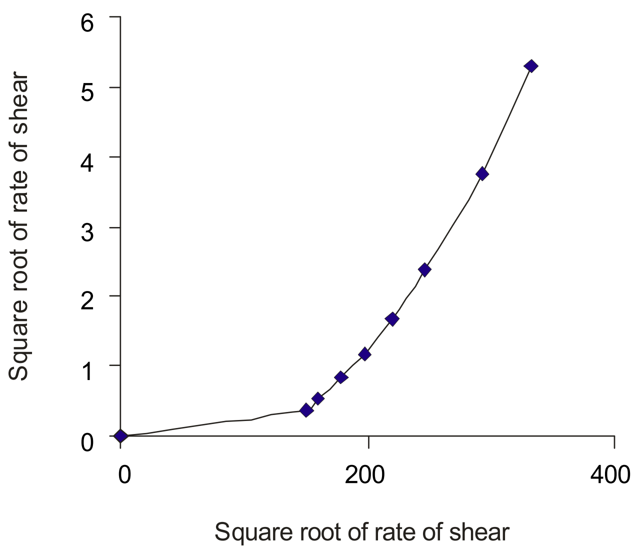

Fig. 8: Casson plots for gel with propylene glycol

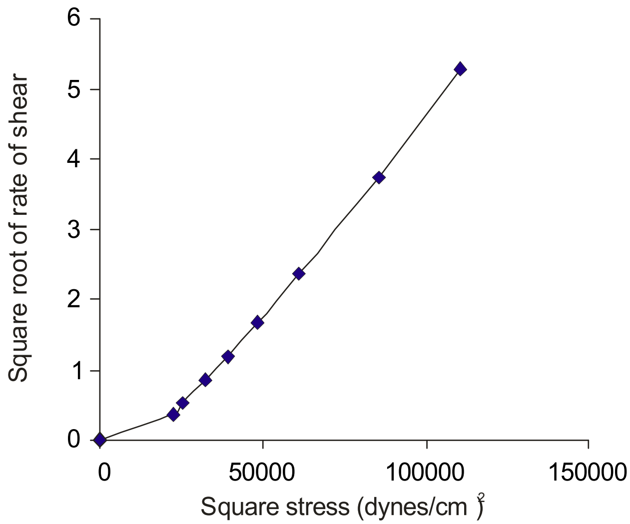

Fig. 9: Fitch plots for gel with propylene glycol

Fitch plots, however; gave lesser yield values from their intercepts and were found to be 14250, 10500 and 16500 dynes/cm^2, respectively for blank gel, gel with polyethylene glycol 6000 and gel with propylene glycol, respectively as shown in Fig 3, 6 and 9. Among these two methods of data graphing, Casson plots are most widely accepted. The hydrotropically gelled potato starch was found to be translucent in appearance with adhesive properties. Hydrotropic salts were also recognized for their ability to increase the solubility of variety of poorly soluble drugs in water. The experimental results obtained in the present studies on rheological behaviour of hydrotropically gelled starches have proved that these gel systems will be ideal carriers for topical applications of poorly soluble drugs due to their shear thinning properties and thixotropy.

ACKNOWLEDGEMENTS

The authors are thankful to Principal, Luqman College of Pharmacy, Gulbarga for providing the facilities for carrying out the work.

REFERENCES

1. A. Darwish, A. T. Florence and A. M. Saleh, Effects of Hydrotropic Agents on the Solubility, Precipitation, and Protein Binding of Etoposide, J. Pharm Sci., **78**, 577 (2006).

2. Shikha Agrawal, S. S. Pancholi, N. K. Jain and G. P. Agrawal, Hydrotropic Solubilization of Nimesulide for Parenteral Administration, International J. Pharmaceutics, **149**, (2004).

3. R. K. Maheshwari, V. Chavda, K. Sahoo and S. Varghese, Novel Application of Hydrotropic Solubilization in the Spectrophotetri Analysis of Diclofenac Sodium in Solid Dosage Form, Asian J. Pharmaceutics, **1**, 30 (2006).

4. R. K. Maheshwari and A. Ajmera, Novel Application of Hydrotropic Solubilization in the Spectrophotetri Analysis of Diclofenac Sodium in Solid Dosage Form, Asian J. Pharmaceutics, **1**, 60 (2006).

5. Etman, R. O. Salama, M. A. Shamsedeen and A. El-Kamel, Solubilization of Etodolac for Parenteral Administration, Indian J. Pharm. Sci., **63**, 459 (2001).

6. E. L. Khordaqui, Hydrotrope-Gelled Starch, Study of Some Physicochemical Properties, International J. Pharmaceutics, **74**, 25 (1991).

7. Cooper and Gunn's, Dispensing for Pharmaceutical Students, 12th Ed. CBS Publication and Distributors, (2000) p. 29, 92 and 207.

8. Indian Pharmacopoeia, Published by the Controller of Publications, Delhi, **Vol. II**, 701 (1996).

9. Harry G. Brittain, Analytical Profiles of Drug Substances and Excipients, Academic Press, An Imprint of Elsevier, **23**, 427 (2006).

10. British Pharmacopoeia, Compound Benzoic Acid Ointment, Volume II, 697 (1980).

11. B. A. Ali, M. B. Zughul and A. A. Badwan, Surface Activity and Energetics of Aggregate Formation in Aqueous Sodium Benzoate and Salicylate Solutions, J. Dispersion Sci. Technol., **16**, 451 (1995).

12. N. Casson, A Flow Equation for Pigment Oil Suspension of the Printing Ink Type-In Rheology of Dispersers Systems, by C. C. Mill (Ed.) Pergamon Press, London, (1959) p.84.

13. E. G. Fitch, Ind Eng. Chem., **51**, 889 (1959).

Accepted : 14.03.2008