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Research Article

SELECTION OF PECTIN AS PHARMACEUTICAL EXCEPIENT ON THE BASIS OF RHEOLOGICAL BEHAVIOR

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ABSTRACT

The aim of this study was to evaluate rheological properties of pectin solutions to determine the influence of polymer concentration, pH, preservatives and heating duration on viscosity, using Brookfield R/S Plus Rheometer. The results shows that dilute pectin solutions are showing Newtonian, but at a moderate concentration they exhibit the non-Newtonian behavior, and the psudoplastic nature was found to increase with concentration. As the pH of the polymer solution lowered there was increase in viscosity of the system observed, this may be due do the carboxyl acid groups on the pectin chains are neutralize i.e. reduction in ionization, and leads to reduction in hydration of the carboxylic acid groups. As a result of reduced ionisation, the polysaccharide molecules do not repel each other over their entire length. The result shows that pectin solutions are stable at broad range of pH. It was observed that as the temperature or pH of the system increases there was decrease in viscosity.

Keywords: Pectin, Rheological behavior, Viscosity, Gelation, Shear stress, Shear rate, Esterification

INTRODUCTION

Rheology is concerned with the description of flow behavior of all types of matter. It is the study of how a material deforms during and after a force is applied. Rheology directly affects product handling and flow characteristics [1]. Pectin is an important polysaccharide with applications in food industry, cosmetics and pharmacy. The present work concerns to the study of rheological behavior of pectin, anionic polysaccharide, which is having carboxylic groups and possible to interact with functional groups in mucus layer. Low methoxylated pectin is prepared by acid treatment in ethanol or isopropanol [2]. Pectin is degraded by colonic pectinolytic enzymes and is not digested by gastric or intestinal enzymes [3, 4]. Because of its water solubility, pectin solubilise in the aqueous fluids of the gastrointestinal tract. Solubility of pectin in aqueous medium can reduce through chemical modification by saponification catalysed by mineral acids, bases, salts of weak acids, enzymes, concentrated ammonium systems and primary aliphatic amines without affecting favourable biodegradability properties. Calcium salts of pectin have reduced solubility and matrix tablets prepared with calcium pectinate showed very good potential to be used in colon-targeted drug delivery systems [5, 6]. Pectin consists of galacturonic acid residues and their methyl esters. The polygalacturonic acid chain is partly esterified with methyl groups and the free acid groups may be partly or fully neutralized with sodium, potassium or ammonium ions [7]. Degree of Esterification values for commercial high methoxyl pectins typically range from 60 to 75% and those for low methoxyl pectins range from 20 to 40%. Pectin has been commercially used in many dairy products as gelling/thickening agent (acid and non acid milk desserts) and as a stabilizer ingredient (acid milk drinks milk/juice blends). Cross-linking of pectin with calcium ions inhibits the release of the incorporated drug by suppressing both the dissolution and swelling of these systems [8].

Pectins are soluble in pure water and form gel. The most important use of pectin is based on its ability to form gel. Low methoxyl pectin may form gels at concentrations higher than 1 % in the presence of divalent cations (calcium) over a wide range of pH. A number of physiological effects of pectin or pectin-containing diets have been described depending on the macromolecular state of pectin; these effects include decreasing serum cholesterol levels, increasing fecal excretion of steroids, interacting with metal ions or as dentistry adhesive [9, 10]. The gelation of low methoxyl pectin, over a wide range of pH, is mainly the result of strong interactions between calcium ions and blocks of galacturonic acid [11]. In a study pectin/poly (lactide-co-glycolide) composite matrices for the delivery of biologically active substances for tissue regeneration were developed. The pectin-containing matrices improved cell adhesion and proliferation when compared to plain p (LGA) matrices, as determined *in vitro* by osteoblast culture [12].

MATERIALS AND METHODS

Materials

Low methoxylated pectin (degree of esterification 28 - 45%) was purchased from Krishna Pectins Pvt. Ltd., Jalgaon, Maharastra, India.

Study of rheological behavior of pectin

The study of rheological behavior of the samples was done using Brookfield R/S Plus Rheometer (cone and plate model). The measuring system used was C-25 Din, which is generally used for heavy liquids like gum, mucilages and polymeric dispersions. Brookfield Rheo-2000 V2.8 software was used for the measurement of the rheological behavior and for calculations.

To record the up and down curve for rheological study of pectin, a block was written in Brookfield Rheo-2000 V2.8 software using the block editing menu. The shear rate [s^{-1}] was increased between 0 and 100 within a period of 120 sec for recording the 'up' curve and it was reduced from 100 to 0 within a period of 120 sec for recording the 'down' curve. The number of measuring points within 120 sec duration was 10. The shear stress [Tau], apparent viscosity [Eta] was recorded [13].

Effect of concentration on rheology

This study was done for the determination of Non-Newtonian behavior. Low methoxyl pectin was used at different concentrations levels namely, 7.5, 10.0 and 12.5%. The solutions were prepared and kept overnight for complete swelling. Their flow behavior was noted at different shear rates at 20°C. The psudoplastic viscosity was determined from the down curve. Apparent viscosity at different shear rates was recorded. The obtained data was plotted as viscosity against shear rate, shear rate against shear stress, log shear rate against log shear stress and log viscosity against concentration.

Effect of pH on the viscosity of pectin solution

The effect of pH on the viscosity of the 10 % pectin solution was studied at different pH values like 1, 2, 3, 4, 5, 6, 7and 8. The pH of the solution was adjusted using 1 N HCl or 1 N NaOH. The apparent viscosities were recorded at 25 rpm (shear rate of 60 s^{-1}). A plot of apparent viscosity verses pH was plotted.

Effect of preservatives on viscosity

The effect of preservative on viscosity of pectin 10 % solution was studied. Various preservatives like sodium benzoate, methyl paraben, ethyl paraben and phenyl mercuric acetate were added to the pectin solution at 0.1 % w/v concentration. The apparent viscosities were recorded at various time intervals at shear rate of 60 s^{-1}.

Effect of heating duration on viscosity

The effect of heating duration on viscosity was studied using 10 % w/v solution of pectin. Pectin solution was heated at 100°C for various time intervals like 1, 2 and 3 h. the apparent viscosity was recorded at shear rate 60 s^{-1}. The apparent viscosity values were noted again after a relaxation period of 7 days.

RESULTS AND DISCUSSION

It was observed that pectin exhibits a non- Newtonian psudoplastic behavior and the psudoplastic nature was found to increase with concentration in all the selected grades of pectin (Fig 1). It was noted that at higher shear stress the flow curve tends to linearity indicating that a minimum viscosity has been attained (Fig 2). The psudoplastic viscosity was found to be inversely related to concentration (Fig 3). This is conformity with the observations made by Kabre et al., which can be expressed by equation below:

Apparent viscosity = e^{kc+b}

Where, 'c' is the concentration of hydrogel. The 'b' and 'k' material constants and depend upon the type of hydrogel. The value of 'b' is given by intercept and that of 'k' is given by the slop of the plot. The determined values of 'b' and 'k' are given in the Table 1.

Table 1: Intercept (b), slope (k) and correlation coefficients (r) for the Kabre's plots of rheological data of low methoxylated pectin.

Concentration	Intercept (b)	Slope (k)	Correlation coefficient (r)
7.5%	-1.636469645	1.554700495	0.998788
10%	-4.471890566	2.323998607	0.997716
12.5%	-8.52129443	3.382312723	0.997964

The lot to lot traces chemical variation and processing variation on these variables was not determined.

For determination of effect of pH on viscosity, 10 % of pectin solution was used. As per the results of Fig 4, there was no direct correlation between pH and viscosity of the pectin solution, but results shows that it had maximum viscosity at pH 1-2. Above pH 2 the viscosity decreases as pH increase. From the result it can be stated that pectin undergoes hydration near the pH 2. When the measurements were conducted on 7th day almost similar results were observed. There was slight increase in viscosity was observed at pH 8. It indicates that hydration occurs at higher pH values.

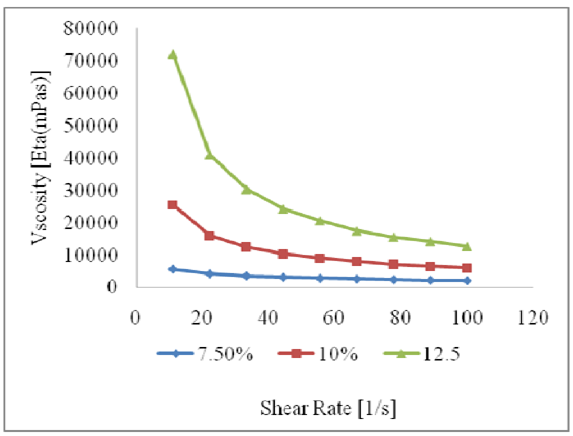

Fig. 1: Viscosity against shear rate plots for different concentrations (7.5 %, 10% and 12.5 %) of low methoxylated pectin

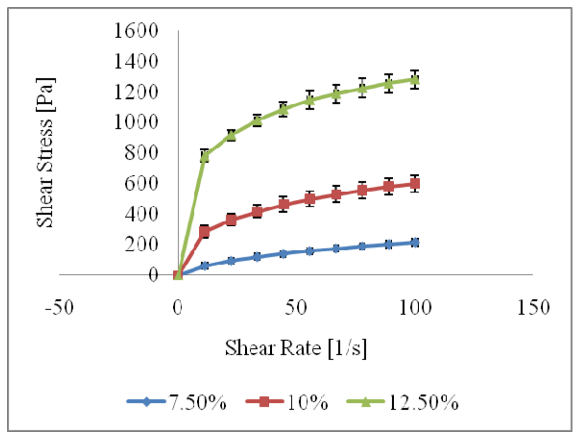

Fig. 2: Rheogram of different concentrations (7.5 %, 10% and 12.5 %) of low methoxylated pectin

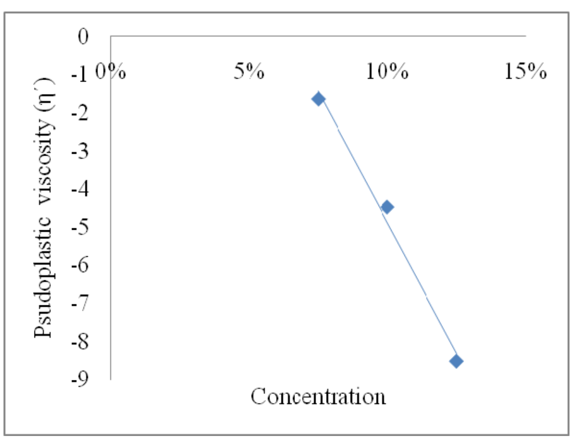

Fig. 3: Relationship between psudoplastic viscosity and concentration of low methoxylated pectin

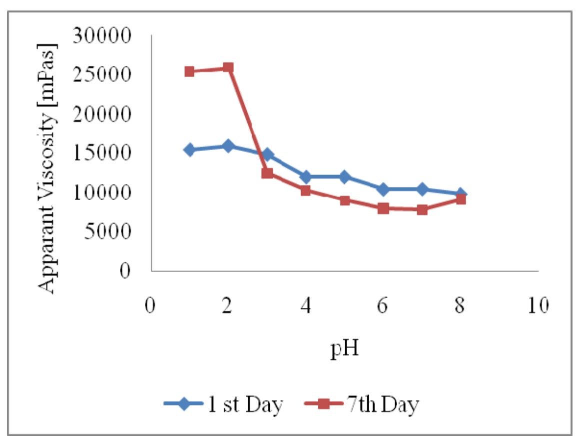

Fig. 4: Effect of pH on viscosity of 10 % w/v low methoxylated pectin on 1st and 7th day

Fig 5 shows that the apparent viscosity of pectin solution, after heating at 100 °C for different duration of time, the viscosity decrease as duration of heating increases. Initially it was found to be increase, due to improved hydration. The viscosity was regained when it was measured on the same sample at the end of 7th day. This indicates thermal stability of pectin.

When preservatives, (sodium benzoate, methyl paraben, ethyl paraben and phenyl mercuric acetate), were added in the polymer solution and the apparent viscosities of the system were measured.

The results indicated that there was no more variation in viscosity in case of sodium benzoate. Hence, sodium benzoate can be considered as ideal preservative for the selected system (Fig 6).

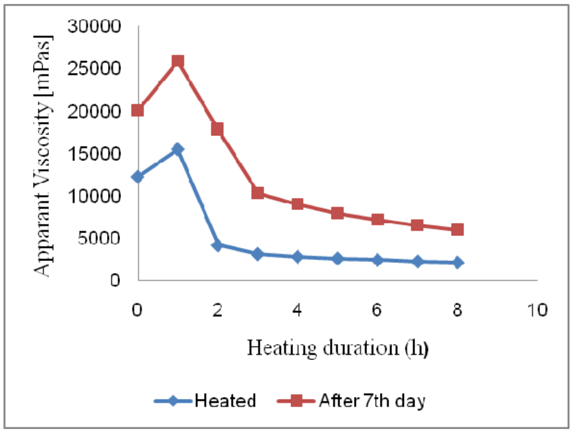

Fig. 5: Effect of heating duration on viscosity of 10 % w/v low methoxylated pectin on 1st and 7th day

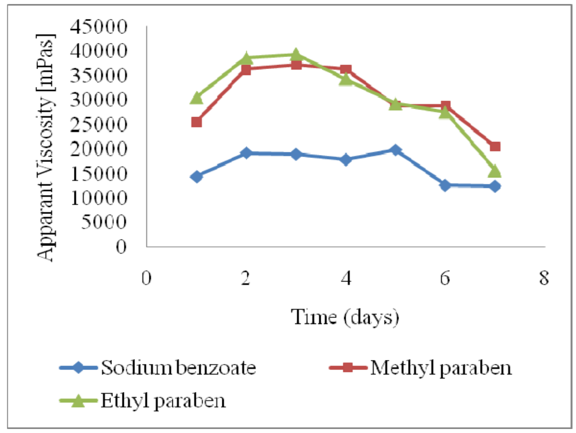

Fig. 6: Effect of different preservatives on viscosity of 10 % w/v low methoxylated pectin

CONCLUSION

The results suggest that pectin exhibits ideal rheological properties for pharmaceutical applications, where pseudoplastic flow is desired feature. As it exhibited concentration dependent pseudoplastic behavior and shows stability over a wide range of pH and temperature, it is suitable excipient for pharmaceutical dosage forms such as suspensions, microspheres and matrix tablets.

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