Available online at www.sciencedirect.com

ScienceDirect

APCBEE Procedia 9 (2014) 192 – 196

Procedia APCBEE

www.elsevier.com/locate/procedia

2013 5th International Conference on Chemical, Biological and Environmental Engineering (ICBEE 2013)
2013 2nd International Conference on Civil Engineering (ICCEN 2013)

Rheological and Swelling Behavior of pH Sensitive Hydrogel Particles

Lomas K. Tomar, Charu Tyagi, Yahya E. Choonara, Pradeep Kumar and Viness Pillay*

University of the Witwatersrand, Faculty of Health Sciences, Department of Pharmacy and Pharmacology, 7 York Road, Parktown 2193, Johannesburg, South Africa

Abstract

pH sensitive hydrogel particles were characterized for their rheological and swelling behaviour at various pH values specific to the gastrointestinal tract simulated conditions. Scanning electron microscopy was used to view the surface morphology of the hydrogels at different pHs. Swelling at pH 7.4 and shrinkage at pH 1.2 confirmed the pH sensitive behaviour of the hydrogel particles. The Linear Viscoelastic (LVE) range was determined by considering G', one of the strain amplitude. Furthermore frequency sweep tests were performed in the LVE range where the storage modulus and loss modulus were determined at constant strain. It was observed that the loss modulus was higher at basic pH while the storage modulus was higher at lower pH. This rheological method can be used to explain the pH sensitive behaviour of hydrogels.

Selection and peer review under responsibility of Asia-Pacific Chemical, Biological & Environmental Engineering Society

Keywords: pH sensitive hydrogel, Rheology, Ammonium persulfate

1. Introduction

Hydrogels are polymeric networks that have the ability to hold water upto a thousand times their weight. This unique nature is attributed to the functionality of the network. The hydrogels along with the swelling capacity have good mechanical strength and biocompatible characteristics [1,2,3], which make them suitable

* Corresponding author
E-mail address: viness.pillay@wits.ac.za

2212-6708 © 2014 Viness Pillay. Published by Elsevier B.V.
Selection and peer review under responsibility of Asia-Pacific Chemical, Biological & Environmental Engineering Society
doi:10.1016/j.apcbee.2014.01.034

for various pharmaceutical and biomedical applications [4]. pH sensitive hydrogels in particular, have been of great interest for the delivery of peptide drugs. These hydrogels protect peptide drugs in the acidic environment of the stomach and facilitates their release in the intestinal region. The drug formulations earlier, before the use of these pH sensitive hydrogels, were required to hold sufficient characteristics to obtain the desired therapeutic effect. Marked pH dependent changes in hydrogel system, the swelling behaviour, changes in structural networks and the mechanical properties, can be characterized by the rheological aspects of the formulation [5]. Rheological determinations are significant from a pharmaceutical viewpoint as they provide adequate characterization details of the behaviour of delivery system during administration of pharmaceuticals and the probable changes occurring during transport and storage [6]. The present study focuses on the evaluation of pH sensitive hydrogel particles in terms of their swelling and rheological behaviour.

2. Materials and Methods

Methacrylic acid (MAA), ethylene glycol methacrylate (EGMA), polyethylene glycol (PEG) (MW 4000) and ammonium per sulphate (APS) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Polyethylene glycol dimethacryalte (PEGDMA) was synthesized in the lab. Sodium hydroxide and HCl were obtained from Merck (Merck Chemicals Ltd, Wadeville, Gauteng, South Africa). All the buffer and solutions were prepared in deionized water.

2.1. Synthesis of pH sensitive hydrogel particles

Copolymeric pH sensitive microparticles were synthesized by free radical suspension polymerization as described in our earlier publication, with certain modifications [7]. Briefly, PEGDMA and MAA were used in molar feed ratio of 1:2 and ammonium per sulphate (1% of monomer concentration) as a free radical initiator. The polymerization reaction was performed at 60°C with continuous stirring at 300rpm, under nitrogen blanket. Water was used as the continuous medium and reaction was proceeded for 4h. The crosslinked particles obtained were repeatedly washed with deionized water in order to get rid of any unreacted monomer and were then dispersed separately in acidic and basic buffer for 6h. The particles were finally lyophilized and stored at 4–8°C until further studies. The scheme of the copolymeric particle preparation is presented in Fig. 1.

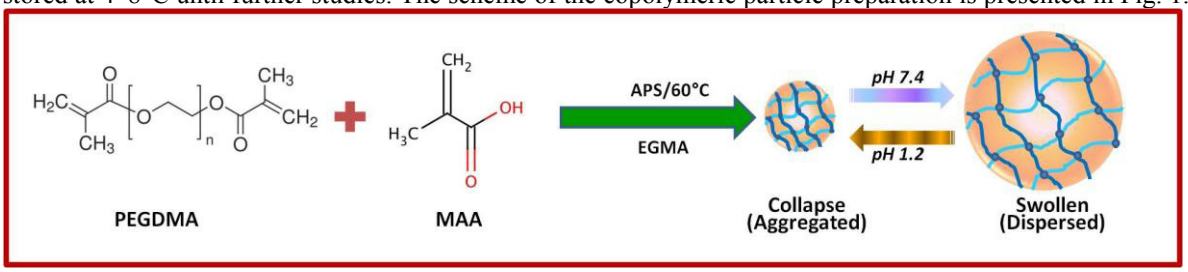

Fig 1. Schematic representation of the preparation of pH sensitive copolymeric hydrogel particles

2.2. Morphological Analysis

Surface morphology of the prepared copolymeric nanoparticles was analyzed using a FEI Phenom™ desktop scanning electron microscope at various magnifications. The particles were prepared for morphological analysis by dispersing in acidic and basic buffer for 6h, followed by lyophilization. The prepared samples were mounted on an aluminium stub and then coated with gold using an EPI Sputter coater

(SPI Module TM sputter-coater and control unit, West Chester, Pennsylvania USA). The coated samples were then analyzed.

2.3. Rheology

The rheological studies were carried out at 37°C using of a Haake Modular Advanced Rheometer System (ThermoFisher Scientific, Karlsruhe, Germany) with parallel plate geometry. Samples were prepared by dispersing the hydrogel particles in basic buffer (pH 7.4) and acid buffer (pH 1.2) for 2h. Hydrogels were filtered and used for rheological studies. A strain sweep test was performed, where G' (γ) function was considered for the determination of linear viscoelastic (LVE) range. Frequency sweep was used to determine the storage modulus, G', and the loss modulus, G", as a function of angular frequency, ω. Oscillation tests provide information on the viscoelastic behavior of the hydrogel particles.

3. Result and Discussion

3.1. Morphological Analysis

The morphology of the prepared copolymeric nanoparticles was analyzed after dispersing the particles separately in two different (acidic and basic) pH medium for 6h, in order to differentiate their pH responsive behavior on a morphological level. Scanning electron micrograph of lyophilized hydrogel particles are shown in Fig. 2. The copolymeric microparticles showed enormous swelling at pH 7.4 (Fig. 2a), whereas at pH 1.5 the particles shrinked appreciably and were observed as aggregates (Fig. 2b). The swelling of particles can be attributed to the carboxylic group ionization at a pH of 7.4, leading to more water uptake and the particles consequently coalesce with each other. At an acidic pH of 1.2 the carboxyl groups present in MAA forms hydrogen bonds with the PEG through its ether groups. The observed morphologies of the hydrogel particulate at two different pH provides a link in confirming pH responsive properties of the polymer system.

3.2. Rheology

LVE range was determined at both acidic and basic pH values by strain sweep against G' and are given in Fig. 3a and 3b, respectively. Results of the frequency sweep in the LVE region are shown in Fig. 4. The Figure shows that storage modulus is higher than the loss modulus at acidic pH in the whole frequency range of LVE, which means the elastic behavior of the hydrogel predominates at this pH value [8]. Inverse results were obtained at the basic pH where with the time loss modulus was higher than storage modulus. The reason for this opposite rheological behavior is the swelling and aggregation of the hydrogel particulate at different pH values. Swelling of the hydrogels is mainly controlled by polymer-solvent interaction, ionic interaction, electrostatic repulsion and elastic interactions. The synthesized hydrogels shows swelling at basic pH because at this pH there is disruption of hydrogen bonding and ionization of carboxylic acid moieties which results in high degree of swelling leading to the viscous behaviour. Hydrogels showed elastic behaviour at pH 1.2 pertaining to the hydrogen bonding occurring at low pH, at inter and intra-particle level which works as a secondary crosslinker [9].

4. Conclusion

Copolymeric hydrogel particulates were prepared and characterized for rheological and swelling behavior at different pH conditions. Hydrogels showed the pH sensitive behaviour, swelling at basic pH while

aggregation at acidic pH, clearly evident from the micrographs. LVE region for the hydrogel samples was determined first and conditions for the frequency sweep were selected. Storage modulus was observed to be higher than loss modulus at pH .2 which shows the elastic behaviour of the particles at an acid pH in comparison to the viscous property of the particle at basic pH. A detailed rheological and physicochemical characterization of hydrogels such as this will lead to the development of formulations for targeted oral peptide delivery.

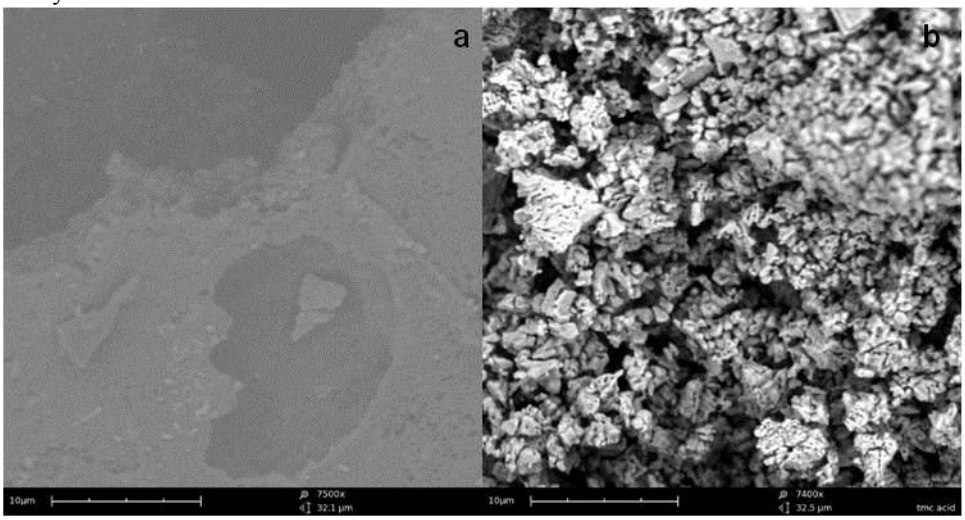

Fig. 2. Scanning electron microscopy of the prepared hydogel particles at (a) pH 7.4; (b) pH 1.2

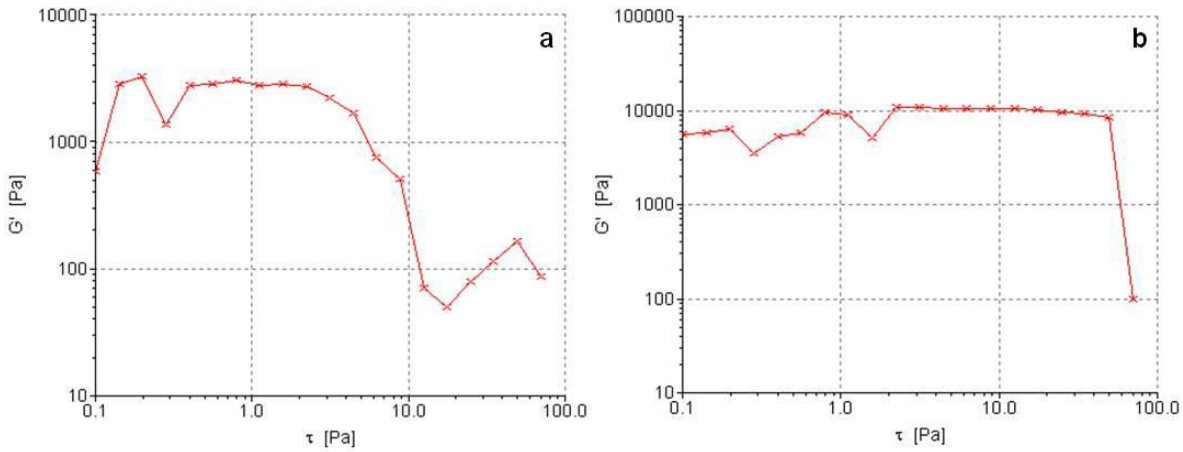

Fig. 3. Strain dependence of the G' at constant angular frequency of 1rad/sec at (a) pH 7.4; (b) pH 1.2

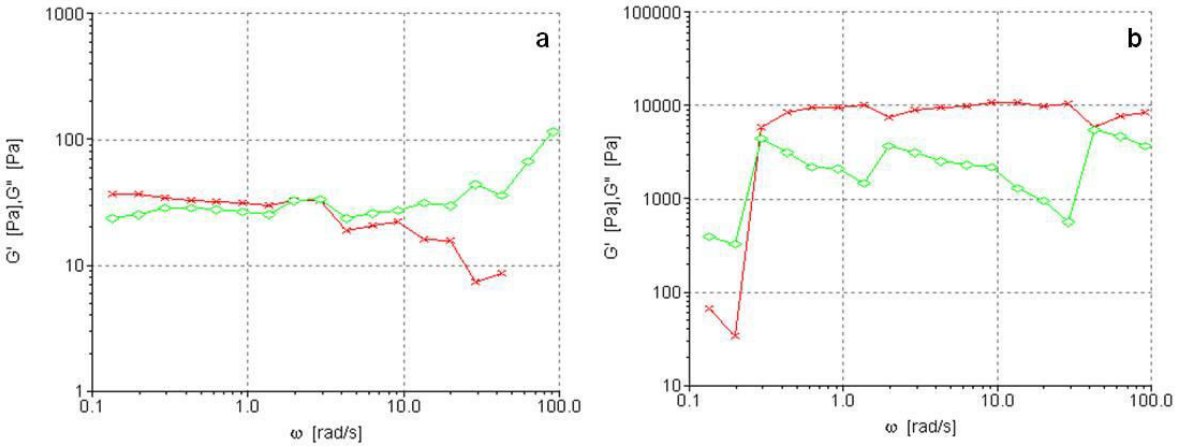

Fig. 4. Angular frequency dependence of the G' and G" at (a) pH 7.4; (b) pH 1.2

Acknowledgements

This research was funded by the National Research Foundation (NRF) of South Africa.

References

[1] Malana MA, Zohra R, Khan MS. Rheological characterization of novel physically crosslinked terpolymeric hydrogels at different temperatures. Korea-Australia Rheology Journal, 2012;**66**:155-62.

[2] Lee C, Shin J, Lee JS, Byun E, Ryu JH, Um SH, Kim DI, Lee H, Cho SW. Bioinspired, calcium-free alginate hydrogels with tunable physical and mechanical properties and improved biocompatibility. Biomacromolecules, 2013;**14**:2004-2013..

[3] Kurokawa T, Furukawa H, Wang W, Tanaka Y, Gong JP. Formation of a strong hydrogel-porous solid interface via the double-network principle. Acta Biomaterialia, 2010;**6**:1353–1359.

[4] Hago E-E, Xinsong L. Interpenetrating Polymer Network Hydrogels Based on Gelatin and PVA by Biocompatible Approaches: Synthesis and Characterization. Advances in Materials Science and Engineering, 2013;**2013**:Article ID 328763, 8 pages.

[5] Heidegrid SK, Eneida JDa-L, Rilton Ade-F, C´Elia RCF, David AM, Joana LMSilveira. Rheological characterization of a xanthan–galactomannan hydrogel loaded with lipophilic substances. Journal of Pharmaceutical Sciences, 2012;101:2457–2467.

[6] Owen DH, Peters JJ and Katz DF, Comparison of the rheological properties of Advantage-S and Replens. Contraception, 2001;**64**:393-396.

[7] Tomar LK, Tyagi C, Lahiri SS, Singh H. Poly(PEGDMA-MAA) copolymeric micro and nanoparticles for oral insulin delivery. Polym Adv Technol 2011;**22**:1760–1767.

[8] Swindle KE, Paul DH, Nathan R. In situ formation of hydrogels as vitreous substitutes: Viscoelastic comparison to porcine vitreous. J Biomed Mater Res. 2008;**87A**:656–665.

[9] Bartili T, Bounekhel M, Cedric C. Swelling behavior and release properties of pH-sensitive hydrogels based on methacrylic derivatives. Acta Pharm, 2007;**57**:301–314.