

**Hyaluronic acid/poly(vinyl alcohol) 블렌드의 농도에 따른
유변학적 특성연구**

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**Effect of concentration on the rheological properties of
hyaluronic acid/poly(vinyl alcohol) blend systems**

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Introduction

Hyaluronic acid(HA) is a water soluble glycosaminoglycan. It is a high molecular weight linear polysaccharide with the repeating disaccharide structure composed of D-glucuronic acid and N-acetyl-D-glucosamin with (1-4) interglycosidic linkages[1]. HA occurs naturally in many living substrates as synovial fluid, vitreous humour, connective tissues, rooster comb and umbilical cord. Indications of pharmacological activity have been demonstrated in the treatment of inflammatory and degenerative joint diseases[2,3]. And HA is also used as a visco-supplementation for the ophthalmic surgery treatment[4] of osteoarthritis of the knees joint. In these applications the rheological properties of HA are important. However, the short residence time of HA due to biodegradability limits the possibility to widen its range of biomedical application. To overcome this problem, many methods have been investigated; associating HA with alginate [5-6], chemically modifying HA[7], and blending HA with other polymers[8], for example.

Bioartificial polymeric materials represent a new class of polymeric materials based on blends of synthetic and natural polymers, designed with the purpose of producing new materials with enhanced properties with respect to the single component. In this paper, we designed the blend of synthetic and natural polymers that have good mechanical properties and biocompatibility[9-10], and enhanced rheological properties. We designed the blend composed of Poly(vinyl alcohol)-borax (PVAs) as synthetic component and Hyaluronic acid (HA) as natural polymer.

HA/PVAs blend system is dependent upon blend composition, borax concentration, degree of hydrolysis of PVA and flow condition such as shear. These effects on the rheological properties and morphology in HA/PVAs blend are investigated.

Theory

Poly(vinyl alcohol) is unique synthetic polymer in that it has a large number of hydroxyl groups. Hydrogen bonds related to the large number of hydroxyl groups play an important role in the physical behaviour of poly(vinyl alcohol).

Aqueous solutions of poly(vinyl alcohol) form aggregated supermolecular structures. These structures contain amorphous and paracrystalline parts[11], the mutual ratio of which depends on experimental conditions during the preparation of solutions, and predominantly on the dissolution temperature[12]. The structure and properties of aqueous solution of poly(vinyl alcohol)-borax complex has been studied. PVA-borax forms the crosslinking and may become a gel under approximate conditions of PVA and borax concentration, ionic strength, pH, and temperate. And its shear thickening behavior has been well recognized.

Experiment

This study was carried out with Hyaluronate, Poly(vinyl alcohol) and borax. HA of molecular weight (3300KDa) is used as received by LGLS in Korea. PVA (Mw: 124-186 KDa, 98-99% hydrolyzed), PVA2(Mw:124-186 KDa, 87-89% hydrolyzed) and borax were purchased from Sigma Aldrich.

The blend preparation is as follows :

- a) 1 wt% HA aqueous solution is prepared with purified water at room temperature for one night by shaking at 300rpm
- b) 4 wt%PVA aqueous solution is dissolved at 106°C (200rpm, 1hr)
- c) 2.0,1.8,1.4,1.2,1.0,0.6,0.2wt% borax aqueous solution is made at 60°C for 30min.
- d) (a) is mixed with (b) at 70°C for 30min.
- e) (d) is mixed with (c) at 70°C for 30min at various blending ratio.

We stained blends using Alcian Blue method for morphology investigation.

Rheological experiments were performed on an RMS 800(Rheometrics Scientific, USA) and Bohlin C-VOR. The morphology of blends is investigated with optical microscope (OLYMPUS BX51, JAPAN), equipped with shearing system (CSS-450).

Results and Discussion

Deviation from linear mixing rule implies the strong interaction between HA and PVA as shown in Figure1. The interaction reaches to a maximum at 20:80 blend ratio. Figure2. shows a various morphology with blending ratio. As blending ratio of HA and PVA increases from 20:80 to 40:60, network structures of the blend gets more stronger. Then some patterns appear at 60:40 and 80:20 blending ratio.

To get more information about HA/PVA interaction, we changed degree of hydrolysis (DH) of PVA that has relation with hydrogen bonding in terms of the number of OH groups of PVA. We named PVA of DH 87-89% as PVA2. The blend of HA/PVAs2 has lower rheological properties. The effect of degree of hydrolysis of PVA could be inferred that hydrogen bonding is the important factor of the interaction in HA/PVAs blend. Adding borax to this HA/PVA blend, it has more

enhanced rheological properties in Figure 2. Though HA/PVA blend without borax shows similar behavior, the interaction was more weaker than HA/PVAs blend. Namely, the presence of borax enhances the interaction of the blends. Figure 3 shows that the rheological properties of HA/PVAs(20:80) blend are enhanced, as the concentration of borax increases. Complex viscosity of HA/PVAs blend with respect to borax concentration is consistent with that of PVA-borax system having various borax concentration.[13].

HA aggregates are in the form of clusters at low borax concentration. As borax content increases, chaining of HA aggregates seems to be caused by morphology which is not contained here. Interesting is that the network structures of HA/PVAs blend are formed both in micro and nano scale. And these micro structures are changing under step shear condition as in Figure 4,5.

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References

1. Fouissac,E. ; Milas M.; Rinaudo,M. , *Macromolecules* 1993,**26**,6945.
2. Asheim,A. ; Lindbald,G. *Acta Vet. Scand.* 1976,**17**,379.
3. Numiki,O. ; Toyosima,M.; Morisaki,N. *Clin. Orthop.* 1982,**146**,260.
4. Miller,D. ; Stegmann,R., Eds. *Healon (sodium hyaluronate) A guide to its use in ophthalmic surgery*; Wiley : New York,1983.
5. Sandra,O. *Biopolymers* 2000,**54**,273.
6. Pelletier,S. *J of Biomedical Materials Research* 2001,**54**,102.
7. Ambrozo,L. *J.M.S.-Pure Appl Chem* 1999,**A36**,991.
8. Cascone,M.G. *Polymer International* 1997,**43**,55.
9. Giusti,P. *Macromol Symp* 1994,**78**,285.
10. Giusti,P. *The polymer Materials CRC: Boca Raton* 1996,538.
12. Braun,D. ; Walter,E. *Colloid Polym Sci* 1980,**258**,376
13. Chen,C.Y. ; Yu,T.L. *Polymer*,1997,**38**,2019.

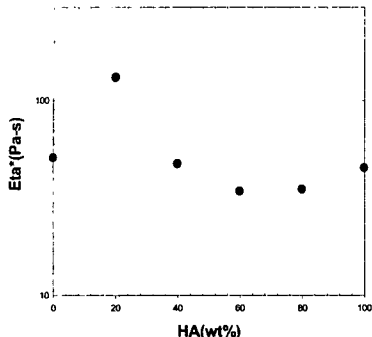


Figure 1.

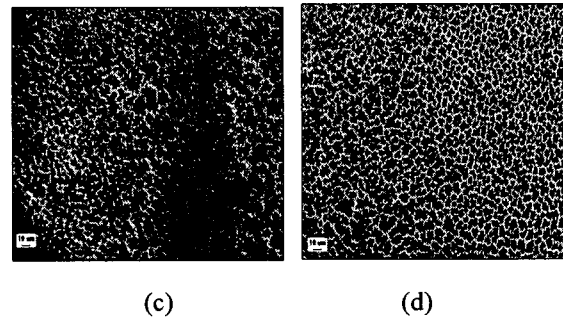
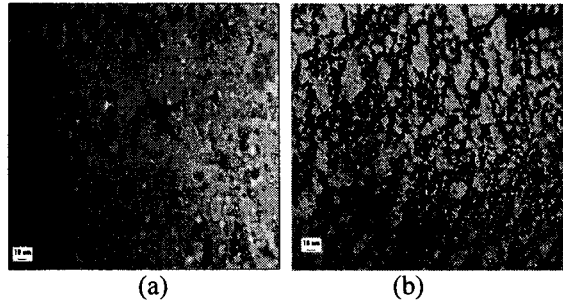


Figure 2. (a) HA:PVAs=20:80,
(b) HA:PVAs=40:60,
(c) HA:PVAs=60:40,
(d) HA:PVAs=80:20

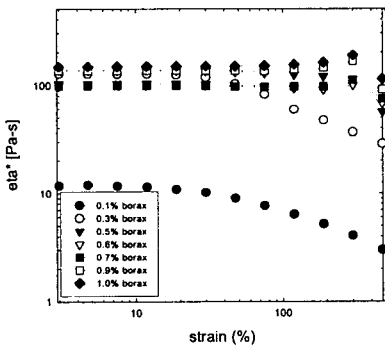


Figure 3.

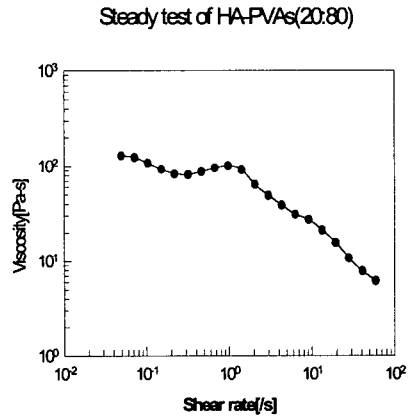


Figure 4.



Figure 5.