学 位 論 文 内 容 の 要 旨
Abstract of Doctoral Dissertation

博士の専攻分野の名称　博士（生命科学）　氏 名　Rajesh Kumar Sharma

Degree requested　Doctor of Life Science

学 位 論 文 題 名
Title of Doctoral Dissertation

Investigation on the Effect of Flow Field on the Amyloid Fibril Formation
(アミロイド線維形成に及ぼす流動場の効果に関する研究)

Amyloids are the insoluble fibrils, formed by the soluble proteins. In vivo, approximate more than 20 neurodegenerative diseases associated with amyloid fibrils have been found in patients suffered with Alzheimer's disease, Prion disease, Parkinson's disease, Diabetes type 2 and Huntington's disease etc. Amyloid fibrils not only form in-vivo but it can also be form in-vitro having the similar structure to those obtained in-vivo.

β-Lactoglobulin, a globular whey protein formed fibrils by heating above its denaturation temperature or by adding denaturants (Alcohol, Urea etc.). Amyloid fibrils of β-Lactoglobulin have advantage in the food industries to change textural properties of the foods. Fibril formation of β-Lactoglobulin associated with a nucleation-elongation growth mechanism. Earlier studies revealed that there are several factors influence to the rate of the nucleation-growth mechanism including shearing, stirring, seeding etc.

In this dissertation, we investigated the effect of flow field (stirring) on the heat-induced fibrillogenesis of β-Lactoglobulin to gain more knowledge about the effect of stirring. β-Lactoglobulin and whey protein isolate (WPI) have been studied earlier using different techniques and shown that shear and stirring enhanced the fibrillogenesis. In this dissertation, we characterized β-Lactoglobulin fibrils using an unique elongational flow birefringence method by using Taylor's Four-Roller Mill (FRM) system. The elongational flow birefringence method has advantage over the traditional shear flow experiments to characterize the polymer molecules in the solution.

The current dissertation has been organized in to four chapters.

A general introduction about the current research has been described in Chapter 1.

In chapter 2, the effect of stirring on the heat-induced fibrillogenesis of β-Lactoglobulin at 80°C and pH 2 has been described. In this study, stirring of two different rates (250 and 474 rpm) were applied during incubation. Sample incubated under rest form was used as a control sample. Fibrils were characterized quantitatively by using flow-induced birefringence method while AFM was used for the morphology of the fibrils. From this study, we investigated that the order of the expected length of the resultant fibrils in both longer and shorter length distributions was those stirred at 250 rpm≈474 rpm >0

rpm.

In chapter 3, we have also described the effect of stirring on the heat-induced fibril formation of the β-lactoglobulin in the presence of reducing sugar (Glucose) at 80°C and pH 7. In this study, we applied stirring same like as those applied in chapter 2 and β-lactoglobulin was incubated with and without glucose under unstirred condition used as control samples. Flow-induced birefringence, X-ray diffraction (XRD), Thioflavin T (ThT) fluorescence and Atomic force microscopy (AFM) techniques were employed to characterize the fibrils and morphology of the fibrils formed. This study revealed that the glucose inhibited the fibrillogenesis of β-lactoglobulin and also fibrillogenesis decreased with increasing stirring rate.

In the final chapter 4, we have been discussed the general conclusion of this work.

In this dissertation, fibrillogenesis of β-lactoglobulin was carried out under flow field (Stirring) in detail can be useful in the food industries and also can clear various aspects about amyloid fibrils.