LOCAL DYNAMICS OF HUMAN INSULIN AND A RAPID ACTING INSULIN ANALOG BY HDX MS ANALYSIS

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INTRODUCTION

Human insulin, used by diabetics to regulate blood glucose, was first introduced in a microbially produced therapeutic drug nearly 30 years ago. It is, however, very challenging to adequately characterize the higher-order structure of both therapeutic products such as insulin and to monitor the changes in oligomeric stability. Human insulin and insulin analogs have identical primary structure, except for the transposition of a pair of amino acids. Lispro is one of the rapid-acting insulin analogs, which has higher tendency to dissociate than human insulin.

In this study, we present an analytical workflow to allow us to detect the difference in the oligomeric dynamics using a Hydrogen Deuterium Exchange Mass Spectrometry (HDX MS) [1]. The HDX peptide analysis on human insulin and Lispro was conducted to identify the location where different deuteration uptakes were observed between human insulin and Lispro. The detected areas were illustrated in various display formats to help understand their flexibility associated with rapid dissociation of insulin oligomers.

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RESULTS

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DISCUSSION

Local dynamics and flexibility of human insulin and Lispro (a rapid acting insulin analog) was analyzed by HDX MS. The results have successfully identified the locations of Chain A 22-24 and Chain B 22-24, where the HDX results showed distinct differences in deuterium uptake.

Our finding in HDX results were well agreed with the regions previously reported for hexamerization and dimerization.

CONCLUSION

Local dynamics and flexibility of human insulin and Lispro (a rapid acting insulin analog) was analyzed by HDX MS. The results have successfully identified the locations of Chain A 22-24 and Chain B 22-24, where the HDX results showed distinct differences in deuterium uptake. Our finding in HDX results were well agreed with the regions previously reported for hexamerization and dimerization.

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