Challenge to Peptide Manufacturing Technologies

Introduction

PeptiStar Inc. was established as a peptide CDMO in September 2017. The headquarters and factory are located in Osaka, where the research building and factory started operations successfully in 2019. From there, we have manufactured more than 100 batches of research level samples (10 mg to 10 g), over 20 batches of non-GMP level products (10 g to 1 kg) and 8 batches of GMP products for early to late phase clinical trials.

One of the key features of PeptiStar is that we have the capabilities to develop innovative manufacturing technology, which is not found in other companies. In addition to a series of peptide manufacturing processes such as synthesis, purification, freeze drying, etc., we have been developing a new technology for analysis every day.

In this article, we would like to introduce our achievements in peptide manufacturing technologies.

Manufacturing Technologies

Microwave Synthesis Method

The microwave synthesis method can raise the temperature of the reaction solutions rapidly by applying microwaves, which can also drastically shorten the reaction time. This enables us to reduce our manufacturing cost, while synthesizing high-quality peptides.

At the research level, the microwave automatic synthesizer is widely utilized as an effective method to synthesize peptides. However, there is no equipment available in regards to large-scale manufacturing. PeptiStar has constructed large-scale facilities in cooperation with its shareholders, which have reactors of 1L, 10 L, and 30 L size to accommodate the gradual scale up of manufacturing according to the development stages (Fig.1).

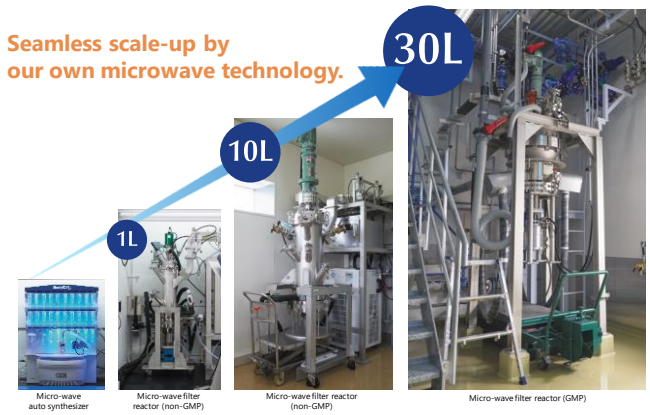

Figure 1 Microwave Synthesis

PeptiStar has already achieved large-scale production using the microwave synthesis method, obtaining excellent yield and quality even after scale up (Fig.2), while realizing significant cost reductions (Fig.3).

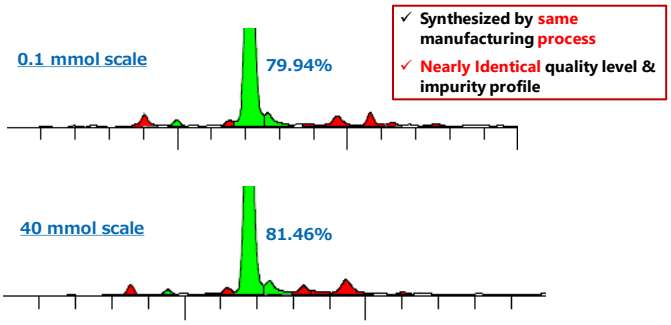

Fig. 2 Quality comparison of model peptide (crude)

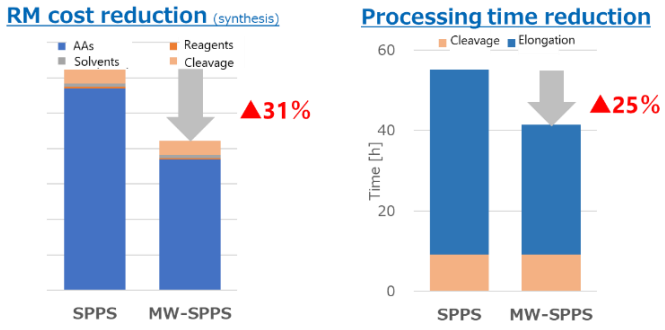

Fig. 3 MW SPPS vs Conventional SPPS

Silylated Tag-Assisted Liquid-phase Peptide Synthesis Method (STag-PS™)

STag-PS™ is a hydrophobic organic tag developed by Sekisui Medical Co., Ltd., which has excellent economical and environmental benefits. In particular, it is a next-generation liquid-phase peptide synthesis method that can efficiently synthesize difficult-to-produce peptides (Fig.4). Because of its high solubility, PeptiStar can complete the synthesis in one pot even for relatively long-chain peptides without precipitation, purification and concentration for each amino acid elongation step. Additionally, we can also reduce the raw material cost, since this method can drastically reduce amino acid equivalence and solvent usage in comparison with the conventional solid-phase peptide synthesis method. Since the reaction can be monitored qualitatively and

quantitatively by HPLC, we can obtain the drug substance at high yield and high purity in a stable manner as impurity control is easily managed. It can also be said that there is no restriction for the scale-up, because we do not need any special equipment such as a filter reactor used in the solid-phase peptide synthesis.

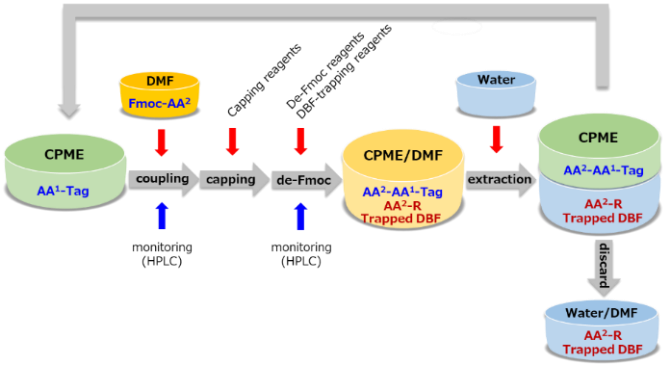

Figure 4. General synthesis scheme using STag-PS™

PeptiStar already has manufacturing experience of using STag-PS and obtained equivalent or better results than solid-phase peptide synthesis in terms of yield and quality (Fig 5).

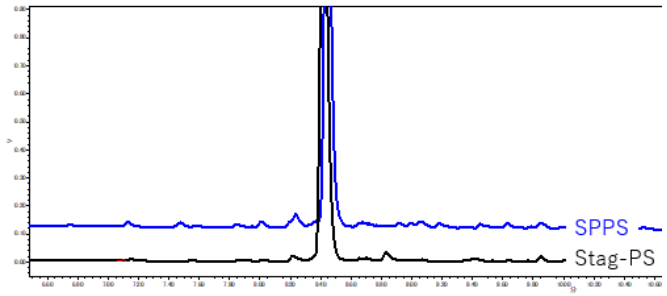

Figure.5 Quality comparison of model Icatibant peptide (crude)

PeptiStar's Manufacturing Strategy

One of the strengths of PeptiStar is that we can choose microwave synthesis or STag-PS™ synthesis methods according to the customer's demands. We usually use the microwave synthesis to get a few mg to several kg of the drug substance. It is especially useful in the early stages of development where speed is the critical factor. Additionally, the scale-up is also quite easy because we have the equipment up to 30 L scale. If the demand for the bulk drug substance reaches the level of several hundred grams to several tens of kilograms, the STag-PS™ synthesis method can be used with the equipment up to 300 L scale, which shortens the production lead time and drastically reduces the production cost (Fig.6).

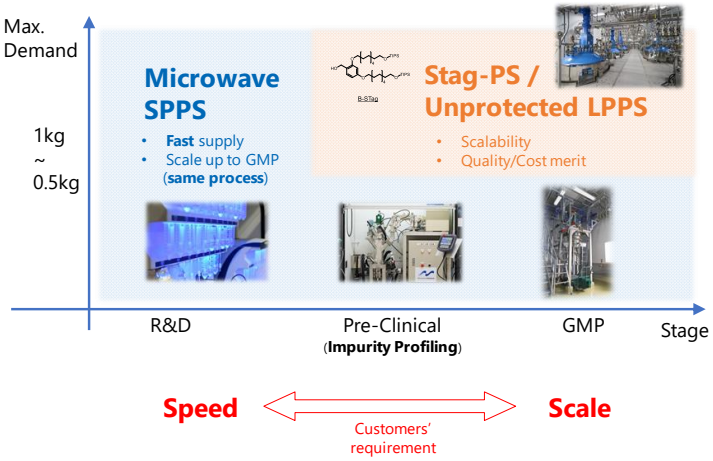

Figure 6 Manufacturing Strategy

The quality is the most concerning issue when the manufacturing method is changed, however, since the STag-PS™ synthesis method and the solid-phase peptide synthesis method have the same basic chemistry, the impurities profiles are also quite similar, and we can achieve the same or better quality (Fig.7).

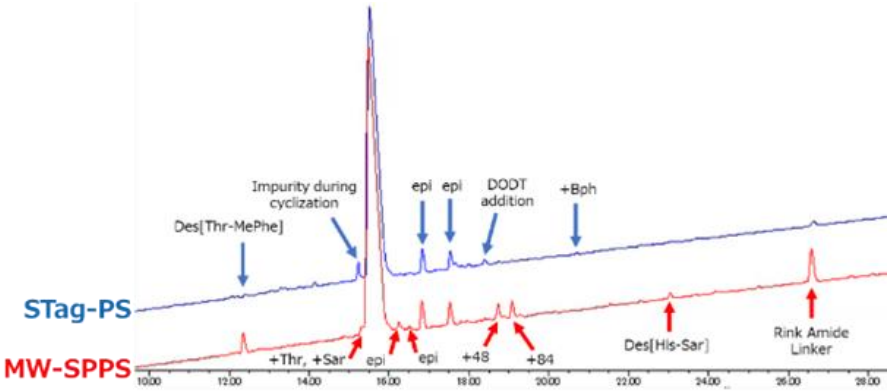

Fig. 7 Quality comparison of model cyclic peptide (crude) between STag-PS™ vs Microwave-SPPS

As explained above, PeptiStar can make the optimum proposal for various requests from the customer by combining our proprietary technologies.

The technologies introduced at this time are only some examples of the capabilities from PeptiStar, so if you are interested, please contact us.

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