TETRAS
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USE OF PEPTIDES IN THE THERAPEUTICS MARKET

A peptide is a class of organic molecules found throughout all of life having various functions in biological processes. A peptide molecule is comprised of multiple amino acids, ranging from 2-50, linked together by what is known as a peptide bond. While not universally agreed upon, once a growing peptide chain consists of 50 or more amino acids it is then considered a protein. With 20 naturally occurring amino acids and an endless number of customized synthetic amino acids, the available combination possibilities and peptide lengths make these molecules so versatile in their functionalities.

Peptides have been well studied ever since the developed theory and discovery in the early 1900's with the research of Emil Fischer. In the 1920's the first isolation and commercialization of animal derived insulin, a 51 amino acid polypeptide, peptide drugs have greatly reshaped our modern pharmaceutical industry. Not until 90 years later was the animal derived insulin

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replaced with a human recombinant substitute. With an increased knowledge of peptide chemistry, the efficacy and potency of insulin has since improved through subtle substitutions and modifications to the amino acids found in the peptide chains. Insulin provides us just one example showcasing the flexibility and customizability of a peptide when used as an active pharmaceutical ingredient (API).

Peptides since are being increasingly used as potential API due to their relative ease of synthesis, general low toxicity, and ease of availability. As per the International Journal of Current Pharmaceutical Research, approximately 60 peptide-based drugs have been approved by the FDA, 140 peptide-based drugs are currently in clinical trials and another 500 peptides are in development.

Peptide therapeutics are being examined in various disease categories such as cancer, autoimmune, neurological and endocrine disorders with cancer being the leading drive in this field due to the rise in mortality and need for chemotherapy replacement. Peptides can be utilized in a number of different ways in treating cancer. This includes using peptides directly as drugs, tumor targeting agents that carry cytotoxic drugs and radionuclides (targeted chemotherapy and radiation therapy), hormones, and vaccines.

Secondly, the prevalent increase in type 2 diabetes has drawn great attention in the world of peptide therapeutics. Available drugs on the market today for the treatment of type 2 diabetes include Byetta, Victoza, and Trulicity. These three therapeutic peptide examples are classified as glucagon-like peptide-1 (GLP-1's) and are responsible for interacting with the bodies receptors to the hormone glucagon. In these cases, the peptide is able to activate specific pathways to trick the body into behaving as if a high concentration of glucose has entered the bloodstream, resulting in the release of insulin.

Insulin, for example, is part of a category of peptides know as hormone mimicking peptides. Other groups of peptides exist such as antimicrobial, alkaloidal, anti-oxidant, and growth factor peptides. The great diversity in functionality of therapeutic peptides is the result of identifying underlying protein interactions throughout the body. The biological effect of protein interactions may include the creation of a new binding site, alter the kinetics of enzyme activities, facilitate the movement of substrates, regulate mechanisms upstream or downstream, or cause destruction of specific proteins. In understanding the direct mechanism of these types of protein interactions, peptides can be constructed to mimic the active biding site of the protein, thus eliciting the same biological response that the protein would cause. Understanding how peptides can be used as substitute components in protein interactions has proven to be an effective method for regulating many biological functions.

As technology advances in protein interaction identification researchers are now able to rapidly measure the effectiveness of these interactions. Some available methods available include Co-immunoprecipitation, pull-down assay, crosslinking protein interaction analysis, label transfer protein interaction analysis, and far-western blot analysis. These methods now make it possible for researches to test and measure the proteins ability to interact with any substrate, such as a peptide. In order to meet the demand for new peptides for use in

such test methods, peptide manufactures are expected to produce a large number of different peptides quickly and effectively dependent on the needs of the researcher.

With peptide demand increasing, contract manufacturing organizations (CMOs) and contract development and manufacturing organizations (CDMOs) are increasing capacity and portfolios to keep constant supply. While increase in facility capacity is one method to increase peptide production, much work is needed in the efficiency of peptide manufacturing. Currently, peptides require complex synthetic processes in their manufacture, including plant and labor-intensive production cycles. Scale-up of batch processes from preclinical to development and then to commercial is very expensive and associated with significant risk of failure to supply – Failure of a Phase 1 or 2 batch is typically $2.2 million to $5.5 million, depending on dose and number of subjects plus a delay of approximately 1 year.

These manufacturing considerations make bringing additional peptide therapeutics to the market a risky and time staking process. As research groups continue to demand more nontraditional, complex peptides, manufactures are needing to introduce new and innovative manufacturing technologies to minimize production costs and times to market. Process automation and innovative peptide synthesis design are increasing the efficiencies of this process and can contribute to the growth and spur of new innovation in the peptide therapeutics market.

Sources

1) *https://www.britannica.com/biography/Emil-Fischer*

2) *https://doi.org/10.1016/j.bmc.2017.06.052*

3) *https://www.diabetes.co.uk/insulin/history-of-insulin.html*

4) *https://www.onlinebiologynotes.com/peptide-types-functions/*

5) *https://www.sciencedirect.com/science/article/pii/S0968089617310222*

6) *file:///C:/Users/mhardison/Downloads/ijms-20-02383.pdf*

7) *https://www.hindawi.com/journals/jaa/2012/967347/*

8) *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5316480/*

9) *https://www.thermofisher.com/us/en/home/life-science/protein-biology/protein-biology-learning-center/protein-biology-resource-library/pierce-protein-methods/overview-protein-protein-interaction-analysis.html#:~:text=Stable%20interactions%20are%20those%20associated,interactions%20that%20form%20stable%20complexes.*

10) *https://www.frontiersin.org/articles/10.3389/fbioe.2015.00211/full*

11) *https://drug-dev.com/therapeutic-peptides-continuous-manufacturing-of-peptides-could-speed-up-development-reduce-costs-improve-quality/*