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The Beneficial Effects of C-peptide for Diabetic Encephalopathy

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ABSTRACT

Diabetes is a disease that millions of people globally are affected by its symptoms along with its complications. Even with treatment plans such as insulin injections or pumps, diabetes remains a widescale, worldwide problem. If a patient is diagnosed with diabetes, they can experience heart and kidney disease, vision dysfunction, oral health deterioration, and nerve damage. However, as recent studies show, a peptide, which was originally used as an early detection tool for diabetes, has exhibited many remunerative characteristics that may benefit diabetes and other complications caused by the disease. More specifically, diabetic encephalopathy, a disease known for cognitive impairment and damage to the nervous system, could improve with the help of C-peptide. With C-peptide's therapeutic effects of improved blood flow, nerve cell regeneration and repair, anti-inflammatory responses, and a decrease in experiencing a stroke, C-peptide has many profitable advantages for treating complications of diabetes related to the deterioration of the nervous system. In this study, the paper will discuss the latest findings on the effects of C-peptide on diabetic encephalopathy, the disadvantages and limits with the use of the substance, areas of uncertainty, and how the new discovery may alter the future. Researchers hope with this new discovery there will be further research done to figure out how C-peptide may help other diseases in the body or may act as a potential cure for diabetes. C-peptide may become a more common and effective candidate for treatment options of diabetes.

Introduction

In today's world, almost 422 million people annually are affected by diabetes (World Health Organization, 2023). Unfortunately, this deadly disease has no cure, which can result in a huge physical and mental toll on the patient and their family. As a result, the world is in high demand for a possible cure or a more effective treatment. Recently, however, scientists have discovered a potential molecule with many positive effects for treating diabetes: C-peptide. C-peptide is a peptide that is made up of 31 amino acids and is derived from insulin from the splicing of proinsulin, the molecule that contains C-peptide and insulin. Although C-peptide was mainly used in C-peptide tests for early detection of diabetes, C-peptide was found to also alleviate the symptoms of diabetes and act as a treatment or medication plan. One specific complication that is primarily discussed in this study is diabetic encephalopathy. Patients who are diagnosed with diabetic encephalopathy experience symptoms of cognitive decline, such as memory loss, confusion, and personality changes. Diabetic encephalopathy affects a large amount of people who are diagnosed with diabetes, which explains its need for a more effective medication. Much of the research that has currently been conducted discusses how C-peptide could specifically provide neuroprotective effects and how C-peptide may result in cognitive improvement for diabetic patients. As scientists try to understand the physiology of C-peptide, they are able to determine how effective C-peptide may become by including it in treatment plans. The study anticipates that research on C-peptide will become more widespread to lead to new treatment approaches and improve other medicines.

Understanding Diabetes

Diabetes is a chronic health condition in which the body is not able to lower blood sugar levels, resulting in sugar level spikes. If not treated, diabetes can lead to heart and kidney disease, possible stroke, cancer, and blindness (Mayo Clinic, 2023). The two types of diabetes are type 1 and type 2. Type 1 is an autoimmune disease in which the pancreas does not make enough insulin to reduce blood sugar due to an attack on islet cells by the immune system. In other words, the body's immune system destroys beta cells, which are responsible for producing insulin for the body. Without beta cells, the pancreas would not be able to respond accordingly when exposed to high levels of blood sugar. Typically, type 1 diabetes is found in young adults and children. In such scenarios, insulin must be administered immediately – otherwise, it might be fatal. However, type 1 diabetes is a rare event compared to type 2 diabetes. Type 2 diabetes is not an autoimmune disorder and is caused by a decrease in insulin production in the pancreas. Simply put, a patient with type 2 diabetes is more insulin resistant. Compared to type 1 diabetes, type 2 diabetes is more likely to be found in older adults, and a patient diagnosed with type 2 diabetes is not in immediate need of insulin. Type 2 diabetes can also be found in obese or overweight patients. The two types of diabetes are equally deadly. Both can lead to substantial permanent damage to a patient's body. Diabetes is treated by insulin pumps or injections to provide a constant supply of insulin. If someone is experiencing symptoms such as weight loss, fatigue, extreme hunger and thirst, and frequent urination, it is advised to talk with a doctor or medical professional about a diagnosis for diabetes. To prevent being diagnosed with diabetes, one must remain physically active, eat plant foods, maintain adequate vitamin levels, cut down on sweetened beverages and foods, and monitor blood sugar levels. By doing these steps, one can decrease their chance of developing the disease and live a healthier lifestyle (Osborn and Biggers, 2020).

The Synthetization of Insulin

When a person eats something that is high in sugar, how will the body respond? Sugar moves directly into the bloodstream, which is detected by hormones in the endocrine system. To prevent sugar spikes in the blood, the endocrine system releases a hormone, insulin, to counteract the sugar and notify the body's cells to absorb it. In addition, insulin signals the liver to absorb the sugar for later use as an energy storage. By doing so, insulin helps lower blood sugar when high to prevent serious, permanent damage to one's organs. Insulin is a molecule that is produced by the pancreas from a secretion of beta cells, or cells controlled by the endocrine system. The pancreas contains sections of beta cells, or islets of Langerhans, that will produce hormones to produce insulin. The process of insulin synthesis starts with protein synthesis, or transcription and translation (Robertson, 2022). The first step in insulin production is transcription. Transcription is the process of creating an RNA strand from its template DNA in the nucleus of the cell. When blood sugar levels are high, the endocrine system signals insulin to be created and for transcription to be initiated. RNA Polymerase, an enzyme that makes an RNA sequence whose bases correspond to the bases on the DNA template, creates an mRNA strand based on the sequence of DNA coding for insulin that will leave the nucleus and be sent to ribosomes in the cell. Once the insulin mRNA reaches the ribosomes, translation has been initiated. Translation is the process of converting the mRNA molecule to a sequence of amino acids, or a protein, by tRNA. tRNA is a molecule that provides the corresponding amino acid to a group of three nucleotides, or a codon. In translation, the tRNA molecule reads a codon of the mRNA molecule and provides the appropriate amino acid for the codon. As the tRNA molecule reads the codons, the amino acid chain soon develops into a proper protein (Clancy, 2008). In this scenario, the insulin molecule is created, which is also known as pre-proinsulin. The pre-proinsulin is then sent into the endoplasmic reticulum where it will be spliced with its signal peptide, creating proinsulin. Lastly, the molecule is sent into the Golgi apparatus for packaging. Here, C-peptide is split from proinsulin, resulting in an insulin molecule with alpha and beta chains at the ends and a C-peptide molecule. The synthesis of insulin and cleavage of C-peptide creates the molecules that are fundamental to the general functioning of the human body (Robertson, 2022).

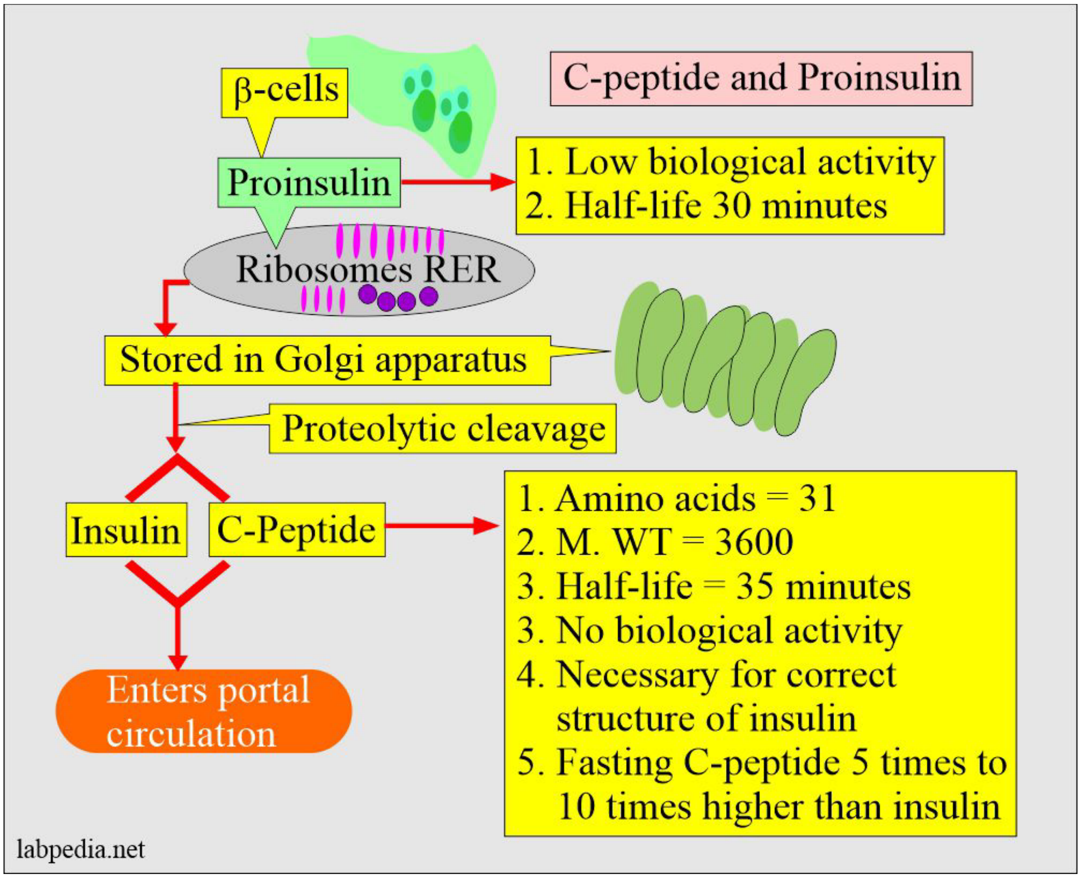

Figure 1. This is a model depicting each step in the production of insulin in a cell. In addition, the figure describes a few characteristics of C-peptide. This figure is from (Labpedia, 2020).

Structure and Derivation of C-peptide

C-peptide is produced during the separation of proinsulin in the synthesis of insulin and is a crucial component in the study of diabetes. The chain of 31 amino acids that connects the A and B terminals of proinsulin that make up the structurally complex C-peptide contains important information about its functions. C-peptide is derived as cleavage from the production of insulin. In this process, C-peptide is removed from proinsulin, and the COOH-terminal portion of the B-chain of insulin opens and is able to acquire the proper shape for effective binding with the insulin receptor. As a result, C-peptide molecules can be released into the bloodstream (Chan et al., 2020). Furthermore, C-peptide exhibits a unique chemical structure, $C_{129}H_{211}N_{35}O_{48}$. The precise arrangement of amino acids in the C-peptide has a significant impact on its stability, folding, and interactions with other biomolecules, which in turn affects how the peptide behaves (Novac et. al, 2019). C-peptide will have the secondary structure of a beta-pleated sheet since it is secreted by beta cells from the endocrine system that regulates the pancreas (Venugopal et al, 2023). The specific amino acid arrangement of the peptide molecule is Glu-Ala-Glu-Asp-Leu-Bln-Val-Gly-Gln-Val-Glu-Leu-Gly-Gly-Gly-Pao-Gly-Ala-Gly-Ser-Leu-Gln-Pro-Leu-Ala-Leu-Gl-Gly-Sea-Leu-Gln (Bhagavan and Ha, 2015).

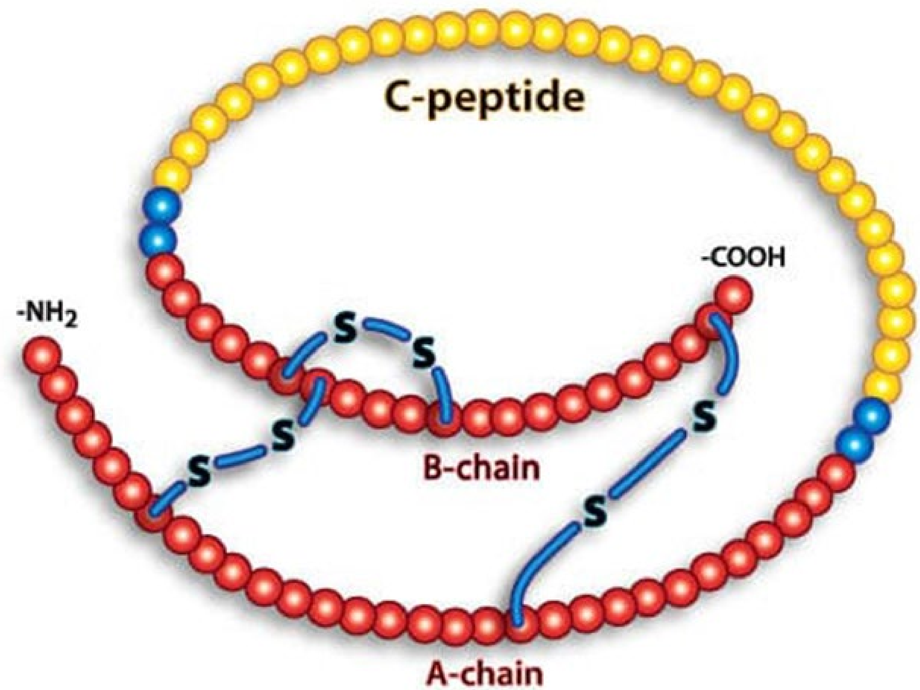

Figure 2. This is a model of the location of C-peptide in an insulin molecule. This figure is from (Clinical Laboratory Science, 2023).

C-peptide Tests

As discussed before, C-peptide is cleaved from proinsulin. Consequently, the amount of insulin that is available to the body is directly related to the amount of C-peptide concentration. Therefore, for doctors to determine what type of diabetes a patient has, they will measure the amount of C-peptide present in a patient with a C-peptide test. Although C-peptide tests cannot officially diagnose a patient with diabetes, they serve as an indicator of diabetes to medical professionals. Typically, patients who are mandated to take a C-peptide test have been diagnosed with hypoglycemia (a sign of diabetes) or a pancreatic tumor. To take a C-peptide test, the patient must give a blood or urine sample that will be collected over a 24-hour period. If a C-peptide test indicates a high level of C-peptide, the patient may have type 2 diabetes, kidney failure, or a pancreatic tumor. On the other hand, if the C-peptide test displays a low level of C-peptide, the patient may have type 1 diabetes, a severe infection, or liver disease. If one would like to improve their C-peptide levels, they will have to make a few necessary changes to their lifestyle to prevent them from falling victim to these diseases. To increase C-peptide levels, one should exercise and increase levels of Omega-3. To decrease C-peptide levels, one should exercise and eat a fiber-rich diet. C-peptide tests can help doctors and medical professionals determine what would be the appropriate treatment plan for the patient and help the patient live a more comfortable lifestyle (Medline Plus).

C-peptide's Neuroprotective Effects

The peptide has a variety of remunerative functions that also contribute to the well-being of the nervous system by reducing oxidative stress and increasing the expression of neurotrophic factors. In an article provided by the Journal of Internal Medicine, oxidative stress is caused as a result of an imbalance of ROS, or reactive oxygen species. If elevated, ROS could oxidize important molecules necessary for survival – such as DNA, lipids, and proteins (Drain et. al, 2017). Therefore, if C-peptide has the ability to reduce oxidative stress, the body will be able to maintain the important molecules required to live. On the other hand, C-peptide has been proven to have an increase in antioxidant enzymes such as SOD, also known as superoxide dismutase. This enzyme functions in neutralizing free radicals, such as ROS, by converting the harmful, free radicals into hydrogen peroxide and water to maintain cellular health and protect the body from progressive oxidative stress. Additionally, C-peptide can revamp the number of neurotrophic factors in the body, which are important to the regrowth of damaged nerves and the survival of the nerves. These neurotrophic factors may include the nerve growth factor NGF and IGF-1. According to the National Library of Medicine, in diabetic rats, there was a decreased level of NGF and IGF-1 and C-peptide provided neurotrophic support and expanded the size of neurofilaments (Ryk et. al, 2020). These factors work together to provide the neuroprotective benefits of C-peptide, making it a desirable treatment option for diabetic encephalopathy. As stated by the description, C-peptide can alleviate symptoms of cognitive deterioration. Therefore, there is a high potential for C-peptide to benefit diabetic encephalopathy, a disease that is mainly caused by the decline of the nervous system and brain health. By reducing the amount of oxidative stress and increasing the expression of neurotrophic factors, C-peptide is a worthy candidate to be used in future treatment plans for consequences of diabetes that result in the degeneration of the nervous system.

Disadvantages/Limits with using C-peptide

Although C-peptide was discovered to have many beneficial, therapeutic effects for the organs and organ systems in the body, there are many limitations to using C-peptide as a treatment course for diabetic patients. For one, if misused, C-peptide with the incorrect dosage of insulin may cause more damage than good. In a study conducted by several scientists, the researchers learned about the interactions between C-peptide levels and insulin treatment for patients who experienced type 2 diabetes. Patients with low C-peptide levels and patients with relatively average/high levels of C-peptide received additional insulin treatment. The results revealed that patients with low C-peptide levels experienced the best outcomes compared to patients with average/high levels of C-peptide. Hence, high C-peptide levels may not be as beneficial as previously thought. In addition, C-peptide is not a widely standardized treatment for hospitals regarding diabetic encephalopathy as it needs further testing for long-term effects and other issues. However, these disadvantages of using C-peptide are not limited to the dosage amounts and availability of the substance. C-peptide also has a short half-life, or the amount of time for the substance's concentration to decrease by half. On average, C-peptide has an estimated half-life of around 30-35 minutes. This results in the high probability that C-peptide will be in lower concentrations in the body in a smaller amount of time. For that reason, C-peptide may not be able to provide as many advantages to the body because of the lack of time it has to provide an appropriate amount of concentration of the substance to serve its purpose of reducing high blood sugar. Therefore, although C-peptide has the potential to become a major treatment plan or medication for diabetes or diabetic encephalopathy, there are still many limits that come with the substance. However, these disadvantages do not limit the abilities of what C-peptide can do for the human body. Although there are some qualms about the usage of C-peptide in the medical field, C-peptide still remains an important molecule that aids in providing remunerative effects for diseases and disorders. (Ko et al., 2009).

Research Behind the Beneficial Effects of C-peptide for Diabetic Encephalopathy

Recently, many scientists and researchers discovered that C-peptide may have positive effects regarding diabetic encephalopathy. Although there are many other treatment plans for diabetes, with further research, C-peptide could be responsible for more effective therapies and possible cures. Many different studies took part in determining how C-peptide could change the way scientists view diabetes. According to an article published by PubMed, one study used several methods to gauge how beneficial C-peptide could be for diabetes. They simulated these experiments by using diabetic BB/Wor-rats that mimic similar symptoms of diabetic encephalopathy, such as nerve cell apoptosis and brain deficits. In one experiment, the groups the scientists used in the experiment included seven-month diagnosed diabetic BB/Wor-rats – one with C-peptide treatment and one without – and BB/Wor-rats without diabetes and had no C-peptide treatment. In order to determine how exposure to C-peptide may affect the brain, the researchers collected the tissue of the BB/Wor-rats to determine its capability. This process consists of the researchers anesthetizing and bisecting the tissue of the brains in the BB/Wor-rats. With the aim of preserving the various proteins that may be produced in the brain in reaction to the C-peptide, one hemisphere of the brain was preserved in liquid nitrogen at -80 degrees Celsius. On the other hand, the other hemisphere was preserved by placing it into a buffered PBS, a solution called Phosphate-Buffered Saline that is used for diluting samples, embedded with 4% paraformaldehyde and paraffin. The researchers conducted this experiment to determine the levels of RAGE (a ligand cell-surface receptor responsible in signal transduction pathways that function for pro-inflammatory responses), GFAP positive astrocytes, or astrocytes that express proteins that function in maintaining the nervous system, and merged images. The researchers concluded by looking at the samples that there was a decreased level of RAGE. A decreased level of RAGE indicates less inflammation – a major symptom of diabetic encephalopathy (Sima et al., 2009). Moreover, the tissue samples showed that C-peptide had a positive effect for the symptoms of diabetic encephalopathy.

In addition, a behavioral study was conducted by the same research team. In this experiment, the scientists made the BB/Wor-rats participate in the Morris Water maze paradigm. The BB/Wor-rats were placed in a circular pool at a temperature of 28 degrees Celsius and submerged 3cm underwater. The pool was then divided into 4 quadrants. The rats were given a two-week training with three attempts to complete the maze for the final day of testing. In this experiment, the rats were timed (in seconds) to determine the latency period for the rats to reach the ending point platform. According to the results, in Quadrants 1, 2, and 4, the C-peptide-treated diabetic BB/Wor-rats were not statistically different from diabetic BB/Wor-rats with no treatment. However, C-peptide-treated diabetic BB/Wor-rats had a much more improved latency period in Quadrant 3 compared to diabetic BB/Wor-rats with no treatment. Therefore, C-peptide was able to help the BB/Wor-rats' performance in the Morris Water maze and showed cognitive improvement (Sima et al., 2009).

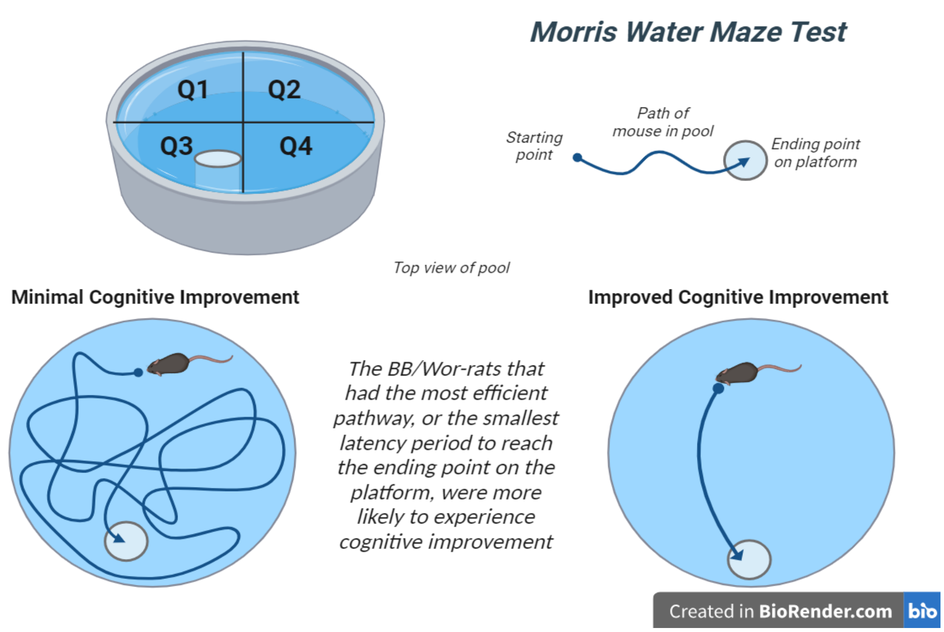

Figure 3. Here is a model that depicts the Morris Water Maze Test visually. This figure was created by Lara Kawle with Biorender.

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In addition, the same group of researchers used clinical data in order to determine how C-peptide may affect the body in BB/Wor-rats. In this experiment, the researchers determined the body weight, glucose levels (mmol/l), glycated Hb (%), serum insulin levels (pmol/l), and serum C-peptide levels (pmol/l) of the control group, the BB/Wor-rats with diabetes with no treatment, and the diabetic BB/Wor-rats with the C-peptide treatment. However, based on the data, the researchers concluded that the C-peptide treatment had no statistical difference in body weight, glucose, glycated Hb, and insulin levels. In spite of that, there was a significant increase in C-peptide levels in the diabetic rats (Sima et al., 2009).

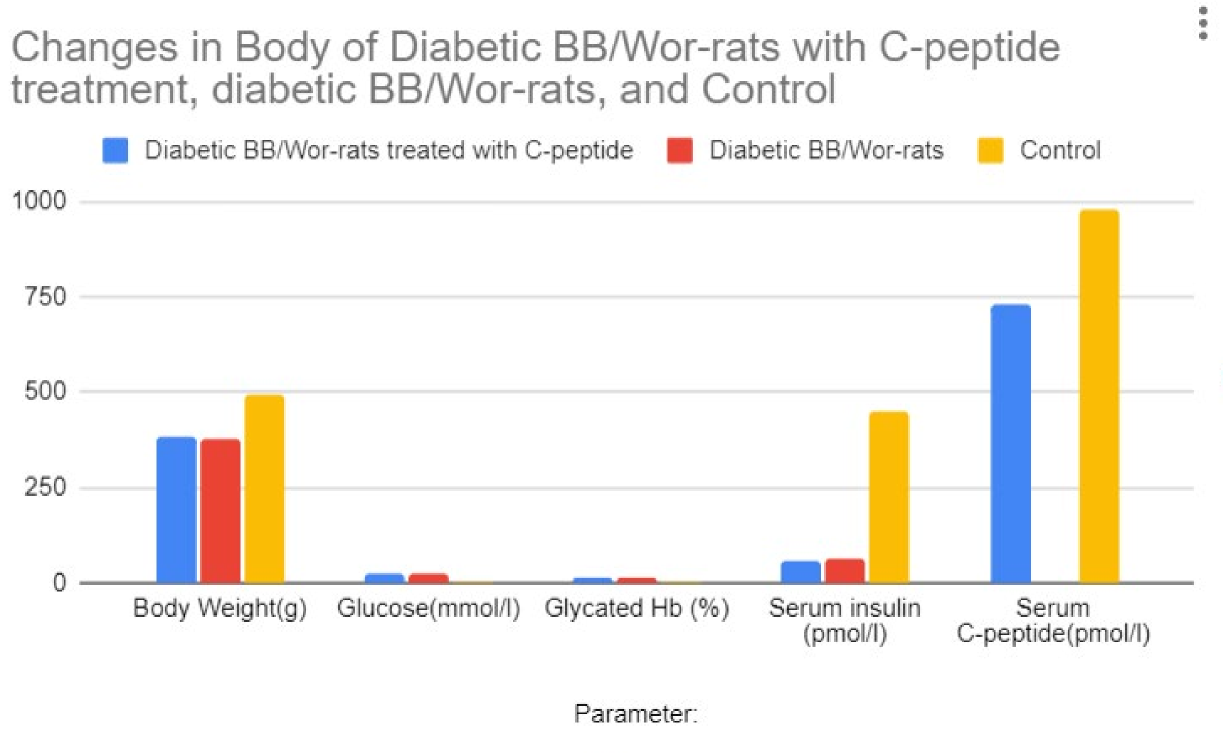

Figure 4. This graph highlights changes in the body in C peptide-treated diabetic BB/Wor-rats, diabetic BB/Wor-rats, and the control group. Data from (Sima et al., 2009). This figure was made by Lara Kawle with Google Spreadsheets.

Experimental Conclusions

The experiments conducted to test how efficient C-peptide may be on diabetic encephalopathy were able to conclude that C-peptide has positive results to prevent many of the consequences of diabetes, such as diabetic encephalopathy. To summarize, C-peptide was responsible for a decrease in pro-inflammatory responses and improved cognitive improvement. These responses by C-peptide could be able to relieve symptoms of diabetic encephalopathy. If C-peptide has the ability to have therapeutic effects for many of the different organ systems in the human body, with more extensive research, C-peptide could soon be discovered to possibly cure degenerative diseases in the nervous system or work as treatment plans for other disorders/diseases. Based on these results of the experiment, C-peptide has the potential for scientists to explore other factors of the molecule that can lead to improved functions of the body (Sima et al., 2009).

Areas of Uncertainty Regarding the Properties of C-peptide

Although C-peptide has been proven to provide curative properties to aid in the general well-being of the human body, there are many areas of uncertainty that scientists require further research. For one, scientists are still reviewing the appropriate dosing amounts for treatments. Without having a full understanding of how different dosing amounts of C-peptide may affect the body, researchers are not able to make an accurate prescription number for C-peptide in medications. This issue is connected to another problem researchers face with using C-peptide in combination therapies for diabetic patients: how C-peptide reacts with other substances and medications. In spite of the fact that C-peptide may have promising results for the body, scientists do not have a full in-depth understanding of how interactions with other molecules may cause the body to react. Misunderstandings about the interactions between the substances may cause devastating reactions in the body. Furthermore, even if C-peptide were to be confirmed to have optimistic results with further research, several other factors must be considered. These factors consist of the changes in functions of the molecule between different ages and sexes of people, the interactions with other hormones, and how accessible this possible medicine could be for our community. Scientists and researchers have a long journey ahead in order to determine how the discovery and incorporation of C-peptide in the medical field will change future prospects. However, C-peptide does show a favorable outlook with its promising functions.

How C-peptide Treatment Affects the Future of Medicine

C-peptide could be used in individualized healthcare strategies in the future of medicine. As researchers gain a better knowledge of how each patient responds differently to C-peptide therapy, it may be possible to construct custom treatments based on each patient's particular genetic makeup and medical background. The use of customized treatment has the potential to maximize therapeutic results and raise patient well-being. C-peptide can aid in more than treating diabetic encephalopathy. It can also help with other complications that may arise with problems similar to diabetes. For example, current research says that C-peptide may serve as a helpful indicator for beta-cell regeneration as well as organ transplantations. Even from the beginning of discussions of the molecule, C-peptide has been proven to have beneficial effects on the cardiovascular, nervous, and renal systems. Its groundbreaking therapies for the body can aid in other things, such as high blood pressure or the potential of a fatal stroke. It has been discovered to enhance the control of kidney blood flow and to improve the dilation of blood vessels, protecting kidney function in diabetics. With these ameliorative effects that come with C-peptide, it has the potential to change the face of medicine for future treatment plans. Therefore, it can be proven that C-peptide not only has beneficial effects for brain health, but also for renal health. Also, C-peptide therapy offers hope for treating diabetic nephropathy, an often fatal consequence of diabetes. Not only does it provide a series of benefits for diagnosing and treating diabetes in the future, C-peptide has the potential to facilitate the prevention of other fatal diseases.

Conclusion

Through the discussion, C-peptide was able to prove how beneficial it can be for future medication plans. Furthermore, C-peptide has the potential to reduce the effects of diabetic encephalopathy by improving brain health and displaying cognitive enhancement. In other words, C-peptide is known for its functions that aid in the health of many of the organs and organ systems of the body, specifically the nervous system. This may include its function of reducing oxidative stress, increasing the number of neurotrophic factors, and aiding in the regrowth of damaged nerves. More than 100,000 patients have died or suffered from diabetes or one of its complications (CDC, 2019). Without new treatment plans or medicines, the mortality rate caused by diabetes will increase. However, C-peptide provides the medical field an opportunity to lower that death rate. With further research and more clinical trials, C-peptide gives hope for a better future in addressing the difficulties of diabetes-related brain issues as the medical community works to fully understand the complicated role of C-peptide in brain health. With greater study, C-peptide therapy might be a useful addition to the available treatments and improve the lives of patients diagnosed with diabetic encephalopathy.

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