6

DEVELOPMENT OF HUMAN GROWTH HORMONES

Revathi A/P Paramasivam, Yuggheshinie A/P Murugananthan, Elizah Mohammed,
Noor Akhmazillah Mohd Fauzi

Faculty of Engineering Technology,
Universiti Tun Hussein Onn Malaysia,
Pagoh Higher Education Hub,
KM 1, Jalan Panchor,
84600 Muar, Johor, Malaysia.

Biotechnology plays significant role in today's lives especially in the scope of medical biotechnology which can be identified as red biotechnology to cure many diseases and for many other purposes after the modifications of the biotechnology has been made for this modern world. Growth hormone deficiency is one the diseases that has been cured by the development of human growth hormone by DNA recombinant technologies or efficient fermentation. Human growth hormone provides important benefits such as maintaining body and bone mass, promoting Iongitudinal growth lipolysis. strengthening muscles, enhancing weight loss and erectile dysfunction, and ensuring а wellfunctioning cardiovascular system. Development of human growth hormones has given good effects to the society, which is made of the consumers, people under the production team, businessmen, economics and the countries. Thus, the development of growth is an effective and successful idea which is very important for developing our lifestyle.

Keyword— Medical biotechnology, growth hormone deficiency, recombinant of DNA, development of human growth hormone

6.1 INTRODUCTION

6.1.1 Biotechnology

Based on the encyclopaedia, biotechnology is the use of biological processes, as through the exploitation and manipulation of living organisms or biological systems, in the development or manufacture of a product or in the technological solution to a problem [1]. Biotechnology is a very wide part of biology that involves biological systems and living organisms and parts to develop or to produce many products which is being so important on a daily basis in our human life which has been frequently overlapping with related scientific fields depending on the tools and its use.

Biotechnology can be also defined as a broad concept that have a hold within a broad scale of ways for improvising organism which is alive based on human needs nowadays such as domestication of animals, cultivation of plants and modifying to these through hybridization and breeding exercise that avail oneself of artificial selection. Biotechnology is actually regarding the basic science of biology such as biochemistry, embryology, microbiology, molecular biology, cell biology

and genetics which gives procedures for basic research in biology that can give support to it.

Biotechnology is the evolution and experimentation that will be done in the laboratory using bioinformatics for exploration, extraction, exploitation and production from any living organism and any source of biomass by means of biochemical engineering where high value-added products could be planned such as reproduced by biosynthesis, forecasted. formulated, developed, manufactured, and marketed for the purpose of sustainable operations and gaining durable patents rights [2]. Biotechnology nowadays covers many different areas such as medical biotechnology, industrial biotechnology, pharmacology biotechnology and agricultural biotechnology. For this report, we chose medical biotechnology as our major area in biotechnology.

6.1.2 Medical Biotechnology

In biotechnology, there are many major areas of biotechnology such as agricultural, industry biotechnology and so on, and one of it is medical biotechnology that also recognised as red biotechnology, which can be defined as a process where an organism is used to make any organism to be healthier by helping the body to fight disease and also to improve health care. Red biotechnology is a very crucial sector of the medical area and widely used in the field of gene therapy, clinical research and trials, and gene therapy such as growth hormone.

The life-threatening diseases has been treated by using engineering in genetics, which have been used to transform the allele of the DNA of bacteria and also different kind of organisms to produce biological based products such as drugs as insulin and growth hormone, and the development and production of various new medicines by utilizing red biotechnology in this modern world.

The potential of this medical biotechnology is tremendous and there are many advantages that can be listed in various branches of medicine such as engineering, product of biochips, cancer research and many more. Most of the research in red biotechnology has been a success to improve the quality of human life. One of the studies in red biotechnology development of growth hormone and that is what we chose for our case study.

6.1.3 Human Growth Hormone

Growth hormone which can be called Somatotropin is manufactured by the master gland also known as pituitary gland and this growth hormone has innumerable purposes including sustaining ordinary body composition and metamorphosis. Growth hormone also better-known as human growth hormones, indeed a mitogen, is actually a peptide hormone or protein hormone of about 190 amino acids that has been amalgamated and discharged by cells which can be exclaimed as somatotrophs where only between one and two milligrams of the hormones has been excreted each day in the anterior pituitary gland, that stimulates many cells in human and animals such as reproduction cell, regeneration cell and most importantly growth of and organisms either human or animals. Growth hormone is very important in human development and also important to increase the concentration of glucose and fatty acids which produce freely [12].

Other than that, growth hormone has many uses in the human body such as increasing calcium level in the body to strengthen the bone and also to escalate the mineralization in the cartilage [13]. Furthermore, human growth hormone also helps to increase the mass of the muscle via sarcomere hypertrophy, to give rise to the production of protein molecules and to develop lipolysis.

Growth hormone also helps us to stimulate or is important in the development or growth of all the internal organs excluding the brain in humans and animals. In addition, growth hormone also helps to stimulate our immune system and reduces liver uptake of glucose. Many more consequences of growth hormone on the body are conceivably listed and that shows how important is growth hormone or Somatotropin in the body humans and animals.

6.1.4 Growth Hormone Deficiency or Overabundance

Even though the growth hormone is very important for humans, there are some who will go through either deficiency or overabundance of the hormone which is secreted by anterior pituitary gland. In our study case, development in growth hormone has been an important thing for those who have been going through deficiency of growth hormone where it can cause more and different problems at different ages. For example, in

children, short body stature and growth failure are the major effects of growth hormone deficiency in a human body. The manifestation of human growth hormone deficiency in grown-up people is not so obvious and can cause deficiencies in strength, energy, and bone mass, and rise in cardiovascular risk.

In 1985, Genentech became the first biotechnology company to launch its own biopharmaceutical product called ProTropin which is actually manufactured growth hormone for children with lack of human growth hormone [14]. Many years ago, growth hormone has been purified from the anterior master gland from a cadaver or a dead human body was used to develop the growth hormone to useful protein or peptide products by using the recombinant DNA which can be used to treat children who were going through growth deficiency.

Development of growth hormone not only has been used for growth deficiency but for other purposes after biotechnology has been modified to this modern world. As the red biotechnology in the field of genetic engineering has been growing from time to time, the advantage of the growth hormone also has been changing and improving as the needs of the products needed by humans nowadays.

6.2 BIOTECHNOLOGY IN DEVELOPMENT OF HUMAN GROWTH HORMONES.

As we know earlier, Growth hormone (GH or somatotropin), is the hormone that stimulates the growth and cell reproduction in humans and other vertebrate animals. Both bone mass and muscle mass to their maximum level depend on the human growth hormones. However, 4 out of 10 people face failures of stimulation of growth hormones in their body, and 2 out of the 10 people do face growth disorder. A short healthy child who grows at a normal rate may be observed only, but the one who stopped growing or grows more slowly than expected will often need additional testing.

As time flies, and modern technologies are developing, biotechnology does contribute in the medical field too.

Biotechnology can be defined as biological knowledge and techniques application for product developing and problems solvent. Molecular biotechnology is subunits of the under medical biotechnology. It is known to employ the tools of molecular biology for example, recombinant DNA and gene cloning, to engineer the genetic information/ blueprint of living organisms to produce useful, marketable products. Generally, we know that protein is the key in every role for major movement forces in every process of all living organisms such as structural support, storage, growth, and catalysis in reactions. Protein engineering is related to protein biotechnology as contributes to the continuous process to obtain protein with desired properties.

Thus, biotechnologists have brought the idea of recombinant proteins in human growth hormones with help of technologies. The idea of recombinant proteins is known as the process where a form of protein is manipulated to produce large quantities of proteins which also have modified gene combinations and sequences. Actually, the resulting proteins from the expression of recombinant DNA are termed as recombinant proteins. Recombinant DNA technology really has played main roles in the medical field such as producing human insulin and also not forgotten human growth hormones. Beside medical, recombinant DNA has been used in agriculture too to improve the nutritional content in the plant. However, the new DNA sequence does not exist under normal circumstances and environmental conditions.

But how has this recombinant protein been produced? The first step is using the recombinant DNA technologies. Three major methods to recombinant DNA using technologies. First, as seen in Figure 1, is the transformation where in a vector which is known as plasmid is inserted a foreign DNA fragment which has been cut [8].

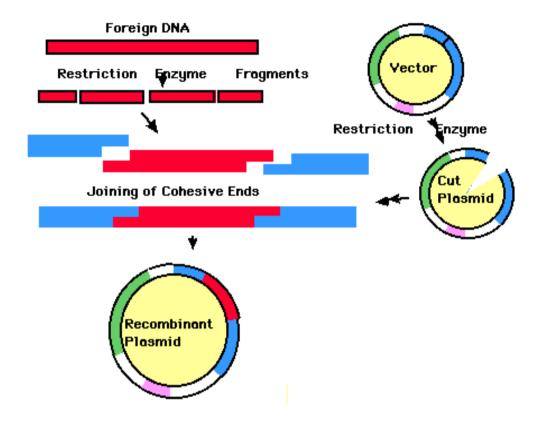


Figure 1: The process of recombinant protein [8].

Next method is known as Non-Bacterial Transformation or known as inserting vectors into host cells as shown in Figure 2. This transformation occurs without requiring the host cell. A foreign DNA injected directly into the nucleus of the recipient cell. To help inject foreign DNA into the recipient cell a method called Biolistic which has high velocity microprojectiles is used [8].

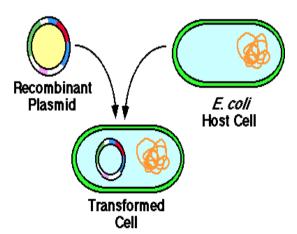


Figure 2: The process of inserting vectors into the host cell [8].

The third method is known as phage introduction, as illustrated in Figure 3. A phage DNA containing foreign DNA is inserted into the host cell's genome.

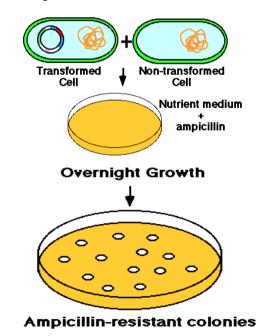


Figure 3: The process of phage introduction [8].

Production of recombinant protein for human growth has been carried out in various ways since the technology has evolved. Different proteins have their different properties thus producing recombinant proteins which are in good quality and purity should be done with the proper requirements and methods. For example, it can be done by obtaining the cDNA and creating expression cloning. So, we can summarize that protein biotechnology does help in developing our human growth as the useful protein peptide is produced biologically in the longest period.

Besides recombinant DNA technologies for developing human growth hormones. producing hiaher and recombinant human growth hormone (rHGH) through efficient fermentation can be carried out. The presence of impurities human growth hormones, for example deamidated forms of recombinant human growth hormones. It seems that separating the impurities is expensive. Thus, producing high purity of human growth hormone through fermentation is the best choice as it saves cost. For the production of hormone through fermentation fed-batch is carried out as it optimizes the fermentation of hormone to prevent formation by-product [4]. For the better genetic stability and scalability of the process, a good condition and parameters will be chosen. In this process. technologists use P. pastoris as the host cell which has two stages for the production of recombinant protein. The cell growth is developed on a fermentable carbon sauce in the first stage, and in the second stage, addition

of an inducer into the inducer of the expression system to initiate the production of heterologous proteins. On the other hand, they state that methanol does start off the expression of recombinant protein. As this productivity is a success, there are high chances that the production of human growth hormone is exceeded. Thus, the fed batch process was carried out to limit cell productivity [5].

Biotechnologists have introduced an expression system to develop human growth hormone, as shown in Figure 4. For this system. Escherichia Coli is the mainstream host to use as it is less costly too [5]. Escherichia coli under alkaline phosphatase (phoA) promoter. We can clearly see that human growth hormones are as important to treating dwarfism, obesity, wound healing and burn injury too. With a combination of genetic engineering, technology came up with an excellent way for heterologous protein production from microbes. After many ideas and proper trials Escherichia coli, which is one of the microbes been prove that it can overcome the lack of human growth hormones. A major complication was maintaining the cultivation medium of recombinant E.coli. Zamani et al. state that it must be done by response surface methodology for recombinant human growth hormone product. However, Patra et al have successfully optimized the solubility of recombinant human growth hormone inclusion bodies from E.coli

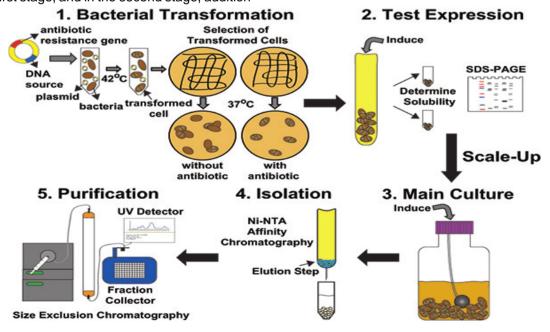


Figure 4: The process of expression system [8].

The development of the human growth hormones has also been carried out through isoform human growth hormones recombinant protein. As we see, human growth hormones have 2 major splicing which are 22kDa protein and a 20kDa protein, which is known as isomers. Using chromatography preparative SDS-PAGE (sodium dodecyl sulphate- separation of protein by mass occur through electrophoresis method) under a parameter, Grigorian with his other technologist isolated relatively had а stable mercaptoethanol-resistant 45 kDa human growth hormones. By removing the reduction through dialysis, they proved that the 22kDa human growth hormones are able to connect and support to produce 45 kDa human growth hormones. This isomer will increase the sequence to a larger mass and thus increase the productivity of human growth hormones too.

As we can see, biotechnology has contributed to the development of human growth hormones. With the presence of advanced technologies, we can solve many problems and defects that arise in the medical field. Finding solutions for defective production of human growth hormones has brought the medical field to a better development.

6.3 ADVANTAGES OF DEVELOPMENT OF HUMAN GROWTH HORMONES.

There are numerous benefits to the development of growth hormone to humans as mentioned before. Even though there are many more advantages, the main purpose of developing the growth hormone is to cure children who are experiencing insufficient growth hormone which causes short stature. Growth hormone is also being used nowadays for children and also adults who are going through a shortage of growth hormone. In addition, not only for their growth, growth hormone can also increase their muscle strength, they will have finger fracture healing, emphasize weight loss, well-built bones, possibility minimize the of cardiovascular disorder, enhancement in erectile dysfunction, reduce the probability of being obesity, for better multiple mental abilities and mood, and peaceful sleep. Moreover, growth hormone is also being used in animals for more products.

First of all, the main advantage of growth hormone development is for some children who are suffering from lack of enough

growth hormone by birth, growth deficiency, to reach their complete height by growing. In developing world countries such as Sudan and Somalia, normal human growth is not as easy and achievable as per other well-developed country due to the malnutrition problems over there. People in that country tend to face many issues during pregnancy. Growth deficiency can also be caused by severe kidney illness, children who have less weight when they are syndrome. Prader-Willi Turner's born. syndrome, pituitary tumor or disease where muscles have been wasted [15]. synthesized growth hormone helps these children to grow to their original height. For example, children who have short stature due to growth hormone deficiency which can be called Turner's syndrome, and kidney failure may be asked to take human growth hormone but children who have normal levels of growth will not grow taller even if they injected or take human growth hormone. Rather than that, Prader-Willi syndrome is a condition where the disorder is based on genetic issues that affects without races and ethnicities consideration. This syndrome makes the affected males or females with the obesity level potentially fatal [15]. Human growth hormone has been a great cure to treat children with this syndrome.

Secondly, after children, human growth hormone helps the adults to be treated who have growth deficiency which can happen by having problems afflicting the hypothalamus, pituitary gland or both. Hypothalamic-pituitary dvsfunction is a disorder where hypothalamus controls and synchronizes body functions of the pituitary gland [16]. Examples of glands affected by this condition are ovaries, testes, adrenal glands and thyroid glands. Adults who have growth deficiency may suffer from deficient thickness of cartilage which can give rise to osteoporosis, lower the mass of exhaustion, muscle. despondency, remembrance and enlargement of body fat surrounding the waist part. From the therapy with the growth hormone injections adults can experience the benefit of the treatment which can help to escalate the thickness of cartilage which can put a stop for simple fractures, to raise the thickness of the mass of muscle, escalate energy levels, to raise the capacity for exercises, reduce body fat and diminish the possibility of heart based problem. Human growth hormone plays a significant role in reducing the risk osteoporosis especially in postmenopausal women whose bone density dropped drastically.

Thirdly, from the therapy with growth hormone injections, it can aid in strengthening

the muscle significantly. A fact that cannot be denied is that human growth hormone ensures and upgrades the physical capacity of humans. Human growth hormone can stimulate collagen synthesis in the tendons and muscles of the skeletal where it can improve physical extent of individuals [17]. That is an important function of human growth hormone in the human body which is to increase muscle strength. Humans that have a lack of human growth hormone literally could not stimulate collagen synthesis in tendons and in skeletal muscles. By having this therapy, it helps to strengthen the muscle more and improves our capability to exercise because we can do more exercise and our muscles will find it difficult to wear off easily. Therefore, this can be an advantage of development of human growth hormone where it can strengthen the muscle more in a way that the body does not undergo the shock of foreign drugs.

Additionally, the other advantage that has been mentioned above is that human growth hormone can improve fracture healing [3]. We can surely have better fracture healing by having the aid of human growth hormone because it can speed up regeneration of cartilage or bone. This is because of the growth factor in the human growth hormone called IGF-1. The purpose of using IGF-1 in human growth hormone is to stimulate the metabolism of bone. The more the metabolism of bone stimulates, the faster and better the fracture can be cured as the metabolism speeds up the regeneration of cartilage or bone. Therefore, we can have better fracture healing because it can speed up the regeneration of cartilage or bone by putting in growth factors such as IGF-1 which is well known to stimulate the metabolism of bone [3]. In simple words, to make a fracture to heal there are several factors involved in the healing as in the hormones and cytokines of the human body where the secretion couldn't be fully reliable and so, the human growth hormone is needed as a remedy to get healed as soon as possible.

Furthermore, the advantage of developing human growth hormone is that it enhances weight loss. People who are experiencing obesity will have a finite feedback on releasing the stimuli for growth hormone and later on prescribing the human growth hormone, they will eventually lose weight and by losing weight, their response of growth hormone can be perfect or partially perfect. This happens when the growth hormone helps to secrete more lipolysis where this enzyme can break down the lipids and necessitate hydrolysis of triglycerides into glycerol and free

fatty acids and that is the cause of losing weight [18]. Accordingly, the advantage of developing human growth hormone is that it can enhance weight loss and because of this we can reduce the possibilities of having chronic diseases as Moreover, human growth hormone has the advantage of helping us to make the bones well-built and strengthen it [3]. The human growth hormone is very crucial for controlling the growth of the bone for the most part when we reach puberty when the growth hormone is released by the pituitary gland after stimulating. It is crucial to have a well-built bone mostly during puberty because that is when our bones will grow more stronger and will remain the same till we grow old. That is why it is important for us to have sufficient human growth hormone during our puberty and development of human growth hormone is very crucial for the ones who are lacking growth hormone.

The other advantage of developing human growth hormone is that it will help to reduce cardiovascular disease risk as adults who are suffering from lack of growth hormone, have more possibility of risk for cardiovascular disease which can lead to shortening the lifetime of the individual [19]. This is because when an adult is lacking or insufficient of human growth hormone, it will lead to many diseases such as obesity. Such diseases can lead to cardiovascular disease such as heart attack which can be caused by coronary occlusion, coronary thrombosis and many more. Coronary occlusion happens when the coronary artery has blockage and it stops or reduces the blood flow to the heart. Coronary thrombosis happens when the artery that supplies the heart muscle with blood to heart has been blocked by a blood clot. This can reduce the blood flow to the heart and can cause heart attack, and this happens mostly to those who are obese because of the blockage by the cholesterol or fat in the artery vein. Adults, who are experiencing a lack of human growth hormone can reduce the probability of getting cardiovascular disease by taking the injection of human growth hormone because they will eventually lose weight and the content of the cholesterol and fat in their body decrease.

Apart from reducing cardiovascular disease risk, developing human growth hormone gives us an advantage as it can give enhancement in erectile dysfunction [20]. There are two types of erectile which are erectile spines and erectile tissue. Erectile spines are defined as something that has the ability to become erect. Based on Oxford dictionary, erectile tissue has a meaning that denoting tissues which are capable of becoming

temporarily engorged with blood, particularly those of the penis or other sexual organs [6]. Erectile dysfunction is when the penis and other sexual organs fails to become erect. Human growth hormone is very important for the sexual organs as well such as male reproductive system. With the intake of human growth hormone, it takes up to three to four months for the erectile dysfunction to fully cure. Lack of human growth hormone can cause erectile dysfunction where the male reproductive organ fails to erect. Thereupon, developing human growth hormone can give benefit to humans especially males where enhancement in erectile dysfunction while reduced human growth hormone in ones' body might undermine sex drive.

Other than giving enhancement in erectile dysfunction, the advantage development of human growth hormone is it can prevent individuals from being obesity. As mentioned above in another point, obesity can many chronic diseases including cardiovascular disease such as heart attack, high blood pressure, osteoarthritis, asthma, diabetes, cancer and many more. Obesity is actually caused by accumulation of fats and cholesterol in the human body. Those cardiovascular diseases, asthma and also high blood pressure can be caused by clotting of veins and arteries by fats or cholesterol, or blood clotting. Osteoarthritis is a common disease happening around the world where mostly people going through obesity or elderly people will suffer from. This disease usually happens to people who are obese because when they walk or stand all their weight has been holding onto their leg. This can cause the cartilage that protects our bones from meeting each other will wear off easily and lead to osteoarthritis. Obesity can also lead to diabetes because of high intake of sugars and cancer. Developing human growth hormone could prevent obese people from all this disease as it can help them to lose weight easily and also it can improve the sensitivity of the insulin in their body so that when they have high intake of insulin their body could detect it and remove it from their body [18]. Thus, we cannot deny that development of human growth hormone benefits us in the way to help obesity individuals to lose weight and from getting chronic diseases as mentioned above.

On top of everything else, development of human growth hormone benefits humans for better multiple mental abilities and mood, and better sleep. Multiple mental abilities can be also called cognitive functions where those functions are intelligence, understanding.

perception, thinking, comprehension, conscious thought, apprehension, reason, awareness, thought, discernment, reasoning, enlightenment, learning and insight. As a human, we need cognitive function to think before doing something and in our daily life and it is very important. As for the people who lack human growth hormone, it is very difficult for them to have a normal multiple mental ability as the growth hormone is playing an important role for the human being to have those abilities. This development of human growth hormone helps adults that have insufficient human growth hormone could go through the therapy and improve their multiple mental abilities and it also can lead to a good mood. Basically, those who are having insufficient human growth hormone will undergo depression and they will be mentally unstable as it causes a lot of disease and disabilities in certain things so, by developing this human growth hormone and by going through the therapy or taking injections, they can have sufficient human growth hormone and be like other humans as well. Not to forget, development of human growth hormone also helps us to get better sleep.

In addition, another advantage of the human growth hormone is to improve the athletic performance because adults who is lacking in growth hormone will prescribe it and it helps them to have more strengthen muscles with increased mass, more active, energized and the capacity to do the exercise will be increased after the therapy of human growth hormone replacement in adults who are being an athlete and it became an advantage for them. Many people nowadays use human growth hormone to improve their athletic capacity so that they can perform well in the sports. Athletes tend to use it by combining it with the anabolic steroids as it gives more benefits where it helps to strengthen the muscle and to improve their ability. Hence, human growth hormone helps to improve athletic performance.

Advantage of human growth hormone is for older people who are using human growth hormone as an anti-aging product [21]. Nowadays people are very concerned about their looks and skin to maintain their beauty and to look young. And they are too desperate to have a solution because as their age increases their looks are getting older because of the consequences when the natural levels of human growth hormone by birth surely will reduce with age as it has been used since we are young. The level of testosterones can be increased by using human growth hormone therapy or injections and that can be the anti-

aging hormone as it can prevent their look and skin from aging easily. Wherefore, human growth hormone can actually increase the level of testosterone and that helps older people from aging easily and early.

The other advantage of developing recombinant human growth hormone than those that has been mentioned above is to have sufficient amount of human growth hormone all time to treat children who are going through growth deficiency and also for adults, who are using human growth hormone as anti-aging product and also for athletic purposes, and also for their health in this modern era. As we know, human growth hormone has been used since the late 1950's. Maurice Raben purified enough growth hormone from human pituitary gland to treat a boy who has been going through growth deficiency [11]. During that time, that is when we started to be more civilized and only after that all the countries started to develop. Before biotechnology arose, before the development of human growth hormone as recombinant human growth hormone, they were using pure human growth hormone which has been extracted from cadaver, dead human body and purified before using it on humans. An issue has occurred by doing so where at one point there will be insufficient human growth hormone when there is a lack of dead bodies in the country. For example, as per the study says, in the late 1970's the autopsy rate in the United States decreased because of the shortage of the available cadaver [11]. This causes the treatment for the growth deficiency children to stopped. As biotechnology recombinant human growth hormone has been created and used worldwide. This recombinant human growth hormone only contains a segment of the hormone and is inserted into the This can cause and ensure the bacteria. amount of human growth hormone to be used for the treatment and so on will be sufficient at all times.

Not only humans, development of growth hormone also gives advantages to humans by injecting the growth hormone in animals. Growth hormone helps the animals to yield more milk and more meat. For example, the bovine growth hormone in cows and the porcine growth hormone in pigs have been used in animals to increase the yield of milk and produce more meat without any harmful effects on humans. This can give a tremendous advantage to the meat seller and also the milk seller as they can sell more milks and meats daily and earn more money. They do not have to be worried about their daily outcome as they

are going to have enough meat and milk to be sold. The customers who are buying meat and milk also will have healthy meat and milk plus the stock will not finish early and easily.

6.4 DISADVANTAGES OF DEVELOPMENT OF HUMAN GROWTH HORMONES

As we know, when there are many advantages of this modern technology, there will be disadvantages also of development of human growth hormone to human beings. As there are many processes to prepare this human growth hormone, there must be many chemicals that have been used to preserve the human growth hormone and also that could cause side effects for the humans. Plus, we can also have those side effects because of excessive human growth hormone in the human body. Human growth hormone in the human body functions to maintain the growth of the organs and tissues and excessive use of it can cause more growth and lead to severe diseases. There are many side effects or we can say disadvantages by taking excessive developed human growth hormone.

First of all, the disadvantage or side effect of taking excessive developed human growth hormone by healthy adults is it might lead them to have Carpal tunnel syndrome [22]. Carpal tunnel syndrome is a normal and usual pain in the hand where it also feels numb when the main nerve in the hand, which can be called as the median nerve that travels through the wrist, is being compressed. The tissue that will compress the nerve is oedematous synovial and it happens because of excessive human growth hormone in an adult body. Excessive human growth hormone can raise the amount water and sodium retention in the extracellular fluid. This is what leads to the Carpal tunnel syndrome for an individual. Consequently, without our known, excessive or developed human growth hormone in our body can lead to side effects as mentioned before.

In addition, another side effect that might be caused by taking an excessive amount of human growth hormone is that it may heightened the body's resistance to insulin. When the insulin resistance in the body increases, it will resist the insulin which has the function to transport the glucose through blood to other tissues of our body such as muscle. The cells in our body will find it hard to detect or

will not be able to respond to the insulin. Humans who are obese will usually experience the insulin resistance and this surely led to diabetes mellitus type 2. This can be found out by the fasting insulin that has been increased. insulin resistance is increased by taking in the human growth hormone because the sensitivity towards the insulin also has been increased which can lead to more intake of glucose than required by the cells [23]. Therefore, the side effect of taking excessive developed human growth hormone is that it will increase the insulin resistance in the body and lead to diabetes mellitus type 2.

Furthermore, as mentioned before as for the Carpal tunnel syndrome, by taking in excessive developed human growth hormone also can cause arms and legs to be swollen and this causes joint and muscle pain. This swelling in the arms and legs is caused by the fluid retention in the tissue on the body where the fluid can be called as oedema. When adults, especially those who have a lack of human growth hormone in their body as for their looks or for the betterment of their athletic performance. consume these developed human growth hormones, they tend to face the fluid retention occurring in their arms and legs which eventually end up in swelling. Initially, the fluid retention is supposed to work on the boosting of protein synthesis. Meanwhile they do not face any particular effect when testosterone is consumed. However, long term consumption of human growth hormone heads to terrible cardiovascular problems. Athletes are faking their body appearances mostly to fulfil the requirement of target set for a particular group having fixed weight range. The thing they are absolutely not aware of is that excessive intake of human growth hormones to bulk up their bodies will ruin their health and risk their career. In real life, one must be awakened to the fact that an immoderate number of hormones, just like food intake, brings nothing but only harmful effects to respective bodies.

6.5 EFFECT OF DEVELOPMENT OF HUMAN GROWTH HORMONES TO THE SOCIETY

There is no doubt that technologies are getting advanced and more improved. This technology has contributed to a lot of new innovations, which help to solve our daily life problems. In the medical field, we have faced several health issues, deflects which need

multiple treatments. As we know, growth hormone defect is caused by less extractions of the hormones from the pituitary gland. In this generation, development of human growth hormones has really given a big impact to society. Most importantly, the number of adult growth hormone deficiency has reduced since biotechnology has contributed to overcome this deficiency.

One of the effects on society that we can talk about since the development of human growth hormones was introduced is that we. as humans, have less number of people who are facing growth problems. Some may feel down and not confident with their height or body mass, as they do have family genetics who have small bodies. This development has helped them to rebuild their confidence since their body size has improved. Without our realization, it boosts our inner positivity, where this positivity vibes to affect a person's daily routine. For example, your energy level will increase, you have more confidence to meet more people and carry out more activities in your daily life. Besides, our sleeping pattern and eating pattern might have improved too. Thus, we can clearly see that development in human growth hormones do bring improvement in a person's confidence and help them.

As we know, human growth hormones are related with our body muscle and stamina. The project of developing human growth hormones by biotechnology has brought the solution to increase our body muscle and stamina. Thus, improve our national can performance too where they can build up their stamina and muscle. This will boost them to increase their exercise capacity. They will be improve more concentrated to their performance in their sports too. The metabolic process in the athlete body will be increased which will supply more energy to each of the body cells in the entire body part. This change occurs as the tissue in the body begins to regenerate which increases the metabolism rate. A well-trained athlete is very important to a country as they will bring the country's name to the international community through sports. Being participants in a specific sport and presenting our country are good enough, but our athletes can win the competition too and make our country feel proud.

Besides that, we can state that human growth hormones not only relate with growth in the point of height and mass, it is also linked to our bones and their strength. Osteoporosis is one disease which is because of a lack of

hormones, which causes the density and the quality of bone to be reduced. This disease does affect our body movement, where patients might face bone pain. As the time increases too. their height of body will decrease. Research has proven that developing human growth hormones can also improve the immune system of our body. Increasing the quantity of growth hormone in the system can get rid of osteoporosis slowly [13]. This development has contributed to the medical field as it helps our doctors to solve the patient's problems besides giving medications only. So, we can clearly see that development in human growth hormones has helped our doctors in their medical field to solve the growth deficiency. Examples of beneficial human growth products are shown in Figure 5 below.



Figure 5: The sample products for human growth hormone [9].

Besides humans, we do inject these growth hormones to the animals. Clearly, we can see that these human growth hormones have increased the body size, muscle cells and improved the immune system while providing healthy bones [8]. Thus, this development also contributes to the agriculture field. For example, as shown in Figure 6, these growth hormones increase the production of milk in mammals and have healthier and quality meals. Thus, this helps the agricultures to improve their business where they can supply a healthy and fresh product. Thus, development of human growth hormones does improve agriculture and the mammalian's health too.

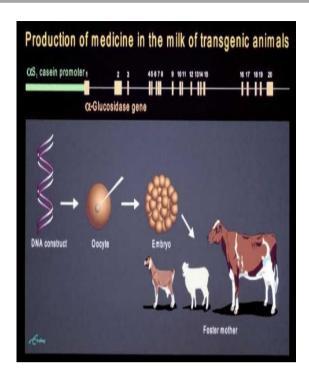


Figure 6: The production of medicine in the milk of transgenic animals [8].

development of human arowth hormones does give an impact to the economy of a county. Beside medical usage to increase growth and body size, this growth hormone is useful in the beauty care field. Human growth hormones do improve and build new cells and tissue and body; thus, it can also increase the level of testosterone. In this beauty care field, growth hormones are added in collagen as an ingredient. There are many collagen products. such as vitamins, face gel or face masks. This collagen improves their skin texture, where the hormones will work on to remove dirty cells that contain impurities and dirt. It helps them to look younger and more confident. This product not only will be selling domestically, but also internationally. Thus, this will improve our country's economy as many foreign entrepreneurs, businessmen, and investors will invest in that product.

Development of human growth hormones has helped improve certain countries' economies too. As the demand of the medication and the process of this development get higher, the medical field needs more people to work on this to increase the production. Thus, it has increased the vacancy of work in our society, which helps to improve their daily lifestyle. Besides that, many new companies have introduced themselves to the medical and business field, to work in the development of human growth hormone production as the

demand increases for many usages. As more companies are being introduced, the vacancy of the work increases too. This also helps to increase the production of human growth hormones. Inadvertently, our economy will improve. As the economics of our country improved well, it helps to improve the lifestyle of our society too. Thus, this development of human growth hormones has given a good effect to the society, who are the consumers, people under the production team, businessman, economics and the countries.

6.6 CONCLUSION

With this advanced technology, many technologists and scientists have contributed their work and innovation to the world to improve our daily lifestyle. Introducing biotechnology has brought better changes and development to many fields such as medical, agriculture, body care, beauty care and food industries. Based on our topic, we can conclude that human growth hormones are very important to our growth in height, body size and make our bones stronger. Due to some genetic disorder, it may affect the growth hormones which lead to growth deficiency in human beings. Introduction of biotechnology to develop human growth hormones has solved the problem of growth deficiency. Through modification of DNA and protein, injection, fermentation of the DNA and isolation, biotechnologists had developed and helped in the deficiency. People who have Dwarfism are really happy and grateful for this development in their human growth hormones.

We can see that applying this development of human growth hormones does give benefits to many parties. However, we must remember that we should not misuse this innovation and development for personal reasons. This is because it might have a bad effect on everyone, mainly on society. Our biotechnologist works hard on it to solve this genetic deficiency, so we should not take advantage of it as this development has its own cost. For example, some parties who are greedy to make more money and carry this development as a business. Nevertheless, we should remember that the development has been introduced not for self-benefits, but for everyone in this society. Thus, we can conclude that, development of human growth is an effective and successful idea which is very important for developing our lifestyle.

REFERENCES

- [1] Red biotechnology. (n.d.). Retrieved from https://encyclopedia2.thefreedictionary .com/Red biotechnology
- [2] Biotechnology. (2020, May 5).
 Retrieved from https://en.wikipedia.org/wiki/Biotechnology
- [3] Price, A. (2019, October 7). The Benefits & Dangers of Human Growth Hormone. Retrieved from https://draxe.com/nutrition/human-growth-hormone/.
- [4] Song, H., Jiang, J., Wang, X., & Zhang, J. (2017, March 4). High purity recombinant human growth hormone (rhGH) expression in Escherichia coli under phoA promoter. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articl es/PMC5398570/.
- [5] Bozkurt, B., & Çalık, P. (2012). Strategy development for therapeutic protein production by Pichia pastoris: human growth hormone. *New Biotechnology*, 29. doi: 10.1016/j.nbt.2012.08.299
- [6] Erectile: Definition of Erectile by Lexico. (n.d.). Retrieved from https://www.lexico.com/en/definition/er ectile
- [7] Bscandlen. (2018, February 23).
 Creating solutions for health and nutrition. Retrieved from https://dnacenter.com/blog/creating-solutions-health-nutrition/
- [8] Brennan, J. (2019, March 2). The Production of Recombinant Human Growth Hormones by Recombinant DNA Technology. Retrieved from https://sciencing.com/productionrecombinant-human-growthhormones-recombinant-dnatechnology-2230.html.
- [9] {BLR 807} Human Growth Hormone SmithKline Beckman BioTechnology General. (1988). *Biotechnology Law Report*, 7(4), 280–281. doi: 10.1089/blr.1988.7.280
- [10] Harvard Health Publishing. (n.d.). Growth hormone, athletic performance, and aging. Retrieved from

- https://www.health.harvard.edu/diseas es-and-conditions/growth-hormone-athletic-performance-and-aging.
- [11] Growth hormone treatment. (n.d.). Retrieved May 20, 2020, from https://www.wikidoc.org/index.php/Gro wth_hormone_treatment
- [12] Robert, D. U. (n.d.). Growth hormone Retrieved from https://www.britannica.com/science/gr owth-hormone
- [13] Vittorio, L. & Vittorio, E. B. (2014). Effect of GH/IGF-1 on Bone Metabolism and Osteoporosis Retrieved from https://www.hindawi.com/journals/ije/2 014/235060/
- [14] Cronin, M. J. (1997). Pioneering recombinant growth hormone manufacturing: pounds produced per mile of height. Retrieved from https://pubmed.ncbi.nlm.nih.gov/92552 18/
- [15] Dana, S. H. (2008). Treatment of short stature and growth hormone deficiency in children with somatotropin (rDNA origin) Retrieved from https://www.ncbi.nlm.nih.gov/pmc/artic les/PMC2727887/
- [16] Soumyadeep, D. & Constance, T. N. (2017). Chapter Six - Erythropoietin and Hypothalamic–Pituitary Axis. Retrieved from https://www.sciencedirect.com/science/article/abs/pii/S0083672917300201
- [17] Simon, D., Katja, M. H., Lars, H., Abigail, L. M., Peter, S., Michael, R., Kenneth, S., Søren, R., Anne-Marie, K., Michael, H. R., Allan, F. & Michael, K. (2010). Growth hormone stimulates the collagen synthesis in human tendon and skeletal muscle without affecting myofibrillar protein synthesis. Retrieved from

- https://pubmed.ncbi.nlm.nih.gov/19933 753/
- [18] Pombo, M., Pombo, C. M., Astorga, R., Cordido, F., Popovic, V., Garcia-Mayor, R. V., et al.(1999). Regulation of growth hormone secretion by signals produced by the adipose tissue. J Endocrinol Invest. Retrieved from https://pubmed.ncbi.nlm.nih.gov/10442 566/
- [19] Isgaard, J. (2004). Cardiovascular disease and risk factors: the role of growth hormone. Retrieved from https://pubmed.ncbi.nlm.nih.gov/15591 764/
- [20] Metro, M.D. (2015). Erectile Dysfunction ED Treatment with HGH and Testosterone. Retrieved from https://www.metro-md.com/erectiledysfunction-ed-treatment-with-hgh-andtestosterone/
- [21] Andrzej, B. (2019). Growth Hormone and Aging: Updated Review. Retrieved from https://www.ncbi.nlm.nih.gov/PMC/arti cles/PMC6305861/
- [22] Mary, A. D. (2021). Human Growth Hormone (HGH). Retrieved from https://www.webmd.com/fitness-exercise/human-growth-hormone-hgh
- [23] Shin-Hye, K. & Mi-Jung, P. (2017). Effects of growth hormone on glucose metabolism and insulin resistance in human. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5642081/