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MATRIC NUMBER: 16/SCI17/002

BTG 406: METABOLIC ENGINEERING

ASSIGNMENT

Write on hormonal regulation of metabolism.

A hormone is any member of a class of signaling molecules, produced by glands in multicellular organisms that are transported by the circulatory system to target distant organs to regulate physiology and behavior. regulation of the vital activities in animals and man through the entrance of hormones into the blood; one of the systems of functional self-regulation, closely connected with the nervous and humoral systems of regulation and coordination of functions.

Hormones, secreted into the blood by endocrine glands, are carried throughout the body and influence the states and activities of various organs and tissues.

Hormones are divided into two groups; according to their type of action. Some hormones act upon specific “target” organs: thyrotropic hormone acts chiefly upon the thyroid gland, adrenocorticotropic hormone (ACTH) upon the adrenal cortex, and estrogens upon the uterus. Other hormones—corticosteroids, growth (somatotropic) hormone, and certain others exert a generalized effect upon all body tissues. Insulin, for example, affects hydrate metabolism by activating the hexokinase reaction, and it can also stimulate the biosynthesis of protein. Testosterone and other androgens intensify processes of assimilation (anabolic effect); their introduction is accompanied by the retention of nitrogen in the body. Glucocorticoids produce various changes in metabolism, stimulate the formation of glycogen in the liver, inhibit the utilization of glucose in the periphery, and intensify the breakdown of proteins (especially in connective and lymphoid tissues). Estrogens stimulate the synthesis of phospholipids and protein in the uterus and cause hydration of the tissues of that organ. Growth hormone intensifies protein synthesis and influences fat, phosphorus, and calcium metabolism.

The effect of hormones upon metabolism is apparently associated with a change in the rate of enzyme reactions; in the majority of cases this is accomplished by activating the enzymes. The effect of hormones on protein biosynthesis is associated with the stimulation of messenger ribonucleic acid (messenger RNA) formation. (Messenger RNA determines the structure of the protein to be synthesized.) Hormonal regulation of metabolism ensures the normal functioning of organs and tissues. Growth and sexual maturation of the body are regulated by the growth and sex hormones. Mobilization of the body’s forces in case of need is also accomplished by hormonal regulation. For example, in the event of danger and the muscular tension produced by it, the entry of adrenalin into the blood is increased, raising the blood sugar level and increasing the blood supply to the heart and brain. Under intensely harmful influences, the manufacture of adrenocorticotropic and other hormones is increased.

The diversity of hormonal activity requires, in order to ensure normal body activity, the precise correspondence of hormone output to the body’s needs. This precise and delicate correspondence is ensured by the mutual influence of nervous, humoral, and hormonal factors. In some cases communication of the nervous system with the endocrine gland is direct. This has been proved for the adrenal medulla: stimulation of the splanchnic nerve leads to the increased secretion of adrenalin. In other cases the stimulus is transmitted along nerve fibers first to the hypothalamus, where substances are then formed (releasing factors) that enter the pituitary and produce the additional secretion of pituitary (so-called tropic) hormones, which in turn stimulate the formation of the appropriate hormone in the peripheral gland. Although releasing factors have not been obtained in pure form, their formation in the hypothalamus has been proved for adrenocorticotropic, luteinizing, follicle-stimulating, somatotropic, and several other hormones.

Hormone secretion is also regulated according to the principle of the feedback mechanism (plus-minus interaction). If for any reason the amount of a given hormone in the body is increased, this leads to inhibition of releasing factor secretion by the hypothalamus, which leads to a decrease in secretion of the corresponding tropic hormone by the pituitary, and finally to a decrease in hormone secretion by the peripheral gland. If, on the other hand, the concentration of a given hormone in the blood decreases (for example, through its accelerated decomposition in the tissues), this leads to increased secretion of the releasing factors, increased secretion of the tropic hormones by the pituitary, and increased biosynthesis of the hormone in the peripheral glands.

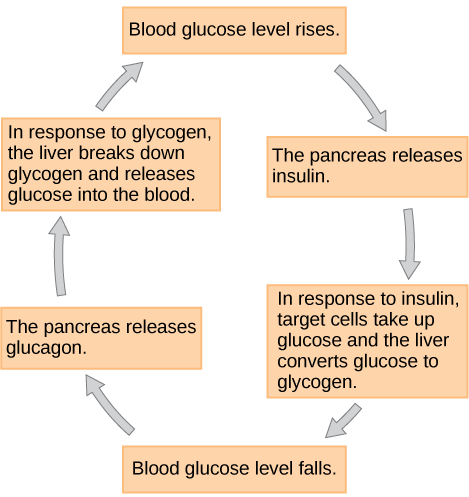
The self-regulation mechanism has definite significance in hormonal regulation. Thus, it has been shown that increased concentration of glucose in the blood leads to increased secretion of insulin and, consequently, to decreased concentration of glucose. Sodium salt deficiency stimulates secretion of aldosterone, a hormone of the adrenal cortex, whose effect is due to acceleration of the processes of reabsorption of sodium salts in the renal tubules, and thereby to their retention in the body. Thus, the system that regulates hormone production ensures the hormonal regulation of metabolism and other body functions.

Hormonal Regulation of Metabolism

Blood glucose levels vary widely over the course of a day as periods of food consumption alternate with periods of fasting. Insulin and glucagon are the two hormones primarily responsible for maintaining homeostasis of blood glucose levels. Additional regulation is mediated by the thyroid hormones.

Regulation of Blood Glucose Levels by Insulin and Glucagon

Cells of the body require nutrients in order to function, and these nutrients are obtained through feeding. In order to manage nutrient intake, storing excess intake and utilizing reserves when necessary, the body uses hormones to moderate energy stores. Insulin is produced by the beta cells of the pancreas, which are stimulated to release insulin as blood glucose levels rise (for example, after a meal is consumed). Insulin lowers blood glucose levels by enhancing the rate of glucose uptake and utilization by target cells, which use glucose for ATP production. It also stimulates the liver to convert glucose to glycogen, which is then stored by cells for later use. Insulin also increases glucose transport into certain cells, such as muscle cells and the liver. This results from an insulin-mediated increase in the number of glucose transporter proteins in cell membranes, which remove glucose from circulation by facilitated diffusion. As insulin binds to its target cell via insulin receptors and signal transduction, it triggers the cell to incorporate glucose transport proteins into its membrane. This allows glucose to enter the cell, where it can be used as an energy source. However, this does not occur in all cells: some cells, including those in the kidneys and brain, can access glucose without the use of insulin. Insulin also stimulates the conversion of glucose to fat in adipocytes and the synthesis of proteins. These actions mediated by insulin cause blood glucose concentrations to fall, called a hypoglycemic “low sugar” effect, which inhibits further insulin release from beta cells through a negative feedback loop.



Diagrammatic representation of the regulation of blood glucose level by insulin and glucagon.

## Regulation of Blood Glucose Levels by Thyroid Hormones

The basal metabolic rate, which is the amount of calories required by the body at rest, is determined by two hormones produced by the thyroid gland: thyroxine, also known as tetraiodothyronine or T4, and triiodothyronine, also known as T3. These hormones affect nearly every cell in the body except for the adult brain, uterus, testes, blood cells, and spleen. They are transported across the plasma membrane of target cells and bind to receptors on the mitochondria resulting in increased ATP production. In the nucleus, T3 and T4activate genes involved in energy production and glucose oxidation. This results in increased rates of metabolism and body heat production, which is known as the hormone’s calorigenic effect.

T3 and T4 release from the thyroid gland is stimulated by thyroid-stimulating hormone (TSH), which is produced by the anterior pituitary. TSH binding at the receptors of the follicle of the thyroid triggers the production of T3 and T4 from a glycoprotein called thyroglobulin. Thyroglobulin is present in the follicles of the thyroid, and is converted into thyroid hormones with the addition of iodine. Iodine is formed from iodide ions that are actively transported into the thyroid follicle from the bloodstream. A peroxidase enzyme then attaches the iodine to the tyrosine amino acid found in thyroglobulin. T3 has three iodine ions attached, while T4 has four iodine ions attached. T3 and T4 are then released into the bloodstream, with T4 being released in much greater amounts than T3. As T3is more active than T4 and is responsible for most of the effects of thyroid hormones, tissues of the body convert T4 to T3 by the removal of an iodine ion. Most of the released T3 and T4 becomes attached to transport proteins in the bloodstream and is unable to cross the plasma membrane of cells. These protein-bound molecules are only released when blood levels of the unattached hormone begin to decline. In this way, a week’s worth of reserve hormone is maintained in the blood. Increased T3 and T4 levels in the blood inhibit the release of TSH, which results in lower T3 and T4 release from the thyroid.

The follicular cells of the thyroid require iodides (anions of iodine) in order to synthesize T3 and T4. Iodides obtained from the diet are actively transported into follicle cells resulting in a concentration that is approximately 30 times higher than in blood. The typical diet in North America provides more iodine than required due to the addition of iodide to table salt. Inadequate iodine intake, which occurs in many developing countries, results in an inability to synthesize T3 and T4 hormones. The thyroid gland enlarges in a condition called goiter, which is caused by overproduction of TSH without the formation of thyroid hormone. Thyroglobulin is contained in a fluid called colloid, and TSH stimulation results in higher levels of colloid accumulation in the thyroid. In the absence of iodine, this is not converted to thyroid hormone, and colloid begins to accumulate more and more in the thyroid gland, leading to goiter.

Disorders can arise from both the underproduction and overproduction of thyroid hormones. Hypothyroidism, underproduction of the thyroid hormones, can cause a low metabolic rate leading to weight gain, sensitivity to cold, and reduced mental activity, among other symptoms. In children, hypothyroidism can cause cretinism, which can lead to mental retardation and growth defects. Hyperthyroidism, the overproduction of thyroid hormones, can lead to an increased metabolic rate and its effects: weight loss, excess heat production, sweating, and an increased heart rate. Graves’ disease is one example of a hyperthyroid condition.