



## Role of hormones in protein metabolism

Pooja Singh\*, Ritu P Dubey, Alka Gupta

Department of Food Nutrition and Public Health, Naini Agriculture Institute  
Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, Uttar Pradesh, India

Corresponding Author: Pooja Singh

### Abstract

Hormones influence a wide range of functions, including growth and development, reproduction, and nutrition metabolism, and they regulate the operation of entire organs. Hormones also regulate blood sugar (glucose) and salt levels, as well as how the body stores and uses energy.

Protein metabolism, which includes the body's production (anabolism) and breakdown (catabolism) of proteins, is mostly regulated by hormones. The majority of hormones either promote the creation of particular proteins, in particular tissues, or more broadly. With a daily turnover of 300–400 g, protein metabolism is an ongoing cycle of synthesis and breakdown. In general, it has been demonstrated that protein anabolic hormones increase the uptake of amino acids by tissues, increase protein biosynthesis through a mechanism separate from the increased uptake of amino acids, increase the labeling of ribonucleic acid (RNA) by tissues in addition to stimulatory effects on precursor entry to stimulate RNA polymerase activity, increase the activity of ribosomes assayed in cell-free systems, change the patterns of polysomes and endoplasmic reticulum, and, in certain cases, stimulate the synthesis of deoxyribonucleic acid (DNA).

**Keywords:** Protein synthesis, insulin, growth factors, humans, anabolism, catabolism, DNA, RNA

### Introduction

Throughout life, proteins are constantly produced and broken down. Maintaining cellular structure, enzyme activity, muscle function, tissue healing, and adaptation all depend on this process, which is called protein turnover. An individual's protein balance can be classified as positive, neutral, or negative based on the ratio of protein synthesis to protein breakdown.

One important regulator of this equilibrium is hormones. Interactions with intracellular signaling pathways, physical activity, and nutritional availability mediate their effects. The relationship between endocrine signals and the mTORC1 pathway—a key regulator of translational activity and muscle protein synthesis—is especially highlighted by recent study (Gharahdaghi *et al.*, 2021) [2]. Since skeletal muscle is the body's primary source of protein, hormone control is particularly crucial in this area. Thus, changes in hormonal state can affect muscle growth, maintenance, and atrophy. The hormonal milieu can be altered by exercise, aging, insulin resistance, fasting, and chronic illness, all of which can change protein turnover (Gharahdaghi *et al.*, 2021) [2].

Main hormones that affect protein metabolism—insulin, growth hormone, IGF-1, testosterone, estrogen, glucocorticoids, glucagon, thyroid hormones, catecholamines.

### Hormonal Regulation of Protein Metabolism

#### Insulin

One of the most crucial hormones in the metabolism of nutrients is insulin. It is secreted by pancreatic  $\beta$ -cells after consuming nutrients and plays a significant part in controlling the metabolism of proteins, lipids, and glucose. Insulin has a potent anti-catabolic impact on skeletal muscle. It helps to preserve muscle protein by inhibiting the breakdown of proteins. However, the availability of amino acids is crucial for insulin to stimulate the synthesis of

muscle proteins. According to Abdulla *et al.* (2016) [1], insulin and dietary amino acids combine to produce an anabolic environment.

Insulin triggers intracellular signaling pathways that include Akt, phosphatidylinositol-3-kinase (PI3K), and downstream elements that control protein turnover. Leucine in particular independently activates mTORC1, which facilitates the start of translation and the synthesis of muscle proteins.

Therefore:

Insulin  $\rightarrow$   $\downarrow$  muscle protein breakdown

Amino acids/leucine + insulin  $\rightarrow$   $\uparrow$  anabolic environment and protein synthesis

In a comprehensive review and meta-analysis, Abdulla *et al.* (2016) [1] showed that insulin significantly inhibits the breakdown of muscle proteins, although its impact on muscle protein synthesis is more reliant on the supply of amino acids. This regulation can be disrupted by insulin resistance, which is increasingly linked to reduced muscle anabolic responses and loss of muscle quality, especially with aging

#### Growth Hormone

The anterior pituitary secretes growth hormone (GH), which is a crucial regulator of protein metabolism and growth. GH helps maintain lean body mass and stimulates tissue growth. Through IGF-1, GH can indirectly affect muscle metabolism and enhance the absorption of amino acids and protein synthesis. Age, dietary status, activity, and the degree of physiological stress all affect its impact. GH should not be viewed as a stand-alone anabolic signal, according to recent study. Interactions with IGF-1, insulin, amino acid availability, and exercise-induced signaling determine its effects (Kraemer *et al.*, 2020) [4]. Exercise length and intensity can have a significant impact on the hormonal reaction. The major effects of GH include;

increased amino-acid utilization, promotion of protein synthesis, support of lean body mass, stimulation of IGF-1 production, regulation of substrate utilization, support of tissue growth and repair.

### **Insulin like growth factor-1**

An essential mediator of GH's growth-promoting effects is IGF-1. Although the liver produces the majority of it, skeletal muscle also synthesizes it locally. By interacting with its receptor, IGF-1 triggers intracellular signaling pathways related to tissue remodeling, protein synthesis, and cellular growth. Thus, one crucial endocrine mechanism regulating muscle growth is the GH/IGF-1 axis. The connection between testosterone, estrogen, and the GH/IGF-1 axis in muscle adaptation was examined by Gharahdaghi *et al.*, (2021)<sup>[2]</sup>. They concluded that rather than functioning independently, hormonal effects on muscle are intimately linked to exercise-induced signaling and amino acid availability. IGF-1 contributes to; muscle protein synthesis, muscle cell growth, tissue repair, muscle remodeling, maintenance of lean tissue.

However, the relationship between circulating IGF-1 and local muscle IGF-1 signaling is complex, and circulating concentrations alone do not completely explain changes in muscle protein synthesis.

### **Testosterone and Protein Metabolism**

One important anabolic steroid hormone that contributes to the growth and upkeep of skeletal muscle is testosterone. It affects anabolic signaling, satellite-cell activity, and gene transcription mainly through the androgen receptor. The significance of testosterone in controlling muscle mass and physical function is still being shown by recent studies. According to Gharahdaghi *et al.*, (2021)<sup>[2]</sup>, testosterone plays a significant role in controlling muscle adaption, especially when it interacts with the androgen receptor and anabolic signaling pathways. Crucially, new research that was released in 2026 looked more closely at the biochemical underpinnings of testosterone's anabolic effects on skeletal muscle. Treatment with testosterone has been linked to gains in strength and muscle growth, confirming its function as an anabolic regulator. Testosterone can promote; increased muscle protein synthesis, increased lean body mass, muscle hypertrophy, satellite-cell activation, improved muscle strength, maintenance of muscle tissue. Testosterone deficiency, particularly in older men, can contribute to reduced muscle mass and impaired physical function.

### **Estrogen and Protein Metabolism**

Estrogen has significant impacts on skeletal muscle even though it is typically considered in reference to reproductive physiology. Skeletal muscle expresses estrogen receptors, and estrogen signaling can affect mitochondrial activity, muscle repair, and exercise adaption.

Gharahdaghi *et al.*, (2021)<sup>[2]</sup> emphasized the significance of estrogen in muscle adaptation, especially in women, where changes in muscle mass and adaptations to exercise may be influenced by hormonal oscillations during the menstrual cycle and menopause. Reduced muscle quality and physical function may result from declining estrogen concentrations after menopause, which are linked to changes in body composition. Thus, estrogen may contribute to; muscle maintenance, muscle repair, regulation of mitochondrial function, exercise adaptation, preservation of muscle quality.

### **Glucocorticoids and Protein Catabolism**

Among the most significant catabolic hormones influencing protein metabolism are glucocorticoids, especially cortisol. Glucocorticoids aid in the mobilization of nutrients required to fulfill elevated energy demands during acute stress. However, skeletal muscle is negatively impacted by long-term glucocorticoid increase. While inhibiting protein synthesis, glucocorticoids promote protein degradation via the autophagy–lysosomal pathway and the ubiquitin–proteasome system. Muscle atrophy may eventually result from this loss of muscle protein (Braun & Marks, 2015)<sup>[14]</sup>. According to Braun and Marks (2015)<sup>[14]</sup>, glucocorticoids can counteract anabolic signals like insulin, accelerate protein breakdown, and decrease translation start. Further studies have shown that long-term exposure to glucocorticoids can cause insulin resistance in skeletal muscle and other tissues (Hwang & Lee, 2021)<sup>[3]</sup>. Glucocorticoid-induced muscle wasting is particularly relevant to; Cushing's syndrome, long term corticosteroid therapy, critical illness, chronic inflammatory disease, cancer-associated wasting, aging-related muscle loss. A 2022 review also emphasized that glucocorticoids can increase muscle protein degradation while decreasing protein synthesis, contributing to muscle atrophy and metabolic dysfunction.

### **Glucagon and Amino-Acid Metabolism**

It has long been known that glucagon, which is released by pancreatic  $\alpha$ -cells, keeps blood glucose levels stable during fasting. But its function goes beyond the metabolism of carbohydrates. In addition to promoting hepatic amino acid use, glucagon also aids in ureagenesis, gluconeogenesis, and amino acid catabolism. According to Zeigerer *et al.*, (2021)<sup>[6]</sup>, glucagon is a pleiotropic metabolic hormone that has significant effects on both whole-body energy homeostasis and liver metabolism. The connection between glucagon and skeletal muscle protein metabolism has also been studied recently. By increasing leucine oxidation, glucagon may decrease the amount of leucine available for mTOR signaling-mediated stimulation of muscle protein synthesis (Fujita *et al.*, 2021)<sup>[5]</sup>. Therefore, glucagon may contribute to; Hepatic amino-acid catabolism, Urea production, Gluconeogenesis, amino-acid oxidation, regulation of circulating amino acids, modulation of muscle protein synthesis. The metabolic role of glucagon is particularly relevant during fasting and conditions characterized by altered insulin–glucagon balance.

### **Thyroid Hormones**

Skeletal muscle physiology, energy metabolism, and mitochondrial function are all significantly impacted by the thyroid hormones T3 and T4. Both protein synthesis and protein breakdown are impacted by thyroid hormone signaling. While thyroid hormone excess or deficit can disrupt muscle protein turnover, appropriate thyroid hormone concentrations are required for optimal muscular development and function. Thyroid hormone signaling, IGF-1, and autophagy in skeletal muscle have all been the subject of recent studies. The connection between autophagy, IGF-1, and thyroid hormone signaling as factors affecting skeletal muscle physiology was covered in a 2024 review. Muscle atrophy may be a result of accelerated protein turnover and breakdown in hyperthyroidism. Weakness and poor physical performance might result from decreased metabolic activity and altered muscle function in hypothyroidism.

Thus, thyroid hormones regulate; Protein turnover, mitochondrial activity, muscle energy metabolism, muscle growth and development, muscle repair and function.

### Catecholamines

Exercise, stress, and other physiological stresses cause the release of catecholamines, mainly noradrenaline and adrenaline. They primarily affect the metabolism of carbohydrates and fats, but they can also affect the metabolism of amino acids and the turnover of proteins. The length and severity of stress, as well as how they interact with other hormones, determine their effects.

Catecholamines aid in the redistribution of energy substrates during acute stress. However, their effects coexist with those of glucocorticoids and other counter-regulatory hormones during chronic stress. As a result, rather than being the result of a single hormone, the hormonal reaction to stress should be viewed as an integrated endocrine response.

### Interaction Between Hormones and Amino Acids

Amino acids are not merely substrates for protein synthesis; they also act as signaling molecules. Leucine is particularly important in activation of mTORC1, which regulates translation initiation.

### Hormonal Regulation During Exercise

Muscle protein synthesis is strongly stimulated by resistance training. Testosterone, GH, cortisol, insulin, and IGF-1 are among the hormones that vary in reaction to exercise. The impacts of these hormones must be considered in addition to mechanical stress and amino acid availability, according to Gharahdaghi *et al.*, (2021)<sup>[2]</sup>.

### Hormonal Changes During Aging and Sarcopenia

Changes in a number of anabolic hormones, such as insulin, testosterone, GH, and IGF-1, are linked to aging. Insulin resistance and persistent low-grade inflammation may arise together. The connection between aging, insulin resistance, and sarcopenia also seems to be related to glucagon and insulin signaling. Recent research has suggested connections between mTOR signaling, glucagon-mediated amino acid oxidation, and age-related muscle mass loss (Fujita *et al.*, 2021)<sup>[5]</sup>. Therefore, hormonal changes associated with aging may contribute to; reduced muscle protein synthesis, increased protein breakdown, reduced muscle mass, reduced muscle strength, sarcopenia, impaired physical function.

### Hormonal Regulation in Metabolic Disorders

Metabolic diseases like obesity, insulin resistance, and type 2 diabetes are closely linked to hormonal imbalances. Insulin's capacity to efficiently control food metabolism is diminished by insulin resistance. Long-term exposure to glucocorticoids can exacerbate muscle protein breakdown and insulin resistance (Hwang & Lee, 2021)<sup>[3]</sup>.

Because skeletal muscle plays a significant role in the metabolism of amino acids and the disposal of glucose, disruptions in muscle endocrine signaling may lead to more widespread metabolic disorders. This creates a crucial connection:

Hormonal imbalance → altered protein turnover → loss of muscle quality → metabolic dysfunction

Therefore, maintenance of healthy endocrine function is important for both protein metabolism and metabolic health.

### Summary of Hormonal Effects on Protein Metabolism

Hormones are crucial for preserving muscle mass and protein balance. Protein synthesis, tissue growth, and muscle maintenance are primarily supported by insulin, growth hormone, IGF-1, testosterone, and estrogen. On the other hand, especially during fasting and stress, cortisol and glucagon encourage the breakdown of proteins and the use of amino acids. Thyroid hormones control muscle metabolism and total protein turnover. Thus, normal protein metabolism and nitrogen balance are maintained by the coordinated action of anabolic and catabolic hormones.

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