

**THE RELATIONSHIP BETWEEN GHRELIN AND FATTY ACIDS**

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**ABSTRACT**

Ghrelin stimulates food intake, initiating a feeling of hunger. In order to regulate the energy balance, the role of ghrelin is important in food intake and regulation of energy balance. Lipids, fatty acids and triglycerides are the primary fuel source for energy in many organisms. Lipids are esters of fatty acids, or compounds that can be esterified; The main building blocks are fatty acids. Fatty acids are the body's energy regulators, and the functional relationship with ghrelin is very important. Approach: It is aimed to summarize the recent information about Ghrelin and fatty acids and their functions in biochemistry and clinical chemistry in body energy regulation and the importance of fatty acids related to ghrelin.

**KEYWORDS:** Ghrelin, Fatty Acids, Lipid.**INTRODUCTION**

Hunger is a feeling and inform the desire to eat and apply to the body. It originates from the needs of the source. This is called homeostatic hunger. Another hunger is hedonic hunger. Hedonic hunger is the hunger felt without the need. Homeostatic hunger opens nervously from the brain.<sup>[2]</sup> This is a process related to his hypothalamus. The place that connects the nerve region of the brain to the endocrine system is the hypothalamus. Hunger is the center of balance management. It is made with hormon secretion.<sup>[1]</sup> When the hunger signal is given with the secretion of the messenger ghrelin. Ghrelin is released in the hypothalamus and signals of hunger are given by signals coming from the intestine. Ghrelin is the most common hormone associated with hunger.<sup>[3]</sup>

In energy metabolism, hunger and satiety are neuropeptide signals in the brain that determine daily eating habits. The part of the nerve centers in the brain is hypothalamic. Ventromedical (VHM) and lateral hypothalamus (LH) in the hypothalamus are the parts that regulate appetite and the amount of nutrients to be taken into the body. While VHM is the region where satiety is felt, LH plays a role in the function of hunger. With the signals coming from these centers, saturation signals come to the brain through hormones released in the intestines. These hormones act on appetite from leptin, insulin and adipose tissue. These hormones secreted by the small intestine have an important role in the formation of a feeling of fullness.<sup>[4]</sup> This event is not only physiological, but it is an important condition that affects appetite mechanisms in eating, taste and taste.<sup>[5]</sup>

Peptides that affect these nutrient intake functions making these arrangements are known as peripheral peptides. Peripheral peptides are produced in the digestive tract and are divided into two parts. Orexigenic and anorexigenic peptides. Orexigenic peptides (ghrelin, neuropeptideY, etc.) stimulate food intake by initiating a feeling of hunger, while anorexigenics (leptin, insulin, etc.) are peptides that stop food intake by creating a sense of satiety.<sup>[3]</sup>

Davis X-A-like cells (ghrelin cells) were discovered in the stomach in 1954<sup>[6]</sup>. It is called "Growth Hormone Secretory" (GHS), which plays a role in the growth hormone release reported in 1976 as a peptide analogue in vitro.<sup>[7]</sup> Ghrelin, known as the cause of our hunger, was discovered in 1999 as a result of the work of Japanese scientists. This lipopeptide found in the stomach fundus is a hormone formed by the peptide bond of 28 amino acids.<sup>[8]</sup> In addition to producing ghrelin in the hypothalamus, it is produced in the pituitary, placenta, kidney and intestine.<sup>[9]</sup> It is produced in salivary gland, thyroid gland, kidney, heart, pancreas, immune system and central nervous system.<sup>[10]</sup>

The name of ghrel is derived from the combination of the word "ghre" and the secretion "relin" from the root of the word "grow", which means development.<sup>[8]</sup> It is a appetite hormone<sup>[11]</sup>. Ghrelin is not just a hormone released from an organ or gland, but rather is produced in many tissues.<sup>[12]</sup> Along with the animal kingdom, it has been reported in plants that there is a ghrelin like substance capable of immuno reacting with human antighrelin.<sup>[13]</sup> Also, the active form of ghrelin found in gram negative bacteria shows structural homology with

lactone of n-octanylethanolamine.<sup>[14]</sup> It is determined that there is a serine acyl transferase enzyme in butter grass, which is an example to us that there is ghrelin in plants.<sup>[15]</sup>

In the human ghrelin hormone, the octanyl group, which is bound to the third amino acid in the series, is an eight carbon fatty acid. This fatty acid is required and activates the hormone ghrelin, which is called active ghrelin active ghrelin (aGAH). The octanyl group containing this fatty acid is active. The nonfatty ghrelin is desecylated ghrelin. This ghrelin is called inactive ghrelin (dGAH).<sup>[16]</sup> dGAH is about 80-90% in circulation.<sup>[17]</sup> Ghrelin hormone is the only peptide hormone whose activity is altered by a fatty acid.<sup>[8]</sup> Ghrelin appears in plasma in two ways. Deoctanyl ghrelin and octanyl ghrelin. Octane ghrelin eight carbon fatty acid is produced as modified with octanoate.<sup>[18]</sup> This event takes place in the endoplasmic reticulum, and the enzyme of ghrelin is o-acyltransferase.<sup>[19,20]</sup>

Medium chain fatty acids and medium chain triglycerides are direct sources of fatty acids in the modification of ghrelin.<sup>[21]</sup> Although the relationship of ghrelin cells with fatty acid is in this way, the mechanisms involved and involved in this event have not been revealed yet, so it is an important function of free fatty acid receptors (FFAR).<sup>[22]</sup> <sup>[23]</sup> In a study in mice, medium chain fatty acids were given. Medium chain triacyl glycerols did not change the total ghrelin amounts but increased the amount of acyl ghrelin in the stomach. It was emphasized that these medium chain fatty acids taken into the body were used for acyl modification of ghrelin.<sup>[17]</sup>

Discovered in 1994, leptin is a single chain protein hormone consisting of 167 amino acids encoded by the obesity gene. Leptin is first identified to be related to saturation and energy balance. It is then determined that it is an effective anti obesity factor with adipose tissue feedback to the hypothalamus. It is one of the most important elements in food intake and body weight regulation in humans. Leptin increases metabolic rate while decreasing food intake.<sup>[24]</sup> However, another study reported that after a diet with a high fat and carbohydrate ratio, 165 low fat women and obese women had a low level of leptin but an increase in ghrelin levels.<sup>[25]</sup>

The first remarkable function of the hormone ghrelin, which has various functions in the body, is appetite and plays a role in energy homeostasis, that is, the balance of fat production.<sup>[26]</sup> It is necessary for the regulation of energy and carbohydrate homeostasis as well as growth hormone secretion.<sup>[27,28]</sup> It has a function in fasting and food intake while regulating short term homeostasis.<sup>[29,30]</sup> However, ghrelin increases weight gain and lubrication and is effective in long term energy regulation.<sup>[31,32,33]</sup>

The more ghrelin is produced in the body, the more fat tissue is produced.<sup>[34]</sup> Intake of foods with high energy

capacity in excessive portions in the intake of food taken into the body in nutrition is characterized by effective and excessive intake stimuli. These foods with high energy capacity are especially rich in nutrients such as lipids and carbohydrates.<sup>[35]</sup> Ghrelin stimulates gluconeogenesis and shows circulating glucose levels in the form of increasing insulin resistance by the release of ghrelin.<sup>[36]</sup> In relation to the homeostasis of appetite and energy balance, the relationship between the neural and peripheral systems that follow the stimulus and functionally takes part in the regulation of the reactions in metabolism, that is to say, with lipids, and therefore with fatty acids is very important.<sup>[37]</sup>

In this review, especially the relationship between the hormones of ghrelin, which is one of the hormones in hunger regulation, on nutrition metabolism with intense fatty diet and fatty acids and lipids, is to draw attention to the studies done so far.

In one study, infusion of ghrelin increased weight gain.<sup>[38]</sup> and at the same time found that it caused appetite and ultimately increased weight.<sup>[11]</sup> In addition to this study conducted in animals, it was observed that the same result was observed in humans. Appetite is opened and obesity is caused.<sup>[38]</sup> The release of the role of ghrelin in energy intake and expenditure, that is, in the energy balance, is quite effective in the body. Increasing the demand for energy intake in linear increase of ghrelin concentration is thought to be related to the feeling of hunger. It is stated that ghrelin increases before eating and decreases rapidly after eating.<sup>[39,40]</sup>

The obesity person is observed to have a low concentration of ghrelin compared to normal subjects.<sup>[41,42]</sup> Accordingly, it suggests that the low ghrelin mechanism may be effective in protecting people who are obese from progressive obesity. When we look at the effect of ghrelin intensity on body fat percentage and body mass index (BMI), the presence of negative relationship is observed. In this context, the concentration of ghrelin in anorexic individuals is high,<sup>[42]</sup> It has been determined that resistance to ghrelin occurs in people with anorexia. Ghrelin concentration is known to be abnormal in people with bulimia, cachectic and prader willi syndrome, among other diseases.<sup>[39]</sup> Although the energy balance for ghrelin is not entirely clear, it is not known how they regulate this hormone.

Adipose tissue contains more than 10% of body weight. Adipocytokines with an energy storage function also act as an active endocrine tissue.<sup>[43,44]</sup> Adiponectin is secreted from adipocytes such as leptin, but unlike leptin, it is specific to adipose tissue.<sup>[44]</sup> Adiponectin plasma levels show a negative relationship with insulin, triglyceride, BMI, subcutaneous adipose tissue, visceral adipose tissue, systolic blood pressure and liver enzymes, while HDL has a positive relationship with cholesterol levels,<sup>[45]</sup> Increases insulin sensitivity. Corrects lipid levels. Adiponectin has many physiological functions

associated with energy balance: the insulin specific role is especially important.<sup>[33]</sup> The mechanism of this weight loss effect has been shown to be associated with increased fatty acid oxidation in the muscles and reduced circulating fatty acid. A decrease in triglyceride concentration has also been observed in muscle and liver tissues.<sup>[46,47]</sup> The high concentration of ghrelin stimulates insulin production, and the inhibited insulin drops, and with the concentration of ghrelin, the body's glucose conversion rate decreases to energy.<sup>[48]</sup>

The role of lipid mechanisms is important in regulating energy balance.<sup>[49,50,51]</sup> The relation of ghrelin cells, which detect lipids, with octanillation and the secretion of ghrelin, which is inhibited by lipids, is an indication that it can be modified with diets. Lipids, especially medium chain fatty acids, determine the presence of the interaction.<sup>[52,53,21,54]</sup> Many studies have looked at the effects of ghrelin levels in mice fed a high-fat diet, and variations in results have been found.<sup>[9]</sup> Due to these features, we can say that the Ghrell's body function is not only a hormone that signals the cavity of the stomach, that is, only hunger, but also an energy sensor. It is a warning system that regulates lipid storage and transmits the signal of rich calories to the central nervous system. In short, it is an energy sensor.<sup>[54]</sup>

When the fatty acids are detected, the interaction of ghrelin in the octanillation is regulated as well as the secretion of the ghrelin. Long chain fatty acid effect was investigated in a study to understand this important mechanism and to understand the role of fatty acid. The effect of long chain fatty acid, alpha linolenic acid, on the release of octanyl ghrel was observed. This effect of alpha linolenic acid is very important in that it inhibits the outbreak of ghrelin and shows that the release of octanyl and desoctanyl ghrel is regulated differently.<sup>[55]</sup>

The stomach and duodenum contain ghrelin hormone, which contains ghrelin cells and detects long chain fatty acids.<sup>[56,57,58]</sup> The strong effect of fatty acids on fatty acids is known in regulating the energy metabolism of lipid while regulating the way fatty acids are stored in animals and plants.<sup>[59]</sup> The warnings going from the periphery to the hypothalamic center, the control mechanism is regulated. Along with adipose tissue, leptin takes part in the brain, carries the information about adipose tissues and causes a decrease in food intake. Therefore, it prevents accumulation of excess oil. On the contrary, ghrelin transmits the brain to the brain, increasing nutrient uptake and adipose tissue.<sup>[60]</sup>

The effects of dietary fatty acids on diabetes, cardiovascular, metabolic syndromes, obesity and many cancers have been intensified. As a result, the anti-inflammatory role of n-6 polyunsaturated fatty acids is noteworthy. The biological roles of these fatty acids have been established.<sup>[61]</sup> In a study to examine the role of gastric ghrel in gene expression, an increase was observed in the group fed with a high fat diet,<sup>[9]</sup> while

others reported a decrease in plasma ghrelin levels by 20-30%.<sup>[62]</sup> A decrease in appetite and nutrient intake was observed when mice with chronic hyperghrelinemia were fed high fat foods in food.<sup>[62]</sup> In another study investigating the effects of high fat diets on the elements of appetite metabolism in different sex groups, it was observed that the group with female mice was over stimulated in the ghrelin.<sup>[63]</sup> The study on the effect of high fat diet on fatty acid composition in women with appetite was conducted in 15 women. These 15 healthy women were given foods containing saturated, monounsaturated or polyunsaturated fatty acids for three days. As a result, saturation response was observed and saturated fatty acid was the highest.<sup>[24]</sup>

In fact, it is very important which fats or fatty acids are in high fat foods. One of the objectives in this review is how effective is the relationship between these fatty acids and ghrelin hormone. It has been known that many working fatty acids, (especially unsaturated fatty acids), have had positive effects on many diseases. In this context, it is thought that this positive effect on the metabolism of ghrelin. It will be very important to concentrate the studies on this subject and to carry out the related studies.

## RESOURCE

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