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Some Biochemical Parameters Secreted from the Adipose Tissues

Mariam H. Abduljalal [1]*, Nuha A. Al-Talib [2], Sura K. Mohialdeen [3]

[1*,3] Department of Biochemistry, College of Medicine, University of Mosul, Mosul, Iraq.
[2]Department of Chemistry, Science College, University of Mosul, Mosul, Iraq.

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Correspondence:
Mariam Hani
mariamhani@uomosul.edu.iq

Abstract

Obesity is a complicated disorder involving an increasing amount of fat in the body. It raises the risk of a variety of illnesses, including heart disease, high blood pressure, certain cancers, and diabetes. Obesity has a complicated origin, comprising a series of interactions between genetics, and hormones, in addition to diet and physical activity. The regulation of whole-body energy is dependent on adipose tissue (fat tissues). It, on the other hand, stores energy in the form of fat and regulates fat mobilization and distribution in the body. It also works as an endocrine organ, producing a number of chemicals such as adipocytokines. Furthermore, fats are burned by beige and brown adipose tissue by dispersing energy in the form of heat in order to maintain a normal body temperature and have been proposed as a potential method of preventing obesity. In this review, we discuss the latest articles on different forms of adipose tissues and their role in metabolism control, with a focus on their endocrine function. The molecular function and clinical importance of various key adipocytokines are described as well.

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1.Introduction

Obesity is a major public health issue because it increases the risk of a variety of diseases, including type 2 diabetes, fatty liver disease, heart attack, hypertension, dementia, stroke, sleep apnea, and some cancers, all of which contribute to a decrease in both life span and quality of life. [1, 2]

Adipose (fatty) tissue

Adipose tissue is not only a passive energy source but it considers one of the biggest endocrine systems in the body which releases big amounts of adipokines that are mostly formed in fat cells in white adipose tissue. adipocytokines are soluble mediators, generated by fatty tissue circulated and transported messages to other organs such as muscle, pancreas, brain, and liver through endocrine processes, thus influencing systemic metabolism. .[3,4,5]

Types of adipose tissues

White adipose tissue (WAT) and brown adipose tissue (BAT) are the two forms of fatty tissue present in humans. They have variable roles and morphologies, but new research has found a third form of adipose tissue called beige or brite adipose tissue.

1. Brown adipose tissue (BAT): it was discovered in 1951, and found in neonates while adult humans either deficit or have a tiny quantity. It is typically present around the neck and the thorax's around the largest blood veins and arteries. the fat cell from brown adipose tissue has numerous mitochondria and tiny fat droplets. [6] Brown fat can make heat by dyscoupling the respiratory chain of oxidative phosphorylation in the mitochondria. Cold exposure activates brown adipose tissue by releasing catecholamines from sympathetic neurons. Chelli (spicy) food or overeating can also trigger brown adipose tissue activation.[7,8]

Although it is clear that brown adipose tissue plays a key role in the prevention and treatment of obesity and diabetes in rats, and that certain medications can trigger the formation of brown fat, the physiological relevance of brown in humans is still being debated. As a result, the development of brown adipose tissue in adult humans is being viewed as a novel effort in the treatment of obesity and linked disorders.[9]

2. White adipose tissue(WAT): Males' white adipose tissue accounted for around 20% of weight, while females' accounted for 25%.[10]
Subcutaneous and visceral white adipose tissue make up white adipose tissue. The major functions of it are to store and release fatty acids, which provide fuel to the body during fasting times. These fatty acids are kept in a huge lipid droplet that takes up over 90% of the cell volume. White fat serves as a metabolic and endocrine regulator.[4,5]

3. brite or Beige (fat cell) adipocyte: is a new type of adipose tissue that has been discovered according to new research. Many subcutaneous fat depots previously categorized as white fat now show brown fat specific markers, earning them the nickname "beige" or "brite" adipose tissue. Browning of white fat occurs when brown adipocytes expressing an dyscoupling protein 1 grow exclusively in white fat anatomical areas. This happens when a person is exposed to rising levels of catecholamine over an extended period of time, like in pheochromocytoma, or a thermogenic stimulus such as expanded cold exposure, which also stimulates brown adipose tissue induction at their conventional anatomical sites (e.g., interscapular depots). Chronic treatment with 3-AR activators can mimic the browning process.[12]

The adipocytokines:
Till 1994, adipose tissue's main known function was to store energy in the form of lipids; however, it has since been realized as a key endocrine organ, producing hormones such as leptin, adiponectine, interleukin 6(IL-6), estrogen, apelin, resistin, and tumor necrosis factor-alpha (TNF). [13] Adipocytokines are a type of cell signaling protein released by fatty tissue; Leptin hormone was the first adipokine identified in 1994. Many types of adipokines have been found since then. These adipokines include the following: [15,16]

1. Leptin

It is one of the most significant hormones derived from adipose tissue. It's a 16-kilodalton protein hormone that regulates energy intake and expenditure. The ob gene, which is generated by adipocytes, codes this protein.[17] The autosomal recessive inheritance of a very obese mouse phenotype was reported in 1950. Hyperphagia, obesity, sterilization, and a range of metabolic and hormonal abnormalities were all linked to this disease. The mouse characteristic ob/ob was named after the mutation, which was found on chromosome 6.[17]
A mouse trait with the same phenotype was discovered in 1966. The trait db/db was named after the mutation "diabetes" that was discovered on chromosome 4. The ob gene encodes a 167-amino-acid peptide chain, which was later named leptin, according to studies published in 1994. [17] Brown adipose tissues (BAT), skeletal muscle, placenta, stomach, ovaries, mammary epithelial cells, liver, pituitary, and bone marrow can all create leptin hormone in addition to white adipose tissue, which is the most common source.[18,22]
The Leptin hormone reduces appetite by it is direct action on the hypothalamic receptors of the brain. Leptin concentrations in women are roughly three times higher than in men, and it is excretion at a higher level at midnight, which is the polar opposite of cortisol hormone secretion.[19]
Obese people have an abnormally high level of leptin in their blood. These people are thought to be resistant to leptin's effects, similar to how patients with type 2 diabetes mellitus (T2DM) are resistant to insulin hormone actions. [20,21]

2. Apelin

In 1998, apelin was discovered to be a peptide. It helps to regulate blood pressure and promotes the development of new blood vessels when activated. The hypotensive impact of apelin hormone is due in part to the generation of nitrogen oxide, a powerful vasodilator that causes the relaxation of blood vessels. [22,23] The hypotensive impact of apelin hormone is due in part to the generation of nitrogen oxide, a powerful vasodilator. Furthermore, water and food intake are controlled by apelin receptors in the brain. It has been discovered that apelin admission enhances water intake while decreasing antidiuretic hormone release in the hypothalamus (vasopressin). Apeline's diuretic action is also linked to its hypotensive impact. [24,25,26]

3. Retinol binding protein 4 cytokines :

This protein is a member of the lipocalin proteins S family and is the blood's particular transporter of retinol (vitamin A). It transports retinol from the liver to the rest of the body. RBP 4 is a critical nutrient for the visual cycle and has been a therapeutic target for eye illnesses. [27,28]

4. Adiponectin

This is a polypeptide hormone with a length of 244 amino acids. Adiponectin was discovered in 1995 and was found to play a role in both the breakdown of fatty acids and the control of glucose. It is generated in fatty tissue and is encoded by an ADIPOQ gene in humans. The hormone adiponectin reduces gluconeogenesis, increases glucose absorption, and improves

insulin sensitivity, all of which have a positive impact on blood glucose levels. It also improves lipid clearance and weight loss, which protects against atherosclerosis. [29,30]
Although adiponectin has been secreted from the fatty tissue, it is levels were shown to be low in obese people. This downregulation hasn't been discussed in detail. The gene was discovered on chromosome 3q27, a region linked to type 2 diabetes mellitus (T2DM) and obesity predisposition. In experiments on mice, adiponectin supplementation improved blood glucose, insulin regulation, and lipid levels. [31, 32, 33]

5. plasminogen activator inhibitor 1

In mammals, there are two plasminogen activators, tissue type plasminogen activator (tPA) and urokinase type plasminogen activator (uPA); both are plasminogen activators and thus fibrinolysis activators. PAI-1 known as serine protease inhibitor (serpin) plays a role in the inhibition of the tissue plasminogen activator and the urokinase. [34]
plasminogen activator inhibitor 1 was found in relatively high concentrations in a variety of illness states, including obesity, cancer, and metabolic syndrome. It's been related to an increased risk of thrombosis in people who have these illnesses. [35,36]

6. Chemerin

It's known as RARRES2 (retinoic acid receptor responder protein 2), and it's been linked to adipocyte differentiation and lipolysis stimulation. [37]
Chemerin is not strongly expressed in brown adipose tissue in mice studies, indicating that it is involved in energy storage rather than thermogenesis. Chemerin levels in humans change dramatically between those with a normal glucose tolerance test result when compared with people with type 2 diabetes mellitus(T2DM). Furthermore, chemerin cytokine levels are linked to body mass index(BMI), lipid profile, and blood pressure. [38,39]

7. Interleukin 6 (IL-6)

It plays an important role in the inflammatory process so it is a pro-inflammatory cytokine. a IL-6 is a cytokine released by muscle and its is level increased in reply to the contraction of the muscle. It is encoded by the Interleukin 6 gene. It rises dramatically in response to exercise and appears before other cytokines in the bloodstream.[40]
Many studies suggested the use of Interleukin 6 as an inflammatory indicator to evaluate the severity of Coronavirus infection in those patients as the highest level was detected in critically ill patients. [41, 42]
Obesity is considered a risk factor to develop severe asthma. Recent evidence suggests that obesity-related inflammation, maybe mediated by the cytokine Interleukin 6, contributes to impaired lung function and aggravation of asthma. [43]
In numerous disorders such as depression, Alzheimer's disease, diabetes, stroke, rheumatism, and intracerebral hemorrhage, Interleukin 6 increases the inflammatory and autoimmune processes.[44,45,46,47] As a result, anti-Interleukin 6 medicines are being developed as a therapeutic for many of these disorders. [48]

8. Visfatin

Visfatin, also known as nicotinamide phosphoribosyl transferase, is an adipokine found in the bloodstream (NAmPRTase or Nampt). The NAMPT gene in humans is responsible for encoding this enzyme. In mammals, this cytokine is considered a rate-limiting protein in (NAD+) the nicotinamide adenine dinucleotide salvage pathway in mammals including human beings, it is role is to change the nicotinamide to nicotinamide mononucleotide, allowing NAD+ production. It promotes the maturation of the vascular smooth muscle cells and reduces neutrophil apoptosis, among other things. Visfatin shows an action similar to that of insulin, which means it lowers blood sugar levels and improves insulin sensitivity by activating insulin receptors. The protein is found in large amounts in visceral fat, and its blood levels have been associated with obesity. [49, 50]

9. Progranulin

Whereas progranulin has been associated with anti-inflammatory activity, its split granulin peptides associated with pro-inflammatory activity. High levels of serum or plasma progranulin in patients with visceral obesity or type 2 diabetes mellitus(T2DM), imply that progranulin may have a role in metabolic diseases. [51] Progranulin is a pleiotropic protein that operates in the brain in a variety of ways. Frontotemporal dementia is caused by mutations in the progranulin gene. Variation in the progranulin gene has been associated with a number of neurological disorders. [52]

10. Resistin.

In 2001, a cysteine rich peptide hormone called resistin was discovered. The human resistin pre-peptide has a molecular weight of 12.5 kDa and is 108 amino acid residues long. In humans, the RETN gene codes for resistin. In primates, pigs, and dogs, immunological and epithelial cells secrete resistin, whereas, in rodents and humans, fat tissue secretes it.[53, 54,55]
It was given the name resistin because of the insulin resistance shown in mice injected with it. Resistin was revealed to be generated and liberated from fat tissue for endocrine functions likely related to insulin resistance, hence its physiologic

involvement in obesity and type 2 diabetes mellitus has been a source of controversy. Other physiological processes such as inflammation and energy homeostasis have also been linked to resistin. [56,57]
Resistin increases the creation of low-density lipoprotein (LDL) while preventing the degradation of LDL receptors in human liver cells. As a result, the liver has a harder time removing bad cholesterol from the bloodstream, and resistin has been associated with high LDL levels. Furthermore, by hastening the deposition of LDL in arteries, resistin raises the risk of heart disease. [58]

11. The chemokine (C-C motif) ligand 2 (CCL2) or known as monocyte chemoattractant protein 1 (MCP1)

CCL2 seems to play a role in many diseases where monocyte infiltration is noted, like atherosclerosis, rheumatoid arthritis, and psoriasis. [14]
Many trials were done using the anti-CCL2 antibodies in the treatment of glomerulonephritis, such experiments show significant reductions in the infiltration rates of the macrophages and the T lymphocytes in the renal tissues thus reduction in renal scarring and impairment.
Moreover, the CCL2 (or MCP1) seems to have a role in many neurodegenerative illnesses involving the nervous system like Alzheimer's disease.
The elevated values of blood glucose and triglyceride (TG) seem to affect the CCL2 promoter region, the increased CCL2 levels in circulation may have an effect on patients with type 2 diabetes mellitus. [22]

12. Omentin

Omentin is a lectin which is a carbohydrate-binding protein that is expressed in human beings in two forms:
1. intelectins-1(hIntL-1) called omentin secreted from fatty tissues
2. interlectin-2 (hIntL-2)

Many studies on interactions have been done to discover it is a function, they conclude that omentin can recognize microbes and perhaps has a role in innate immunity. Other studies concluded a possible role for omentin in the physiology of insulin in obese people. [59]

2. **Conclusion (Bold, 12 pt)**

Adipose tissue is important in the maintenance of systemic metabolic homeostasis because of its significant impacts on energy storage, endocrine function, and adaptive thermogenesis. Obesity and its complications have been linked to adipose tissue malfunction as a cause. Understanding adipose tissue biology and pathology is therefore crucial for identifying novel and potentially therapeutic targets for obesity-related disorders prevention and therapy. Adipokines are a collection of peptides produced by adipose tissue and referred to as adipokines together. Changes in adipose mass in obesity alter the synthesis of most adipose secreted components. Obesity has been related to a number of metabolic irregularities, as well as an increased risk of cardiovascular disease, diabetes, cancer, and a number of other disorders. The hypotheses have evolved that adipose tissues, by their released substances, may play a role in these disorders. Several adipokines, like plasminogen activator inhibiter 1, Interleukin 6, and resistin, are higher in obese people and have been linked to hypertension, poor fibrinolysis, and insulin resistance.

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بعض المعلمات البيوكيميائية التي تفرز من الأنسجة الدهنية

مريم هاني عبد الجلال *[1]، نهى عبدالقادر الطالب [2] ، سرى خيرالدين محي الدين [3]

[3،*1] فرع الكيمياء الحياتية، كلية الطب، جامعة الموصل، الموصل، العراق.
[2] قسم الكيمياء، كلية العلوم، جامعة الموصل، الموصل، العراق.

الخلاصة
السمنة هي اضطراب معقد ينطوي على زيادة كمية الدهون في الجسم. يزيد من خطر الإصابة بالعديد من الأمراض مثل أمراض القلب وارتفاع ضغط الدم والسكري وبعض أنواع السرطان. للسمنة أصل معقد ، حيث يشتمل على سلسلة من التفاعلات بين الجينات والهرمونات ، بالإضافة إلى النظام الغذائي والنشاط البدني. للانسجة الدهنية أمر بالغ الأهمية في تنظيم طاقة الجسم كله. وفي الوقت نفسه ، تخزن الأنسجة الدهنية الطاقة على شكل دهون وتنظم تعبئة وتوزيع الدهون في الجسم ، من ناحية أخرى ، تعمل كعضو من الغدد الصماء وتنتج مجموعة متنوعة من المواد. علاوة على ذلك ، تحرق الأنسجة الدهنية ذات اللون البني والبيج الدهون عن طريق تشتيت الطاقة على شكل حرارة من أجل الحفاظ على درجة حرارة الجسم الطبيعية ، وقد تم اقتراحها كطريقة محتملة للوقاية من السمنة. في هذه المراجعة ، نناقش أحدث المقالات حول الأشكال المختلفة للأنسجة الدهنية وقاعدتها في التحكم في التمثيل الغذائي ، مع التركيز على وظيفة الغدد الصماء. كما تم وصف الوظيفة الجزيئية والأهمية السريرية للعديد من الخلايا الشحمية الرئيسية.