Asprosin is a hormone that is released by the white adipose tissue. It stimulates the release of glucose, which is produced in the liver, into the blood. Asprosin targets many organs including the skeletal muscle, pancreas, liver, and cardiac system. In addition, asprosin stimulates appetite leading to weight gain. It also influences glucose metabolism, cell apoptosis, and insulin resistance. Furthermore, it has been implicated in some medical conditions such as obesity and diabetes.

**Key point**
Asprosin has a regulatory effect on glucose metabolism, appetite, cell apoptosis, and insulin resistance.

**Introduction**
Asprosin is a hormone that is released by the white adipose tissue which stimulates the release of glucose from the liver into the blood circulation. The white adipose structure is the main resource of asprosin. Asprosin is a cleavage product of the C-terminal of profibrillin which is encoded by the FBN1 gene (1). Romere et al were the first to introduce asprosin as a new adipokine in 2016. They reported that patients with neonatal premature aging (NPS) have decreased appetite, lean bodies, low insulin levels with normal blood glucose levels. They noticed that these patients do not produce asprosin. Therefore, they concluded that asprosin may influence the metabolism of carbohydrates and lipids (1).

Asprosin and its effects on the neurons and central nervous system
Asprosin crosses the blood-brain barrier (BBB) and impacts the central nervous system (CNS). It increases the activity of the AgRP neurons through a G proteins-cAMP-PKA pathway. This results in the inhibition disorders (CVDs) (3). Asprosin has also been reported to have implications in pregnant women with GDM, their neonates, and obese children (4-8).

Basu et al have recently proposed a new subclass of protein hormones called ‘caudamins’, which include asprosin, that may be used in therapeutic drugs to treat metabolic syndrome, cancer, and other diseases (9). In this review we aimed to present the mostly recent publication on asprosin.

**Method of the study**
For this narrative review study, relevant articles were searched in Scopus, Embase, EBSCO, Web of Science and Google Scholar and also in PubMed/Medline. The following search terms such as asprosin, appetite, glucose metabolism and insulin resistance were employed to retrieve the published papers on this subject.

**Asprosin and its effects on the neurons and central nervous system**
Asprosin crosses the blood-brain barrier (BBB) and impacts the central nervous system (CNS). It increases the activity of the AgRP neurons through a G proteins-cAMP-PKA pathway. This results in the inhibition
of the POMC neurons leading to appetite stimulation, food consumption, and weight gain (1,3,10).

**Asprosin and its effects on the hypothalamus**
Asprosin increases the activity of the AgRP neurons through the activation of the G proteins-cAMP-PKA pathway in the hypothalamus and, in turn, stimulates appetite.

**Asprosin and its effects on the liver**
Asprosin increases the production and release of glucose in the liver by binding to OLFR734 and through the GPCR (G protein-coupled receptor), which stimulates the CREB (adenyl cyclase-PKA-cAMP responsive element binding) pathway.

**Asprosin and its effects on the pancreatic β-cells**
Asprosin binds to Toll-like receptor 4 (TLR4) and through the TLR4/JNK pathway in the pancreatic β-cells, stimulates the production of reactive oxygen species (ROS) and cytokines leading to inflammation, cellular dysfunction, apoptosis of pancreatic β-cells, and decreased insulin secretion. In addition, the β-cells of the pancreas can excrete asprosin during hyperlipidemia (11,12).

**Asprosin and its effects on the skeletal muscle**
Asprosin affects the skeletal muscle by the inflammation and endoplasmic reticulum (ER) stress through the PKC8/SERCA2-mediated pathway. This leads to insulin resistance (IR) and glucose intolerance (3,13).

**Asprosin and its effects on the myocardial mesenchymal cells**
Asprosin inhibits the apoptosis (induced by oxidative stress) of myocardial mesenchymal cells (MSCs) through the activation of the ERK1/2-SOD2 pathway (3,14).

**Asprosin and its effects on glucogenesis**
Some studies have reported that asprosin has glucogenic effects. On the other hand, some studies could not confirm the glucogenic effects of asprosin. Consequently, the glucogenic effects of asprosin are still controversial (3).

**Asprosin and its effects on appetite**
Some studies have reported that asprosin has orexigenic and appetite-stimulating effects. On the other hand, some studies could not confirm the orexigenic effects of asprosin. Consequently, the orexigenic effects of asprosin are still controversial (3).

**Asprosin and its effects on other hormones**
It has been reported that asprosin does not affect the serum levels of glucogenic hormones including glucagon, epinephrine, norepinephrine, and glucocorticoids (1). On the other hand, an association between asprosin and ghrelin (an orexigenic hormone) is also existed. Both of these substances can activate a common part of AgRP neurons. Although decreased levels of asprosin decrease the activating effects of ghrelin on AgRP neurons, the receptors of ghrelin do not affect the activating effects of asprosin on AgRP neurons. Furthermore, studies have reported that asprosin does not affect leptin, an anorexigenic hormone (3,10).

**Asprosin and its association with obesity**
The effect of asprosin on obesity is controversial and the mechanism by which asprosin affects obesity is still unclear. Patients with NPS have decreased serum asprosin levels and appetite, and lean bodies which indicate a role for asprosin in obesity by affecting appetite (1,10). Several studies have reported an increased serum level of asprosin in obese individuals and mice and a positive association between serum asprosin levels and waist circumference and triglyceride (TG) (15,16). A study reported that the levels of asprosin before bariatric surgery are associated with more decrease in body weight at six months after surgery. However, a study reported that asprosin did not change the whole bodyweight of mice (13). There is a positive association between serum asprosin levels and waist circumference and TG (15,16). Asprosin activates the AgRP- neurons (which have orexigenic effects) and inhibits POMC neurons (which have anorexigenic effects). This results in the stimulation of appetite and increased fat tissue and weight (2,3).

**Asprosin and its association with diabetes**
Increased plasma levels of asprosin have been reported in patients with IR, impaired glucose regulation (IGR), and newly diagnosed type 2 diabetes mellitus (T2DM) (1,15). In addition, there is an independent link between the serum levels of fasting glucose and asprosin levels in patients with T2DM (3,15). Furthermore, a study on type 1 diabetic mice reported that they had increased levels of asprosin (17). The response of serum asprosin levels to the alterations in the serum levels of glucose is also impaired in patients with T1DM and T2DM. Furthermore, the plasma levels of asprosin are increased in pregnant women diagnosed with gestational diabetes mellitus (GDM) and the umbilical cords of these patients’ neonates (3,4).

**Asprosin and its association with polycystic ovary syndrome**
Studies have reported that female patients with polycystic ovary syndrome (PCOS) have significantly increased serum asprosin levels. In addition, there has been a positive association between serum asprosin levels and serum levels of HbA1C (hemoglobin A1c), Apolipoprotein B (ApoB), low-density lipoprotein-cholesterol (LDL-c), and testosterone. In addition, the serum asprosin level is an independent risk factor for PCOS (3,18,19).
Asprosin and its association with cardiovascular disorders

It has been reported that asprosin could be a potential biomarker for diagnosing unstable angina and assessing the severity of acute coronary syndrome (ACS) with unstable angina (20). In addition, pretreatment of asprosin on MSCs promoted the homing of MSCs, enhanced the ejection function, and decreased myocardial remodeling after myocardial infarction (MI). The apoptosis of MSCs which is induced by hydrogen peroxide \((H_2O_2)\) was inhibited via the activation of the ERK1/2-SOD2 pathway (3, 14).

Asprosin in pregnant women and their newborns

The plasma levels of asprosin are increased in pregnant women with GDM, preeclampsia (PE), severe preeclampsia (SPE), and macrosomic fetus (MF) and are also increased in their neonates. However, the level of asprosin is lower in both pregnant women with intrauterine growth restriction (IUGR) and their newborns. In addition, the plasma levels of asprosin in pregnant women diagnosed with GDM are associated with the plasma levels of asprosin in their neonates. The level of asprosin has been reported to be higher in female neonates compared to males. Asprosin has also been reported to be expressed in the placenta (4-6).

Asprosin in obese children

The level of asprosin has been reported to be increased in obese children with higher levels in the female gender compared to males (6-8).

Table 1. The effects of asprosin (1,3,10-14)

| Effects of asprosin | Neurons and the CNS | Hypothalamus | Liver | β-cells of the pancreas | Skeletal muscle | MSCs | Glucogenesis | Appetite | Other hormones |
|---------------------|---------------------|--------------|-------|------------------------|-----------------|------|--------------|----------|---------------|
|                     | Asprosin crosses the BBB and impacts the CNS. | Asprosin increases the activity of the AgRP neurons through G proteins-cAMP-PKA pathway via the inhibition of the POMC neurons leading to appetite stimulation, food consumption, and weight gain. | Asprosin increases the activity of the AgRP neurons by the activation of G proteins-cAMP-PKA pathway resulting in appetite stimulation. | Asprosin binds to TLR4 and through the TLR4/JNK pathway, stimulates the production of ROS and cytokines resulting in inflammation, cellular dysfunction, apoptosis of pancreatic β-cells, and decreased insulin secretion. | Asprosin affects the skeletal muscle by the inflammation and ER stress through the PKCδ/SERCA2-mediated pathway leading to IR and glucose intolerance. | Asprosin inhibits the apoptosis of MSCs which is induced by oxidative stress by activating the ERK1/2-SOD2 pathway. | The glucogenic effects of asprosin are still controversial. Some studies have reported that asprosin has glucogenic effects. Other studies could not confirm the glucogenic effects of asprosin. | The orexigenic effects of asprosin are still controversial. Some studies have reported that asprosin has appetite-stimulating effects. Other studies could not confirm the orexigenic effects of asprosin. | Asprosin does not affect the serum levels of glucogenic hormones (glucagon, epinephrine, norepinephrine, glucocorticoids). There is an association between asprosin and ghrelin (an orexigenic hormone). Decreased levels of asprosin decrease the activating effects of ghrelin on AgRP neurons. The receptors of ghrelin do not affect the activating effects of asprosin on AgRP neurons. Both asprosin and ghrelin can activate a common part of AgRP neurons. Asprosin does not affect leptin (an anorexigenic hormone). |

A summary of the effects of asprosin and its implications in some disorders are shown in Tables 1-3.

Authors’ contribution

Both authors, SH and PN have made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

Conflicts of interest

The authors report no conflict of interest.

Ethical issues

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the authors.

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The level of asprosin is higher in obese children with higher levels in female obese children compared to males.

| Asprosin's association with some medical disorders |
|--------------------------------------------------|
| **Obesity**                                      |
| The effect of asprosin on obesity is controversial and the mechanism by which asprosin affects obesity is still unclear. |
| Patients with NPS have decreased serum asprosin levels and appetite, and lean bodies indicate a role for asprosin in obesity by affecting appetite. |
| Several studies have reported an increased serum level of asprosin in obese individuals and mice and a positive association between serum asprosin levels and waist circumference and TG. |
| A study reported that the asprosin levels before bariatric surgery is associated with more decrease in body weight at 6 months after surgery. However, a study reported that asprosin did not change the whole bodyweight of mice. |
| Asprosin activates the AgRP+ neurons (which have orexigenic effects) and inhibits POMC neurons (which have anorexigenic effects). This results in the stimulation of appetite and increased fat tissue and weight. |
| Plasma asprosin levels are increased in patients with IR, IGR, newly diagnosed T2DM. |
| There is an independent link between the serum fasting glucose and asprosin levels in patients with T2DM. |
| **Diabetes**                                     |
| There are increased levels of asprosin in type 1 diabetic mice. |
| The response of serum asprosin levels to the alteration of serum glucose levels is impaired in patients with T1DM and T2DM. |
| The plasma levels of asprosin is increased of pregnant women with GDM and in the umbilical cords of these patients’ neonates. |
| Female patients with PCOS have significantly increased serum asprosin levels. |
| There is a positive association between the asprosin levels and serum levels of HbA1C, ApoB, LDL-C, testosterone. |
| The serum asprosin level is an independent risk factor for PCOS. |
| **CVDs**                                         |
| Asprosin could be a potential biomarker for diagnosing UA and assessing the severity of ACS with UA. |
| The apoptosis of MSCs which is induced by H2O2 is inhibited by the activation of the ERK1/2-SOD2 pathway. |

**Abbreviations:** Triglyceride (TG), Insulin resistance (IR), Impaired glucose regulation (IGR), Type 2 diabetes mellitus (T2DM), gestational diabetes mellitus (GDM), Polycystic ovary syndrome (PCOS), HbA1C (hemoglobin A1C), Apolipoprotein B (ApoB), LDL-C (low-density lipoprotein-cholesterol (LDL-C), Cardiovascular disorders (CVDs), Unstable angina (US), Acute coronary syndrome (ACS), Ejection function (EF), and Myocardial infarction (MI).

Table 2. Asprosin’s association with some medical disorders (1-7,10,13-21)

| Asprosin in certain populations (4-8) |
|---------------------------------------|
| **Pregnant women and their newborns** |
| The plasma levels of asprosin in pregnant women with GDM, PE, SPE, and MF are associated with insulin resistance and glucose intolerance. |
| The level of asprosin is lower in both pregnant women with IUGR and their newborns. |
| The plasma level of asprosin is higher in female neonates compared to males. |
| Asprosin in the placenta. |
| **Obese children**                    |
| The level of asprosin is higher in obese children with higher levels in female obese children compared to males. |

**Abbreviations:** Gestational diabetes mellitus (GDM), Preeclampsia (PE), Severe preeclampsia (SPE), Macroscopic fetus (MF), and Intra-uterine growth restriction (IUGR).

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