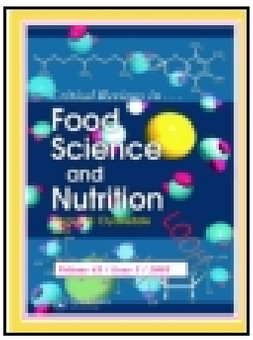

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REVIEW

Effects of nutritional status on serum fetuin-A level

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ABSTRACT

Fetuin-A is a glycoprotein structured molecule which is mostly released by the liver. As a multifunctional protein, fetuin-A has positive effects on health such as calcification, cardiovascular diseases and tumor development processes with various mechanisms, whereas it plays a negative role in the processes of obesity, diabetes and fatty liver disease. There are a large number of studies reporting that serum fetuin-A levels are affected by several dietary factors. It is reported in some of these studies that several nutrients increase fetuin-A release, while some others have adverse effects. It is put forward that some nutrients such as dairy products, curcumin, niacin, palmitate, coffee and alcohol consumption decrease fetuin-A level, and dietary omega-3 fatty acids intake may increase fetuin-A concentration. In addition, it is indicated that high blood glucose levels increase hepatic fetuin-A release by activating extracellular signal-regulated kinase 1/2 enzymes and increased plasma free fatty acids do the same effect by increasing NF-$_{\kappa}$B activity. Despite these studies in the literature, there is not any review evaluating fetuin-A, chronic diseases and nutrition together. Therefore, in this study, the relationship between serum fetuin levels and some diseases and the effects of nutrients on fetuin A levels were investigated with possible mechanisms.

KEYWORDS

Fetuin-A; nutritional status; nutrient intake; obesity; curcumin; resveratrol

1. Introduction

Fetuin-A is also known as α2-Heremans-Schmid glycoprotein which consists of 2 amino-terminal cystatin and one smaller carboxy-terminal domain, and is mainly synthesized by liver parenchymal cells (Brown et al. 1992; Srinivas et al. 1993). Human homolog of fetuin-A (Pedersen 1944), distilled from fetal cattle serum for the first time, was discovered by Heremans, Schmid and Bürgi in 1961 (Schäfer et al. 2003).

Fetuin-A takes role in calcification, insulin sensitivity and apoptosis processes (Kaden et al. 2007; Zheng et al. 2009). Although fetuin-A is a multifunctional protein, its roles in diabetes and kidney disorders could be examined further (Miura et al. 2018; Ochieng et al. 2018). In addition, it is considered that fetuin-A may be correlated with some physiological processes such as cardiovascular diseases and calcification (Ketteler et al. 2003; Ochieng et al. 2018; Schäfer et al. 2003). These data indicate that fetuin-A glycoprotein has many biological functions.

Different studies have shown that fetuin-A may be positively associated with obesity (Blumenthal et al. 2017; Ix et al. 2006). There are also studies which suggest that low and high dietary energy intake may affect serum fetuin-A concentrations (Choi et al. 2013; Samocha-Bonet et al. 2014). However, there are a limited number of studies on this subject in the literature.

Serum fetuin-A level is a biomarker known to be affected by some dietary factors (Nimptsch et al. 2015; Roshanzamir et al. 2017; Yamada et al. 2015). It is reported in some of these studies that several nutrients increase fetuin-A level, while some others have adverse effects (An et al. 2012; Nimptsch et al. 2015; Yamada et al. 2015). It was found out that some nutrients such as dairy products, curcumin, niacin, palmitate decrease fetuin-A levels (Kaushik et al. 2009; Nimptsch et al. 2015; Öner-İyidoğan et al. 2013). It is stated that alcohol consumption can also decrease fetuin-A levels (Joosten, Schrieks, and Hendriks 2014; Ley et al. 2014). In a single study examining the omega-3 fatty acids and fetuin-A concentration, it was put forward that omega-3 fatty acids supplementation can increase fetuin-A concentration (An et al. 2012).

Although there are different studies examining the correlation between serum fetuin-A level and dietary energy and nutrient intake in the literature, the lack of a review evaluating these studies shows the importance of this review. This review examines fetuin-A's structure, biological functions, and the effects of dietary factors on serum fetuin-A levels through a wide perspective.

2. Structure and biological functions of fetuin-A

2.1. Structure of fetuin-A

Fetuins are glycoproteins with both N-linked and O-linked carbohydrate side chains (Nawratil et al. 1996). Fetuin-A, linked by a short link peptide of 40 amino acids, consists of

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a long A chain and a short B chain. The chain A consists of 282 amino acids and the chain B 27 (Nawratil et al. 1996).

Fetuin-A is a glycoprotein structured molecule which weighs 60 kDa, is mostly released by the liver and has a serum concentration ranging between 0.5 and 1.0 g/L (Schlieper et al. 2007). Fetuin-A can be synthesized in the kidneys, choroid plexus and all major organs during fetal development as well as liver tissue (Westenfeld, Jahnen-Dechent, and Ketteler 2007). In addition, fetuin-A (Westenfeld et al. 2007), an acute phase reactant such as albumin, is present in large amounts in blood and cerebrospinal fluid and accumulates in high concentrations in calcified bone (Nawratil et al. 1996).

2.2. Fetuin-A's biological features and correlations with diseases

Fetuin-A undertakes important biological functions in diseases such as calcification, cardiovascular diseases, tumor progression, diabetes, obesity, and fatty liver disease (Figure 1).

Beginning, continuation and inhibition of calcification is a physiological process that is affected by many molecules, and a number of biomarkers can be used to follow up this process (Nafakhi, Al-Nafakh, and Al-Mosawi 2016; Small et al. 2017). It is considered that fetuin-A can be one of these potential biomarkers (Carracedo and Bäck 2018). It is reported that fetuin-A increases solubility of crystals by generating complexes with calcium and phosphor and acts as a calcification inhibitor (Di Minno et al. 2017; Ix et al. 2007). It is also stated that fetuin-A can inhibit calcium and phosphor incubation and crystallization for more than 9 days in physiological pH. The crystallization occurs just within hours in the absence of fetuin-A (Price and Lim 2003). Low serum fetuin-A concentrations are correlated with increased calcification levels in end-stage renal disease patients (Moe et al. 2005; Wang et al. 2005). In addition, low serum fetuin-A concentrations were found to be correlated with progression of severe vascular and valvular calcification, and increased cardiovascular diseases risk (Ketteler et al. 2003; Stenvinkel et al. 2005).

The effect shown against TGF-β1 (transforming growth factor-β1) is one of the most important biological effects of fetuin-A in cell culture. It is reported that fetuin-A acts as antagonist of TGF-β1 (Demetriou et al. 1996; Tajirian, Dennis, and Swallow 2000), and may specifically inhibit tumor growth with this effect (Swallow et al. 2004). In addition, fetuin-A administration induced increased secretion of pro-inflammatory cytokines (Hennige et al. 2008; Lee, Lim, and Yang 2015).

Progress in diabetes is controlled by various risk factors such as lifestyle habits, body composition and genetic susceptibility (Guo et al. 2017). Studies in the literature show that increased serum fetuin-A levels may be one of the risk factors of diabetes (Ochieng et al. 2018; Srinivas et al. 1993). It is reported that fetuin-A, an endogenous inhibitor of insulin receptor tyrosine kinase, may cause insulin resistance (Auberger et al. 1989; Guo et al. 2018; Srinivas et al. 1993). It is stated that fetuin-A may decrease insulin sensitivity by suppressing adiponectin production in adipose tissue (Hennige et al. 2008; Ix and Sharma 2010). In addition, obesity-induced insulin resistance and fat accumulation were found to be decreased in mice undergoing fetuin-A inhibition (Mathews et al. 2006; Mathews et al. 2002). Increased serum fetuin-A levels are correlated with insulin resistance in human studies, as well (Mori et al. 2006; Stefan et al. 2006). In line with these data, it can be considered that

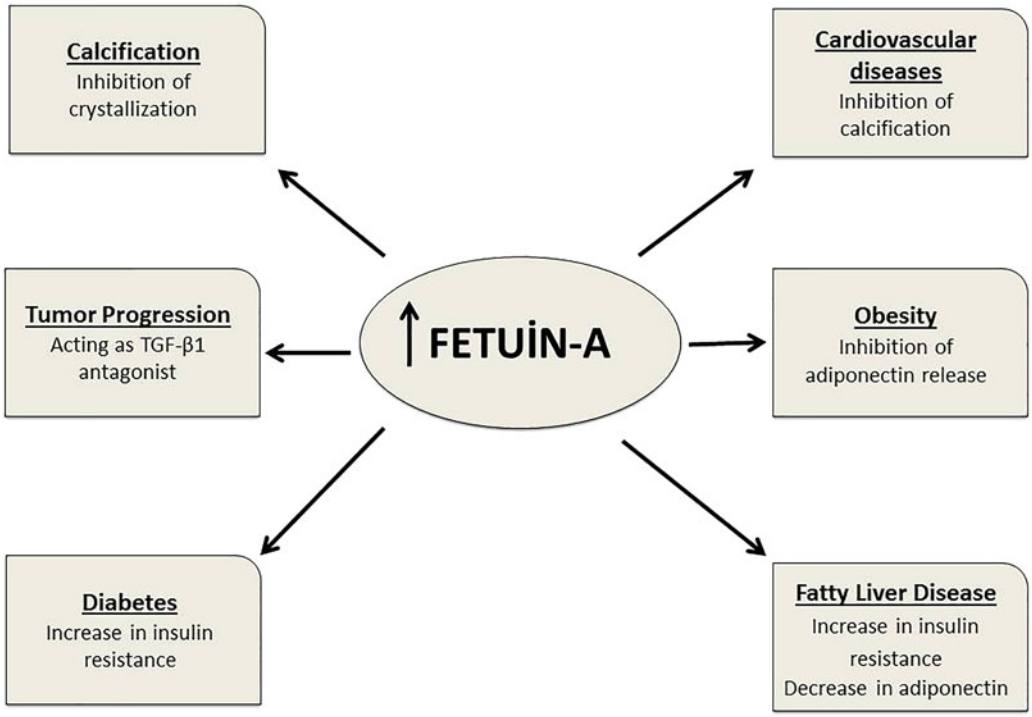

Figure 1. Main biological features of fetuin-A.

Table 1. Effects of obesity on fetuin-A level.

Author and reference	n	Study design	Conclusion
(Reinehr and Roth 2008)	50 individuals	1-year exercise, behavior and nutrition therapy.	Serum fetuin-A levels decreased with weight loss ($p < 0.05$).
(Yang et al. 2011)	40 individuals	3-month exercise therapy.	BMI values of participants decreased; however, the difference in their serum fetuin-A levels was not statistically significant ($p > 0.05$).
(Ix et al. 2009)	508 individuals	Body compositions and serum fetuin-A concentrations of participants were measured at 5-year interval.	Individuals with most increase in visceral adipose tissue also had the most increase in serum fetuin-A concentration ($p < 0.05$).
(Mathews et al. 2002)	23 mice	Evaluation of body composition and body weight increase of fetuin-A knockout mice.	Fetuin-A knockout mice resisted body mass increase and their body fat ratio decreased.
(Blumenthal et al. 2017)	16 individuals	6-month exercise and weight-loss diet therapy.	Participants' weight loss increased along with their plasma fetuin-A levels after the therapy ($p < 0.05$).
(Roshanzamir et al. 2017)	214 individuals	Participants' fetuin-A levels and anthropometric measurements were evaluated.	There was a positive correlation between their serum fetuin-A levels and BMI values.
(Xu et al. 2011)	5469 individuals	Evaluated participants' serum fetuin-A levels and obesity.	There was a positive correlation between serum fetuin-A levels and BMI values ($p < 0.05$).
(Mathews et al. 2006)	42 mice	Evaluated diet-induced obesity risk of fetuin-A knockout mice.	Diet-induced obesity risk of fetuin-A knockout mice decreased ($p < 0.05$).

increased serum fetuin-A level may increase the risk of type 2 diabetes by causing insulin resistance.

Increase in body fat and nan-alcoholic liver fat is another clinical consequence of increased serum fetuin-A levels leading to insulin resistance and inhibition of adiponectin release in adipose tissue (Hennige et al. 2008; Ix and Sharma 2010; Mori et al. 2006). The studies specifically focusing on body weight gain report that diet and exercise therapy may reduce the risk of insulin resistance, fatty liver disease and obesity by decreasing serum fetuin-A levels (Ix and Sharma 2010; Stefan et al. 2006).

3. Effects of obesity on fetuin-A level

Obesity has a multifactorial etiology resulting from the interaction of metabolic, genetic and environmental factors (Archer, Lavie, and Hill 2018; Weinsier et al. 1998). Rapid increase in the prevalence of obesity around the world makes it necessary to find out the causes of obesity and to develop preventive strategies (Flegal et al. 2012; Ogden et al. 2014). This is one of the main purposes of determining the correlation between fetuin-A level and obesity (Thakkinstian et al. 2014). There are various human and animal studies in the literature reporting that the increase in serum fetuin-A level is in direct proportion to the risk of obesity (Mathews et al. 2006; Thakkinstian et al. 2014). However, the relationship between fetuin-A and obesity, and the mechanisms that give rise to this correlation are not yet clear (Thakkinstian et al. 2014). There are possible mechanisms regarding this correlation (Fisher et al. 2009; Mathews et al. 2006). One possible mechanism is that fetuin-A increases obesity risk by creating insulin resistance through endogenous inhibition of insulin receptor tyrosine kinase (Guo et al. 2018; Mathews et al. 2006). Another possible mechanism is that fetuin-A level is parallel to obesity-related gene polymorphisms (Fisher et al. 2009; Thakkinstian et al. 2014). It is also reported that increase in serum fetuin-A level may increase obesity risk by preventing adiponectin release. Table 1 summarizes the studies examining the correlation between fetuin-A level and obesity in the literature.

In general, studies showed that exercise and/or diet therapy decreased serum fetuin-A levels by causing body weight losses (Table 1). Some studies showing that there is a correlation between increased serum fetuin-A level and body mass index (BMI) (Kalabay et al. 2002; Stefan et al. 2006). Brix et al. analyzed fetuin-A levels of 75 morbid obese patients (65 women, BMI $= 45.6 \pm 8.1\,kg/m^2$) and 38 healthy individuals of control group (21 women, BMI $= 26.0 \pm 5.5\,kg/m^2$) before and after bariatric surgery with body weight loss. It was found out in the study that fetuin-A levels of the morbid obese group were higher than the control group before body weight loss. Another result of the study was that body weight loss caused a statistically significant decrease in fetuin-A levels ($p < 0.05$) (Brix et al. 2010). In contrast to these studies, it was observed in another study that exercise and diet therapy caused an increase in serum fetuin-A levels (Blumenthal et al. 2017).

Taking the results of these studies into consideration, it is suggested that determination of the correlation between fetuin-A levels and obesity may contribute to prevention and treatment of obesity. For this purpose, further experimental studies are required to better understand the mechanisms of action of fetuin-A on obesity and to make definitive judgments.

4. Effects of nutritional status on fetuin-A level

There are studies in the literature evaluating the effects of dietary energy limitation, dairy products, meat, fish, coffee and alcohol consumption and protein, omega-3, palmitate, curcumin, turmeric, resveratrol and niacin intake on fetuin-A levels (Figure 2) (Kaushik et al. 2009; Lee et al. 2015; Ley et al. 2014; Nimptsch et al. 2015; Öner-İyidoğan et al. 2013; Stefan and Häring 2013; Yamada et al. 2015).

4.1. Effects of dietary energy on fetuin-A level

While the changes in body weight is the most important effect of dietary energy intake, it may also create different results in metabolism (Al-Regaiey 2016). For this purpose, many studies have been carried out on the effects of the

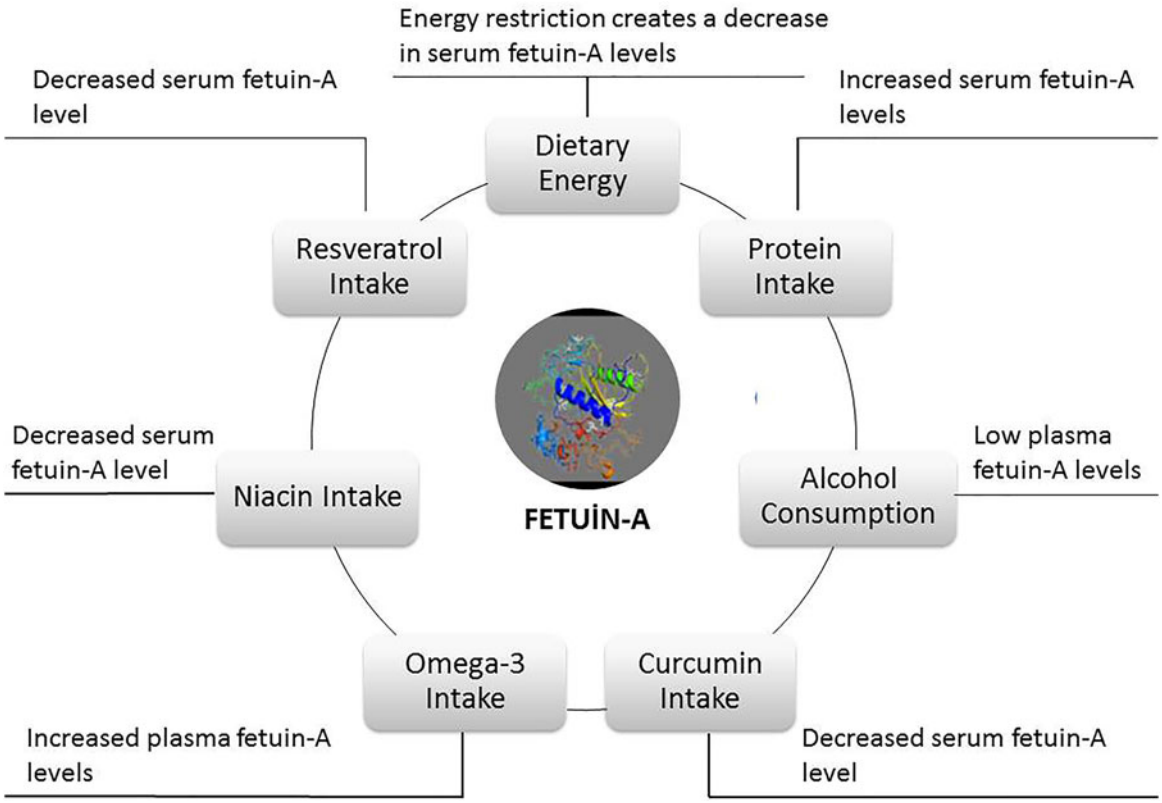

Figure 2. Effects of nutrients on fetuin-A.

energy content of the diet on human health (Ma et al. 2018; Nikhra 2018).

The studies examining the correlation between dietary energy density and fetuin-A levels are also part of these studies (Choi et al. 2013; Hwang et al. 2014). Choi et al. (2013) searched the effect of 30% dietary energy restriction on plasma fetuin-A level with seventy-six overweight women with type 2 diabetes. The study showed that 12-week-calorie restriction caused significiant decrease in hepatic expression and circulating levels of fetuin-A levels (Choi et al. 2013). In another study conducted with 40 healthy individuals to evaluate the effects of 28-day overfeeding (1,100 ± 100 kcal/day above baseline energy requirement, increasing mean dietary fat intake from 34 ± 1% to 45 ± 1% of energy intake) on serum fetuin-A levels, it was found out that increased energy intake also increased serum fetuin-A levels (Samocha-Bonet et al. 2014). Hwang et al. (2014) evaluated the effects of short and long term calorie restriction on fetuin-A level which were not found to be statistically significant (Hwang et al. 2014).

In line with these data, it can be concluded that dietary energy limitation or increase may have a direct effect on serum fetuin-A levels but more randomized controlled studies are still needed.

4.2. Effects of some nutrients and alcohol consumption on fetuin-A level

Nutrition has significant effects on human health with many different mechanisms (Mahan and Raymond 2016). Therefore, there are a large number of studies in the literature on the effects of dietary habits on diseases and the biomarkers associated with diseases (Icer, Gezmen-Karadag, and Sozen 2018; İçer and Gezmen-Karadağ 2018; Nimptsch et al. 2015). Recently, fetuin-A is one of the most important biomarkers examined within the scope of this subject (Blumenthal et al. 2017; Yamada et al. 2015). The increase in the number of studies which examine the correlation between diseases and fetuin-A level, and better understanding of the effects of nutrition on fetuin-A level boosted other studies in this field (Carracedo and Bäck 2018; Öner-İyidoğan et al. 2013).

There are very limited data on through which mechanisms nutritional habits can effect serum fetuin-A level (Nimptsch et al. 2015). Studies mostly focused on the correlation between dietary energy limitation, obesity, and serum fetuin-A levels (Blumenthal et al. 2017; Choi et al. 2013; Thakkinstian et al. 2014). However, there are also studies evaluating the correlation between consumption of some nutrients and serum fetuin-A level (Roshanzamir et al. 2017; Yamada et al. 2015). In the study conducted by Roshanzamir et al. (2017) to evaluate the correlation between Healthy Eating Index-2010 and fetuin-A levels, it was found out that there is a negative correlation between high-quality diet and serum fetuin-A levels (Roshanzamir et al. 2017). Another study showed that high glucose and fructose levels in blood increased fetuin-A release by activating extracellular signal-regulated kinase 1/2 enzyme (Haukeland et al. 2012). Yamada et al. (2015) found out that the diet combination including low protein and phosphate

decreased serum fetuin-A level (Yamada et al. 2015). It can be considered that glycoprotein structured fetuin-A can be affected by protein content of diet.

In the study conducted by Nimptsch et al. (2015) to evaluate nutrient intake of participants and its effects on plasma fetuin-A level by using their 24-hour food consumption records, it was determined that dietary increased dairy product consumption decreased fetuin-A concentrations. In addition, the study could not find a statistically significant correlation between fetuin-A concentrations and dietary vegetable, meat or fish consumption. In the statistical analyses of the study, there was not a correlation between dairy product consumption and fetuin-A levels when protein content of diet was excluded. There was not a remarkable change in the results when fat and calcium which are important compounds of dairy products were excluded in statistical analyses (Nimptsch et al. 2015). It is reported that there is an inverse correlation between consumption of dairy products and obesity and insulin resistance ($p < 0.05$) (Pereira et al. 2002). Additionally, it was indicated in the previous sections of this publication that fetuin-A affects insulin sensitivity.

Coffee consumption is associated with many biomarkers (Wedick et al. 2011; Zhang and Zhang 2018). Investigations of the relationship of coffee consumption with fetuin-A have been limited to three studies (Dickson et al. 2015; Jacobs et al. 2014; Wedick et al. 2011). In two of these studies, while the consumption of coffee was inversely related to fetuin-A levels (Jacobs et al. 2014; Wedick et al. 2011), one study did not find a relationship between coffee consumption and fetuin-A level (Dickson et al. 2015). Coffee consumption may be related to the fetuin-A level. However, it is not possible to reach an absolute judgment as there is only three study regarding this subject in the literature.

In contrary to the studies indicating that moderate alcohol consumption may have various positive effects on health, there are other studies claiming that increased alcohol consumption may increase the risk of a number of diseases (Baliunas et al. 2009; Ley et al. 2014; Liangpunsakul and Chalasani 2012). How fetuin-A, undertaking important roles in insulin resistance and adiponectin release, is affected by alcohol consumption is also an important research subject (Ley et al. 2014; Mori et al. 2006). Ley et al. (2014) searched the effect of alcohol consumption on plasma fetuin-A level with 1331 participants. The study showed that high alcohol consumption is correlated with low plasma fetuin-A levels (Ley et al. 2014). Another study conducted with 568 individuals aging between 13–80 also found an adverse correlation between alcohol consumption and fetuin-A concentrations (Nimptsch et al. 2015). In a study evaluating the effects of alcohol consumption on fetuin-A concentration, Joosten et al. (2014) determined that moderate alcohol consumption increased fetuin-A concentration in male participants and there was not a statistically significant correlation in female individuals (Joosten et al. 2014). Although the physiological mechanisms to explain the correlation between alcohol consumption and fetuin-A are not yet clear, a negative correlation can be suggested. However, in order to reach absolute judgment, it is very important consider the amount of alcohol consumption and the type of alcoholic beverage consumed.

4.3. Effects of curcumin, resveratrol, omega-3, palmitate and niacin intake on fetuin-A level

The effects of nutrients on diseases and biomarkers are mostly related to different food items in nutrients (Mahan and Raymond 2016). Therefore, there are some studies in the literature evaluating the effects of some nutrients such as curcumin, resveratrol, omega-3, palmitate and niacin on fetuin-A levels (An et al. 2012; Ghaffari et al. 2017; Kaushik et al. 2009; Mukhuty et al. 2017; Öner-İyidoğan et al. 2013).

Curcumin is the main bioactive compound of ginger obtained from the roots of the plant called *Curcuma longa*, a member of the Zingaberaceae family (Ammon and Wahl 1991). It is claimed that curcumin, a polyphenolic and hydrophobic compound, has potent antioxidants, anticarcinogens, anti-inflammatory and hypoglycemic properties (Ammon and Wahl 1991; Jacob et al. 2007; Manjunatha and Srinivasan 2007). In addition, it is reported that curcumin decreases serum triglyceride levels and have hypo-lipidemic effects on rats fed with high fat diet (Jang et al. 2008). It was explained in the previous sections that obesity caused by high fat diet increases fetuin-A concentrations through various potential mechanisms. Therefore, the effects of curcumin, which is known to have hypo-lipidemic effects, on fetuin-A concentrations is another current research subject. Although the mechanisms effects of curcumin on hepatic fetuin-A release are not yet fully clear, there are two possible mechanisms. One of these mechanisms is that curcumin supplementation inhibits hepatic fetuin-A release by regulating peroxisome proliferator-activated receptor-γ (PPAR-γ) receptors (Ochi et al. 2014; Seyithanoğlu et al. 2016). Other possible mechanism of the curcumin is reducing expression of hepatic fetuin-A by activating AMP-activated kinase (AMPK) (Öner-İyidoğan et al. 2013; Tang and Chen 2010). Seyithanoğlu et al. (2016) evaluated the effects of curcumin supplementation on hepatic fetuin-A release by supplementing 1.5 g/kg curcumin to the rats fed with high fat diet for 16 weeks. The study found out that hepatic fetuin-A release levels of rats decreased after curcumin supplementation (Seyithanoğlu et al. 2016). Another study showed that increased ginger consumption has not any statistically significant effect of serum fetuin-A levels (Ghaffari et al. 2017). Öner-İyidoğan et al. (2013) searched the effects of curcumin supplementation on serum fetuin-A levels of rats fed with high fat diet. The study demonstrated that curcumin supplementation (100 and 400 mg/kg bw/day curcumin) prevented liver fat accumulation and decreased serum fetuin-A levels ($p < 0.05$) (Öner-İyidoğan et al. 2013). According to these data, it can be considered that curcumin supplementation may contribute to the treatment of obesity by decreasing fetuin-A levels. However, further clinical studies are needed to support this hypothesis.

It is reported that combination of fetuin-A with fatty acids increases the risk of Type2 diabetes and cardiovascular

diseases by increasing insulin resistance and inflammatory signals on adipose tissue (Pal et al. 2012). It is indicated that increased plasma free fatty acids increase hepatic fetuin-A release in liver by scaling up NF-$_K$B activity (Dasgupta et al. 2010). It is also reported that fetuin-A levels may cause insulin resistance alone or along with free fatty acids in the patients with high dietary energy intake (Lee et al. 2017; Samocha-Bonet et al. 2014). In the study carried out by Lee et al. (2017) to examine whether there is any mutual interaction between plasma free fatty acids and fetuin-A concentrations of participants after 12-week exercise intervention, it was found out that there is not a mutual interaction between plasma free fatty acids and fetuin-A concentrations; however, plasma fetuin-A concentrations of participants decreased after the exercise intervention (Lee et al. 2017). Another study demonstrated that free fatty acids increased fetuin-A release from pancreatic β cells (Mukhuty et al. 2017). Okamoto et al (2018) found out that serum butyrylcholinesterase and fetuin-A levels are positively correlated (Okamoto et al. 2018). These data prove that dietary increased free fatty acids intake can affect fetuin-A concentration by increasing plasma free fatty acids.

An et al. (2012) evaluated plasma fetuin-A levels of 23 individuals out of 43 dialysis patients aging between 20 and 80 by supplementing 3 g/day of omega-3 fatty acids for 6 months. The results showed that omega-3 supplementation increased plasma fetuin-A levels (An et al. 2012). In line with these results, it can be considered that increase in dietary omega-3 fatty acids intake may also increase serum fetuin-A levels. However, these results must be supported with further research in order to reach absolute judgment regarding this subject.

There are studies in the literature reporting that serum fetuin-A concentrations and dietary niacin intake affect blood lipids (Andersen et al. 2008; Dahlman et al. 2004; Grundy et al. 2002; Vogt et al. 2007). These studies suggested that dyslipidemia risk has positive correlation with serum fetuin-A concentrations and negative correlation with niacin intake (Andersen et al. 2008; Dahlman et al. 2004; Grundy et al. 2002; Vogt et al. 2007). The study conducted by Kaushik et al. (2009) to evaluate fetuin-A levels of 15 patients with metabolic syndrome before and after niacin supplementation (500 mg/day in the first week, 1000 mg/day in the second week, and 1500 mg/day in the 3th-6th weeks) for 6 weeks found out that there was a statistically significant decrease in serum fetuin-A levels of patients after the supplementation. At the end of the study, it is stated that niacin intake may increase fetuin-A gene expression by increasing endogenous glucocorticosteroid level (Kaushik et al. 2009). As a consequence of study results and its adverse effects on dyslipidemia, dietary niacin intake can be considered to have possible effects on serum fetuin-A levels. However, it is not possible to reach an absolute judgment as there is only one study regarding this subject in the literature.

It is indicated that fetuin-A release decreases adiponectin release, while dietary resveratrol intake increases adiponectin release (Dalamaga et al. 2013; Hennige et al. 2008). It is reported that the decrease in the release of adiponectin increases the risk of many diseases such as nonalcoholic fatty liver disease, insulin resistance and obesity (Dalamaga et al. 2013; Kawano and Arora 2009). It can be considered that there is a correlation between fetuin-A level and resveratrol intake due to its adverse effects on adiponectin release level. Lee et al. (2015) evaluated serum adiponectin and fetuin-A levels of obese rats fed with high fat diet by supplementing 8 mg/kg/day of resveratrol for 4 weeks. The study demonstrated that resveratrol supplementation increased serum adiponectin level and decreased serum fetuin-A level. Another result of the study is that serum adiponectin level and serum fetuin-A level have an adverse correlation (Lee et al. 2015). In the light of these data, it can be concluded that resveratrol supplementation may have positive effects on health by affecting serum fetuin-A and adiponectin levels.

5. Conclusion

Serum fetuin-A concentration, which is thought to have many controversial effects on health, is a glycoprotein that decreases due to dietary energy limitation. Although its mechanisms have not been fully explained yet, it can be considered that consumption of dairy products, coffee and alcohol, and dietary intake of curcumin, resveratrol and niacin may also decrease serum fetuin-A concentrations. In contrast to these negative correlations, it can be claimed that omega-3 intake may increase serum fetuin-A concentrations. According to these data, it can be concluded that fetuin-A is a biomarker affected by nutritional status. Clear explanation of the correlations between diet and serum fetuin-A concentration may contribute to keep serum fetuin-A concentration at certain levels. However, it is necessary to conduct further research to reach absolute conclusions and determine by which mechanisms nutrients show this effect on fetuin-A concentrations.

Disclosure statement

No potential conflict of interest was reported by the authors.

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