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Professional paper

ADVANCED GLYCATION END PRODUCTS IN FOODS

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Abstract

Advanced glycation end products (AGEs) are products formed as a result of Maillard reaction, which is a chemical reaction between the carbonyl group of carbohydrates and free amino groups of amino acids. AGEs can be produced endogenously as part of normal metabolism or ingested exogenously with food. AGEs cannot be eliminated from metabolism, but they can be slowed down and reduced with appropriate methods. The amount of AGE formation in foods depends on various factors such as food composition (protein > fat > carbohydrate), cooking method, temperature and time, humidity, pH and the presence of antioxidants. While AGEs are found naturally in uncooked foods of animal origin, new AGEs can be formed in foods as a result of heat treatment. Especially, processes such as grilling, roasting and frying increase and accelerate the formation of new AGE. Consuming foods containing high amounts of AGE causes diabetes as well as many chronic diseases such as cardiovascular, neurodegenerative and kidney diseases. Therefore, it is important to reduce the amount of exogenous AGE that will enter the body by applying methods to reduce the formation of AGEs in processed foods. As a result consumption of foods with high AGE content should be reduced, processed foods should be avoided, and the cooking temperatures and cooking methods should be controlled during the preparation of the food. The purpose of this review is to determine the effects of various food preparation methods on AGE production and to examine the AGE content of commonly consumed foods.

Keywords: Advanced glycation end products, AGE, Maillard reaction, food, nutrition, health

1.Introduction

Heat treatments effect important functions in food preparation by improving digestibility, ensuring microbiological safety, and developing flavor. During cooking, significant chemical changes can occur that improve the sensory quality of food, but some undesirable chemical changes can also occur. This can lead to the loss of nutritional components of some foods and the reduction of their nutritional value, as well as harm health through the formation of toxic substances (Pedreschi & Murkovic, 2018). Maillard reaction is one of the most important reactions that occur during heat treatment applied to foods, and it greatly affects the basic quality characteristics of foods such as flavor, aroma, color, and texture. In fact, this reaction is used to produce foods with sensory qualities that are demanded by the consumer. However, Maillard reaction products, which are produced with a non-enzymatic process, can be harmful to human health, even though they have a positive effect on the sensory quality of the food (Bastos, Monaro, Siguemoto & Séfora, 2012). Advanced glycation end products (AGEs) are products formed as a result of Maillard reaction, which is a chemical reaction between the carbonyl group of carbohydrates and free amino groups of amino acids. AGEs can occur endogenously in the body as well as exogenously in food (Demirel & Yıldıran, 2018; Rahman & Rostam, 2020). Although the formation of AGEs is a part of normal metabolism, it can become pathogenic if AGEs in tissues and circulation reach extremely high levels (Ulrich & Cerami, 2001). While AGEs are found naturally in uncooked foods of animal

origin, new AGEs can be formed in foods as a result of cooking. Especially some processes such as grilling, roasting, and frying increase and accelerate the formation of new AGE (Uribarri et al., 2010).

Today, with the improvement in living standards, the consumption of processed foods is increasing and the harmful substances in terms of food safety, which result from these changes in dietary habits, pose a serious risk to human health (Nie, Li, Qian & Wang, 2020; Zhang, Wang, & Fu, 2020). In recent years, especially the increase in the consumption of processed foods has increased the intake of exogenous AGE and the exposure to AGEs (Yılmaz & Karabudak, 2018). AGEs are formed in processed and ultra-processed foods in accordance with the degree of processing. For example, modern foods are often processed with high heat and as a result, high levels of AGE occur (Uribarri et al., 2010; Yıldız & Wiley, 2017).

AGEs ingested have an effect on human health depending on the absorption and distribution of the compounds, and consumption of foods with high amounts of AGE causes many chronic diseases such as cardiovascular, neurodegenerative, and kidney diseases, as well as diabetes (Nowotny, Schröter, Schreiner & Grune, 2018; Rahman & Rostam, 2020). AGEs accumulate slowly in circulation and tissues. However, the accumulation of AGEs increases with age and greatly speeds up with chronic diseases such as diabetes, kidney disease, and cardiovascular disease (Šebeková, Klenovics& Šebeková, 2014; Stirban, Gawlowski& Roden, 2015).

Fresh or minimally processed foods should make up 80% of the daily diet in order to reduce the accumulation of AGEs (Yıldız & Wiley, 2017). To prevent the formation of AGE compounds, not only the amount and composition of the food, but also the way the food is prepared, such as the cooking temperature, the cooking method, and the duration of the heat application are very important. Foods with high lipid and protein content contain more AGE, while foods high in carbohydrate content such as fruits, vegetables, and milk have low AGE concentrations. Using methods such as boiling and steaming instead of using dry and high heat for cooking results in less AGE formation. Cooking at lower temperature and for shorter time helps to reduce AGE production as well. As a result, daily AGE intake can be significantly reduced by selecting the right food and the correct food preparation techniques (Goldberg et al., 2004; Kutlu, 2016; Radoi, Lixandru, Mohora & Virgolici, 2012; Vlassara, Woodruff & Striker, 2017).

The purpose of this review is to determine the effects of various food preparation methods on AGE production and to examine the AGE content of commonly consumed foods such as meat and meat products, oils, grain products, milk and dairy products, vegetables and fruits.

2. Foods and AGEs

The formation of advanced glycation end products and their effectiveness in metabolism are closely related to processing and cooking of food. (Yıldız & Wiley, 2017). Among the main factors determining the amount of AGE formation in foods, there are various factors such as the composition of the food (protein> fat> carbohydrate), cooking method temperature and time, humidity, pH level, the speed and variety of the Maillard reaction, and the presence of antioxidants. For example, foods rich in protein and fat can reach a higher AGE concentration with an increase in cooking time and temperature, although they already have a high AGE concentration. In short, the higher the temperature processing (frying> grilling> boiling) is during the preparation of the food, the higher AGE concentration will be in the food (Goldberg et al., 2004; Kandaraki & Kandarakis-Dimanti, 2018; Kutlu, 2016; Sharma, Kaur, Thind, Singh & Raina, 2015). Figure 1

shows the effect of frying, grilling, and boiling processes used during food preparation on AGE concentration in foods (Kandaraki & Kandarakis-Dimanti, 2018).

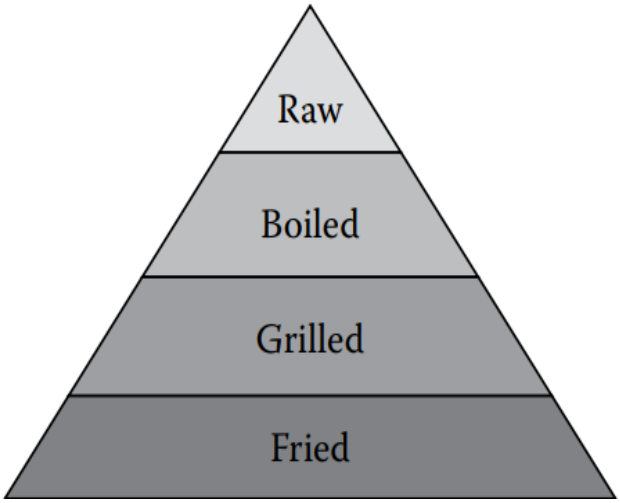

Figure 1. The AGEs Pyramid (Kandaraki & Kandarakis-Dimanti, 2018)

AGEs can be reduced with various treatment options that are used to prevent the effects of AGEs. However, since there are not enough studies on pharmacological interventions, serious problems may arise if they have side effects. Therefore, reducing AGEs with alternative diet options should be preferred instead of pharmacological interventions. Recommendations for reducing AGEs ingested with food can be summarized as follows (Cai et al., 2004; Sharma et al., 2015).

- Low cooking temperatures should be used instead of high cooking temperatures.
- Methods such as boiling and steaming should be preferred instead of frying, roasting, and grilling.
- Since high temperature and low humidity levels will increase the formation of AGEs ingested, attention should be given to the cooking method and time-temperature adjustment.
- Acidic ingredients such as vinegar and lemon juice should be added to foods during preparation.
- Plants containing antioxidant and phenolic substances such as green tea should be added to the diet.
- Foods should be consumed fresh with every meal as much as possible.

In a study, samples from lean beef were marinated in acidic solutions of vinegar and lemon for 1 hour before cooking, and then new AGE formation was detected in cooked meat. Beef (25 g) was cooked for 15 minutes at 150°C marinated or non-marinated in 10 ml of vinegar (A) of 10 ml of lemon juice (B) for 1 hour. As a result, it was found that beef marinated in vinegar or lemon produced less AGE compared to cooked samples. Antioxidants in foods prevent the formation of AGE by acting as an AGE inhibitor. Lemon and vinegar are foods with high antioxidant content and as a result of marinating the meat before cooking, the antioxidant capacity is increased and the meat is softened. This process of marinating prevents the meat from getting in contact with heat for a long time by decreasing the cooking time. Depending on the antioxidant capacity, the amount of AGE is also reduced. The effect of acidic environment on AGE content of beef is shown in Figure 2 (Uribarri et al., 2010).

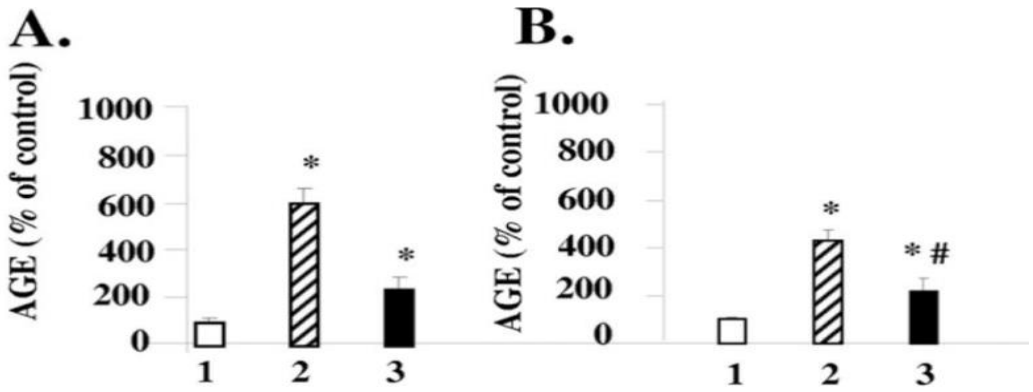

Figure 2. Effect of acidic environment on the AGE content of beef (Uribarri et al.,2010)
1 = Raw beef, control sample
2 = Roasted beef with no vinegar or lemon
3 = Roasted beef after marinating with either vinegar or lemon for 1 hour

The amount of AGE increases above 20.000kU/day by consuming foods that are heat treated with methods such as grilling and roasting. This situation negatively affects human health and increases the risk of disease (Uribarri et al., 2010). There is limited data on the consumption of AGE in the general population. In a study conducted with healthy adults in New York, it was found that the average daily consumption of AGE was 14,700 kU/day (Uribarri et al., 2007).
Vlassara et al. (2016) conducted a 1-year study by dividing obese individuals with metabolic syndrome into two groups. One group of participants consumed foods with low AGE levels (L-AGE), while the other group consumed foods with high AGE levels (Reg-AGE), which they usually preferred out of habit.After the participants were individually instructed on how to reduce AGE intake in their diet by simply changing the cooking time and temperature without changing the quantity, quality, or composition of the food, they were specifically asked to avoid frying, baking, or grilling, and were encouraged to boil or steam their food. An example of a participant's daily dietary AGE intake on the L-AGE diet is shown in Table 1. As a result of this study, it was revealed that L-AGE diet can improve insulin resistance in obese people with metabolic syndrome, which is an important risk factor for type 2 diabetes. It also provides clinical evidence that high levels of AGE are associated with diets rich in AGE and this is among the factors that increase the risk of insulin resistance.

Table 1. Sample of daily dietary AGE intake (Vlassara et al.,2016)

Meal	**High AGE Diet (Reg-AGE)**			**Low AGE Diet (L-AGE)**		
	Item	**Portion**	**AGEs**	**Item**	**Portion**	**AGEs**
Breakfast	Fresh Fruit Cup	½ cup	15	Fresh Fruit Cup	½ cup	15
	Fried Eggs	1	**1200**	**Boiled Egg**	1	**75**
	Toasted Bagel	112g	**200**	**Fresh Bagel**	112g	**120**
	Cream Cheese	5 ml	500	Cream Cheese	5 ml	500
	Skimmed Milk	240 ml	2	Skimmed Milk	240 ml	2
	Coffee	240 ml	19	Coffee	240 ml	19

Lunch	Orange Juice **Grilled Chicken** Green Salad Caesar Dressing Bread,white Margarine Iced Tea Apple	120 ml 84 g 1 cup 30 ml 1 slice 5 ml 360 m 1 medium	3 **5200** 0 200 10 900 5 15	Orange Juice **Poached Chicken** Green Salad Caesar Dressing Bread,white Margarine Iced Tea Apple	120 ml 84 g 1 cup 30 ml 1 slice 5 ml 360 m 1 adet	3 **1000** 0 200 10 900 5 15
Dinner	Cantaloupe Wedge **Grilled Steak** Mashed Potato Carrots Coffe With Milk Muffin (Bran)	¼ small 84 g 1 ½ cup 240 ml 1	20 **6600** 20 10 5 102	Cantaloupe Wedge **Beef Stew** Mashed Potato Carrots Coffe With Milk Muffin (Bran)	¼ small 84 g 1 ½ cup 240 ml 1	20 **2200** 20 10 5 102
Total AGEs(kU)			**15.026**			**5221**
Total Energy, kJ/day			**7.94**			**7.77**

In line with the data in Table 1, it was found that obese individuals with metabolic syndrome consume significantly more dietary AGE compared to healthy obese individuals, even while consuming similar amounts of calories. L-AGE can offer a suitable treatment goal to reduce the risk of type 2 diabetes in obese people without a change in calorie intake or significant weight loss. L-AGE has been found to reduce insulin resistance in obese people at risk, and because it is a difficult process to lose weight, it can be considered as a new additional approach (for example, other than calorie restriction or drugs) for insulin resistance treatment (Vlassara et al., 2016).

In a study conducted, a three-day "individual food consumption record" was kept for 200 volunteers between the ages of 18-28. According to the three-day "individual food consumption record" data provided by the students, the daily amounts of AGE taken by the students was calculated by comparing them with 549 foods with known AGE contents. The average AGE intake level of the individuals participating in the study was found to be 8900.75 ± 302.33 kU, the daily AGE intake level was found to be 10570.92 ± 794.57 kU for the male individuals and it was found to be 8534.12 ± 318.97 kU for the female individuals ($p>0.05$). As a result, as the AGE contents of fried foods, meat cooked at a high temperature, high-fat and processed foods are higher compared to vegetable-based and less processed foods, individuals with western-style eating habits have higher dietary AGE intake levels (Erim & Garipoğlu, 2020).

In another study, AGE contents of mixed fruit juices, one of the frequently consumed food products, were investigated. 11 different mixed fruit juice samples examined were purchased from various markets in Istanbul. The total AGE contents of the samples were found in the range of 535-6517 µg / 100 mL and it was found that they contain high levels of AGE (Çatak, 2020).

Many food products contain AGE more or less, and the AGE contents of food groups such as meat and meat products, fats, grain products, milk and dairy products and vegetables and fruits are given below.

2.1Meat and meat products: Meat and meat products provide most of the nutrients necessary for human health and are a rich source of protein and micronutrients (vitamins A, B_6, B_{12}, D, E and iron) (Yılmaz & Geçgel, 2009). AGE contents of some meat and meat products are given in Table 2 (Uribarri et al., 2010).

Table 2. AGE contents of some meat and meat products (Uribarriet al., 2010)

FOOD ITEM	AGE kU/100 g
Beef Steak Grilled	7416
Beef Stewed	2443
Chicken Breast Broiled (Skinless)	5828
Chicken Breast Poached (Skinless)	1076
Lamb Leg Broiled	2431
Lamb Leg Boiled	1218
Salmon Fillet Poached	2292
Salmon Fillet Broiled	3347

High AGE levels were detected in the meat and meat products group. This is due to the high content of AGE in foods with high protein and fat content, such as meat and meat products. When foods prepared with similar methods were compared, beef, chicken meat, and fish meat were found to contain the highest levels of AGE, respectively. The AGE content of lamb meat was found to be relatively lower compared to other meat products. The amount of AGE content in the food also depends on the cooking methods.The AGE content of boiled or steamed chicken is about a quarter of that of roasted or grilled chicken. Frying, grilling, and roasting cause a higher level of AGE content compared to boiling and steaming. For example, grilled chicken meat contains more AGE than boiled red meat (Goldberg et al., 2004; Sharma et al., 2015; Uribarri et al., 2010).

2.2Fats: Fats have an important place in human nutrition because they contain some essential fatty acids and fat-soluble vitamins (A, D, E, K) and are an important source of energy. Fat-rich foods are divided into two as animal fats and vegetable fats according to their source, and it is recommended that 25% of the energy coming from the daily diet comes from fat (Demirci, 2011). AGE contents of some fat types are given in Table 3 (Uribarri et al., 2010).

Table 3. AGE contents of some fat types (Uribarri et al.,2010)

FOOD ITEM	AGE kU/100 g
Butter	26480
Margarine	17520
Mayonnaise	9400
Canola Oil	9020
Corn Oil	2400
Olive Oil	11900

Sunflower Oil	3940
Safflower Oil	3020

Fats, especially those of animal origin, have a high content of AGE even in their uncooked form compared to other food groups. Among the items of this group, spreadable products such as butter, margarine, and mayonnaise have the highest AGE content level, followed by oils such as olive oil and canola oil (Goldberg et al., 2004).

2.3Grain products: As the main food source, grains that meet the daily energy needs of more than 60% of the world's population contain high levels of carbohydrates as well as protein, and some fat (Ay, 2020). In addition, being rich in vitamins, minerals, dietary fiber, and proteins makes grains an excellent source of high-value nutraceuticals and bioactive compounds (Agyei et al., 2020). AGE contents of some grain products are given in Table 4 (Uribarri et al., 2010).

Table 4.AGE contents of some grain products (Uribarri et al., 2010)

FOOD ITEM	**AGE kU/100 g**
White Bread (1 slice)	83
Toasted White Bread (1 slice)	107
Bagel	107
Toasted Bagel	167
Biscuit	1470
Corn Flakes	233
Pancake(homemade)	973
Pasta (cooked 8 minute)	112
Pasta (cooked 12 minute)	242
White Rice (cooked 10 minute)	9
White Rice (cooked 30 minute)	32
Potato Chips	2883
Pretzel	1757

Compared to the meat and fat groups, the grain products group generally contains lower amounts of AGE. The reason for this may be that this group has a high level of water, antioxidants, vitamin, and carbohydrate content. Even when grains such as pasta and rice are cooked, their AGE levels do not increase much. However, the AGE content of processed grain products such as chips, crackers, and biscuits is high. This may be due to the addition of ingredients such as butter, oil, and cheese, which significantly accelerate the formation of AGE during dry heat treatment. Although the AGE amounts of these snacks are far below those found in meats, they may pose a significant health risk for people who consume more than one snack per day (Story, Hayes, & Kalina, 1996; Uribarri et al., 2010).

2.4 Milk and dairy products: Milk is considered a complete food for humans as it contains most of the essential nutrients. Milk and dairy products such as milk, yoghurt, and cheese in our daily diet are consumed especially for their protein and calcium content. It is also an important source of many nutrients, especially vitamins (A, B_2, B_{12}, D) and minerals (P, Mg). All age groups,

especially adult women, children, and young adults, should consume milk and dairy products every day (Singh & Sachan, 2011; Ünal & Besler, 2008). AGE contents of some milk and dairy products are given in Table 5 (Uribarri et al., 2010).

Table 5. AGE contents of some milk and dairy products (Uribarriet al., 2010)

FOOD ITEM	AGE kU/100 g
Cottage Cheese	1453
Cheddar Cheese	5523
Parmesan Cheese	16900
Fat Free Milk	2
Whole Milk	5
Yogurt (Vanilla)	3

Within the milk and dairy products group, cheese has the highest level of AGE (Goldberg et al., 2004). Although cooking is known to trigger the formation of new AGEs in foods, high amounts of AGE have been detected even in uncooked and animal-based foods such as cheese. The reasons for this are the pasteurization process and the waiting period at room temperature. Full-fat or aged cheeses such as Parmesan cheese contain more AGE than low-fat cheeses such as cottage cheese and cheddar cheese. In addition, the AGE content of foods with high water content such as milk and yogurt is low (Sharma et al., 2015; Uribarri et al., 2010).

2.5 Vegetables and fruits: Vegetables and fruits, which are important sources of vitamins and minerals, contain low calories as well as high level of fiber, cellulose, and organic acid content. Due to these properties, vegetables and fruits, which have a regulating effect on the digestive system, constitute the basic nutritional resources of people (Ay, 2020). AGE contents of some vegetables and fruits are given in Table 6 (Uribarri et al., 2010).

Table 6. AGE contents of some vegetables and fruits (Uribarri et al., 2010)

FOOD ITEM	AGE kU/100 g
Apple	13
Banana	9
Cantaloupe	20
Orange Juice	6
Canned Carrots	10
Celery	43
Cucumber	31
Onion	36
Tomato	23
Canned Corn	20
French Fries	1522
Dried Fig	2663

The AGE content of vegetables and fruits is considered to be at a negligible level (Nowotny et al.,2018). This is because vegetables and fruits have high water content as well as low protein and fat content. In addition, vegetables and fruits are rich in antioxidants. Antioxidants are thought to

lower the AGE content of foods. Freezing, canning, or juicing fruits and vegetables do not affect their AGE content, but drying increases their AGE content. Nevertheless, AGE contents of dried fruits remain at lower levels compared to foods of animal origin (Uribarri et al.,2010).

3. Conclusions

AGEs in foods and their relationship with nutrition have been one of the most frequently examined research topics in recent years. The level of AGE intake through food can be reduced by carefully selecting food, changing the cooking method and adjusting the time-temperature relationship correctly. In general, with a diet in which the consumption of red meat, fat, fast food, and processed foods are decreased and consumption of foods such as boiled meat and fish, whole grains, vegetables and fruits are increased, the intake of AGEs can be reduced, which protects against various disease risks.

Future studies should continue to investigate the health effects of exogenous AGEs and recommendations for safe eating should be improved. Considering the possible health risks of AGE intake through food, individuals should be informed about advanced glycation end products and acquire healthier eating and cooking habits. In addition, there is a need to detect the level of AGE content in all foods and to develop additional methods to reduce the formation of AGE during food processing.

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