
SHORT COMMUNICATION

Advanced Glycation End Products and Nutrition

M. KRAJČOVIČOVÁ-KUDLÁČKOVÁ, K. ŠEBEKOVÁ, R. SCHINZEL¹,
J. KLVANOVÁ

Institute of Preventive and Clinical Medicine, Bratislava, Slovak Republic and ¹Institute of Physiological Chemistry, University of Würzburg, Würzburg, Germany

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Summary

Advanced glycation end products (AGEs) may play an important adverse role in process of atherosclerosis, diabetes, aging and chronic renal failure. Levels of N^ε-carboxymethyllysine and fluorescent AGE values were estimated in two nutritional population groups – alternative group (vegetarians - plant food, milk products, eggs) and traditional group (omnivorous subjects). Vegetarians have a significantly higher carboxymethyllysine content in plasma and fluorescent AGE values. Intake of proteins, lysine and monosaccharides as well as culinary treatment, consumption of food AGEs (mainly from technologically processed products) and the routes of Maillard reaction in organism are the substantial sources of plasma AGEs. Vegetarians consume less proteins and saccharides. Lysine intake is significantly reduced (low content in plant proteins). Subjects on alternative nutrition do not use high temperature for culinary treatment and consume low amount of technologically processed food. Fructation induced AGE fluorescence is greater as compared with that induced by glucose. It is due to higher participation of a more reactive acyclic form of fructose. Intake of vegetables and fruit with predominance of fructose is significantly higher in vegetarians. Comparison of nutrition and plasma AGEs in vegetarian and omnivorous groups shows that the higher intake of fructose in alternative nutrition of healthy subjects may cause an increase of AGE levels.

Key words

N^ε-carboxymethyllysine • Fructose • Vegetarian diet • Advanced glycation end products

The non-enzymatic reaction of reducing carbohydrates with lysine side chains and N-terminal amino groups of macromolecules (amino acids, proteins, phospholipids and nucleic acids) is called the Maillard reaction (Njoroge and Monier 1989) or glycation. The latter products of this process, termed advanced glycation end products (AGEs), adversely affect the functional properties of proteins, lipids and DNA (Ledl and Schleicher 1999). In long-lived tissue proteins, these

chemical modifications accumulate with age and may contribute to the pathophysiology of aging and long-term complications of diabetes, atherosclerosis and renal failure (Vlassara *et al.* 1994, Makita *et al.* 1994). AGEs are produced from monosaccharides as glucose and fructose, but also from dicarbonyl compounds derived from the Maillard reaction, autoxidation of sugars and other metabolic pathways, e.g. glycolysis (Thornalley 1990, Wells-Knecht *et al.* 1995). The mentioned routes of

Table 1. Group characteristic, levels of N^ε-carboxymethyllysine, values of fluorescent AGEs, intake of proteins, lysine, saccharides and intake of fruit and vegetables with higher fructose content as compared to glucose content

	Nutrition	
	Traditional	Alternative
Number of subjects	19	19
<i>Average age (years)</i>	30.5 ± 6.9	36.1 ± 10.8
<i>BMI (kg/m²)</i>	23.8 ± 1.7	22.0 ± 2.1 **
<i>Period of vegetarianism (years)</i>	–	7.2 ± 4.2
<i>N^ε-carboxymethyllysine (ng/ml)</i>	427 ± 65	525 ± 129 **
<i>N^ε-carboxymethyllysine (ng/mg of prot.)</i>	5.59 ± 0.96	7.58 ± 1.74 **
<i>Fluorescent AGEs (AU/ml x 10³)</i>	9.91 ± 2.06	13.07 ± 3.34 *
<i>Fluorescent AGEs (AU/mg of prot.)</i>	130 ± 26	190 ± 52 **
Intake (g/day)		
<i>Proteins</i>	88.6 ± 22.6	63.8 ± 18.2 ***
<i>Lysine</i>	3.95 ± 1.43	2.41 ± 0.82 **
<i>Saccharides</i>	415 ± 104	393 ± 78
<i>Vegetables (F>G)</i>	75.3 ± 37.8	117.5 ± 51.7 ***
<i>Fruit (F>G)</i>	340 ± 156	601 ± 139 ***
<i>Apples (5.6 g F; 3.0 g G)</i>	140 ± 100	396 ± 101 ***
<i>Dried apples (20.1 g F; 11.0 g G)</i>	3.1 ± 2.6	11.8 ± 6.5 ***
<i>Citruses (F>G)</i>	14.1 ± 15.2	66.8 ± 45.6 ***
<i>Honey (37.9 g F; 31.4 g G)</i>	2.26 ± 1.78	8.42 ± 6.65 ***

Results are expressed as means ± S.D.; * $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$; AGEs – advanced glycation end products AU – arbitrary units; glucose and fructose content is expressed as g/100 g of product.

Maillard reaction in organism and exogenic AGE values from food (mainly culinary and technologically processed) may be a major source of intracellular and plasma AGEs (Thornalley 1990, Takeuchi *et al.* 2000).

In this report we investigated the AGE products (N^ε-carboxymethyllysine levels /CML/ and fluorescent AGE values in plasma) in alternative nutrition group of adults (vegetarians /lactoovo/) in comparison to the traditional group (Table 1). The groups were randomly selected from 155 subjects (district Bratislava, Slovak Republic). The levels of CML in plasma were analyzed after proteinase K digestion in triplicate by competitive ELISA using monoclonal antibodies 4G9 (Mellinghoff *et al.* 1997) against CML developed by Roche Diagnostics (Germany). N-(carboxymethyl)-aminocaproic acid served as a standard. Fluorescence of 50-fold diluted plasma samples was estimated in duplicate on Fluorite 1000 analyzer at 350/450 nm (Muench *et al.* 1997).

Besides blood analysis and antropometric characteristics, dietary habits were assessed by a food frequency questionnaire. The nutrient content was calculated using the package "Nutrition" based on the Slovak food composition database. All vitamins and trace elements were consumed only in their natural form. Student's t test was used for statistical analysis.

CML levels (Table 1) are significantly higher in vegetarians. In an alternative nutrition group, the fluorescent AGE values are also significantly higher. CML, a major product of oxidative modification of glycated proteins, has been suggested to represent a general marker of oxidative stress and long-term damage of proteins in aging, atherosclerosis and diabetes (Ledl and Schleicher 1999). Vegetarians consume less proteins and saccharides (Table 1). The lysine intake (Table 1) is significantly reduced (low content of plant proteins). Subjects on alternative nutrition do not use high

temperature for culinary treatment. They prefer heat treatment at lower temperature for short period of time. Some milk products, especially heat-treated and products with added sugar or stabilizing agents, have a higher content of CML (Drusch *et al.* 1999). Lacto-ovovegetarians consume significantly lower amount of milk products (together 220 ± 17 g/day vs. 469 ± 41 g/day in traditional nutrition). After excluding all the above mentioned dietary possibilities of the increase AGE products in individuals consuming alternative nutrition we focused on composition of the consumed monosaccharides.

Fluorescence as an index of advanced glycation increased linearly for human serum albumin incubated with glucose and exponentially when fructose was added to the incubation medium (Jakuš *et al.* 1998). Measurements of relative fluorescence showed that fructation induced AGE fluorescence was greater than AGE fluorescence induced by glucose (Jakuš *et al.* 1998). It is due to higher proportion of more reactive acyclic form of fructose vs. glucose. From the ratio of prevalence of the acyclic to cyclic form of monosaccharide results the relative reactivity for AGE production (Beswick and Harding 1985), because only the acyclic forms of sugar participate in the glycation process.

A typical difference of alternative nutrition in comparison to traditional nutrition besides a higher

consumption of whole grain products, sprouts, seeds and plant fats also concerns the significantly higher intake of fruit and vegetables (Krajčovičová-Kudláčková *et al.* 1995, 1996). Many species of vegetables and fruit have higher proportion of fructose in comparison to glucose. Intake of fruit and vegetables with higher content of fructose vs. glucose and intake of apples and honey evaluated from the dietary questionnaires indicated that fructose consumption is significantly higher in vegetarians as compared to subjects on a traditional diet (Table 1). Fresh and dried apples have almost a twofold content of fructose vs. glucose and their consumption is higher in vegetarians. Furthermore the intake of honey is three times higher in vegetarians.

Comparison of nutritional regime and values of AGEs shows that the higher intake of fructose in alternative nutrition of healthy subjects may cause an increase plasma AGE values. Protective effect of regular consumption of vegetables and fruit dominantly concerns the prevention of free-radical diseases. The risks of alternative nutrition may be reduced by better choice of foodstuffs. Our finding of elevated plasma AGE concentrations in vegetarians should prospectively be followed from the point of their pathophysiological relevance.

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Reprint requests

M. Kudláčková, Ph.D., Institute of Preventive and Clinical Medicine, Limbová 14, SK-833 01 Bratislava, Slovak Republic