

Effects of Different Herbal Teas on Reducing the Bioaccessibility of Methylglyoxal in Crackers under Stimulated Gastrointestinal Digestive System

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Abstract: The present study aims to determine the bioaccessibility of methylglyoxal (MGO) in crackers and investigate the effects of herbal teas on reducing the formation of MGO under *in vitro* digestion system. Different herbal teas were added in crackers to reduce MGO formation under *in vitro* system. MGO levels were determined by High-Performance Liquid Chromatography. The amounts of MGO in cracker samples at initial and after *in vitro* digestion were ranged from 51 to 104 µg/100 g and 274 to 408 µg / 100 g, respectively. After *in vitro* digestion, the bioaccessibility of MGO values was increased up to 628%. Also, it was found that polyphenol-rich herbal teas such as black, green, turmeric, and rosehip significantly reduced MGO bioaccessibility in crackers. The addition of these herbal teas as antioxidants in cracker formulations or consumption of herbal teas along with snack foods may be recommended.

Keywords: food processing; advanced glycation end products; methylglyoxal; crackers; bioaccessibility.

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1. Introduction

Processed foods are widely consumed in today's modern diet [1]. Food processing techniques can lead to the formation of α -dicarbonyl compounds (α -DC) in processed foods due to high-temperature processes, nutrition composition, low moisture, and pH [2]. α -DC such as glyoxal (GO), and methylglyoxal (MGO) can be derived from Maillard reaction, caramelization, sugar autoxidation, and lipid peroxidation. The pathway through which α -DC are produced depends on food composition and processing conditions. Caramelization occurs over 120 °C or pH between 3-9, whereas Maillard reaction requires 50 °C and pH in the range of 4-7 [3]. Sugar autoxidation takes place under all conditions that are relevant for food processing, especially in alkaline pH. Lipid peroxidation may contribute to α -DC accumulation in foods due to storage and process conditions [4]. α -DC compounds react with amino groups of proteins to form final advanced glycation end products (AGEs) and advanced lipoxidation end products (ALEs) [5]. The highly reactive AGEs and ALEs such as N- ϵ -carboxymethyl

lysine (CML) and N- ϵ -carboxyethyllysine (CEL) are formed by the reaction of α -DCs with the lysine group of amino acids, respectively [6].

AGEs are heterogeneous groups of molecules that can be formed endogenously or exogenously. The formation and accumulation of AGEs in the human body disrupt cell structure and functions, which causes oxidative stress and inflammation. AGEs play a direct role in developing age-related chronic degenerative diseases, diabetes mellitus, cardiovascular diseases, cancer, and central nervous system disorders [7]. Similar to AGEs, ALEs can be produced from α -DCs. ALEs are lipid peroxidation products formed due to interaction between oxygen-derived free radicals and polyunsaturated fatty acids [8]. Lipid peroxidation is a serious problem in the food industry because it degrades food quality, alters texture properties, and reduces shelf life. Besides, lipid peroxidation causes inflammation in the human body. This increases the risk of atherosclerosis, age-related chronic conditions, cancer, and neurodegenerative disease. Considering all these adverse effects, it is important to prevent lipid peroxidation formation in foods. Lipid peroxidation is induced by exogen and endogen factors such as enzymes, heat, metal ions, radical species, and reactive oxygen species [9]. Food fat composition is also one of the most important determinants, especially polyunsaturated fats are at greater risk for lipid peroxidation than saturated fats [10]. Apart from these, the oxidation process of lipids increases under gastric digestion due to prooxidant conditions in the gastrointestinal tract such as low pH of gastric juice, presence of oxygen incorporated into food during mastication, and metallic ions [11]. Since digestion is dynamic, AGEs formation reactions or lipid peroxidation may increase or decrease digestive tract conditions [12]. Therefore it is important to know MGO formation *in vitro*.

Current strategies for reducing lipid peroxidation include changing processing conditions, reducing total fat or increasing saturated fat temperature, modifying packaging, coating foods to reduce oxygen exposure, and adding antioxidants [13]. Antioxidants are compounds capable of inhibiting or delaying oxidation by scavenging free radicals and preventing radical chain reactions [14]. Phenolic antioxidants inhibit lipid peroxidation by binding these lipid alkoxyl radicals [15].

Crackers are one of the most preferred processed snacks food, with major ingredients such as flour, fat, and salt. However, crackers are convenient for α -DC formation due to low moisture, lipid oxidation, and sugar autoxidation [16]. There is limited study about the formation of lipid peroxidation products such as malondialdehyde (MDA), 4-hydroxy-2-hexenal (HHE), and 4-hydroxy-2-nonenal (HNE) under *in vitro* gastrointestinal conditions, however, there is no study about the formation of α -DC in the gastrointestinal system [11]. The present study aims to determine the formation of the MGO, which is one of the most potent precursors of AGEs in crackers, and investigate the effects of herbal teas on reducing the formation of MGO under *in vitro* gastrointestinal system conditions.

2. Materials and Methods

2.1. Samples.

In this research, four different polyphenol-rich herbal teas, including *Camellia sinensis* (black tea and green tea), *Curcuma longa* (turmeric), *Rosa canina* L. (rosehip) teas, and five different cracker samples were obtained local market in Istanbul, Turkey. Sample type and main contents of tea samples and crackers are shown in Table 1.

2.2. Materials.

Methylglyoxal (40%), methanol, acetonitrile, KCl, NaCl, CaCl₂·2H₂O, NaHCO₃, pepsin (porcine gastric mucosa, ≥ 250 units/mg solid), alpha-amylase (*Aspergillus oryzae*, 1.5 U/mg), pancreatin (porcine pancreas, 8 × USP), lipase (porcine pancreas, 100-500 units/mg protein), bovine serum, mucin, urea albumin, bile salts, uric acid were obtained from Sigma-Aldrich (St. Louis, MO, U.S.A).

In this study, the bioaccessibility of MGO in crackers samples was studied using *in vitro* stimulated human digestive system. The present *in vitro* system consisted of the stomach, mouth, and small intestinal medium [17].

Saliva: 16 mL urea (2.5 g/100 mL), 30 mg uric acid, 3.4 mL NaCl (17.5 g/100 mL), 560 mg α-amylase, and 50 mg mucin were dissolved in 1000 mL volumetric flask using deionized water. The final volume (adjusted pH 6.8) was completed with deionized.

Gastric juice: 36 mL of CaCl₂·H₂O (2.22 g/100 mL), 13 mL of HCl (37 g/L), 2 g of bovine serum albumin, 5 g pepsin, and 6 g mucin was dissolved in 1000 mL volumetric flask using deionized water. The final volume (adjusted pH 1.5) was completed with deionized water.

Duodenal juice: 18 mL of CaCl₂·2H₂O (2.22 g/100 mL), 12.6 mL of KCl (9.0 g/100 mL), 4 g bovine serum albumin, 18 g pancreatin, and also 3 g lipase was dissolved in 1000 mL volumetric flask, and the volume completed with deionized water. The final pH adjusted to 8.0.

Bile juice: 20 mL of CaCl₂·2H₂O (2.2 g /100 mL), 136.6 mL of NaHCO₃ (17 g/200 mL), 3.6 g bovine serum albumin, and 60 g bile was dissolved in 1000 mL volumetric flask using deionized water. The final volume was completed and adjusted pH 7.0.2.3.

2.3. *In vitro* digestion procedure.

In this study, to determine the most effective tea concentration, 2, 4, and 6 ml of each tea sample were added to cracker number 1. Then, the effective tea concentration was added to each cracker sample in the simulated digestive systems. The teas were prepared as indicated on the label as follows one the bag (2 g) was brewed in 200 ml water at 100 °C for 5 min. Then, it cooled down to 37 °C for *in vitro* digestion. One portion of medium cracker and one portion of tea are 50 g and 200 mL, respectively indicated on the labels.

The bioaccessibility of the GO and MGO in cookies was determined using an *in vitro* simulated human digestive system. This *in vitro* simulated method was a modified version of that described previously by Yaman *et al.* (2019) [17]. Saliva, gastric, duodenal, and bile juices were prepared as 1000 mL and shown in Figure 1.

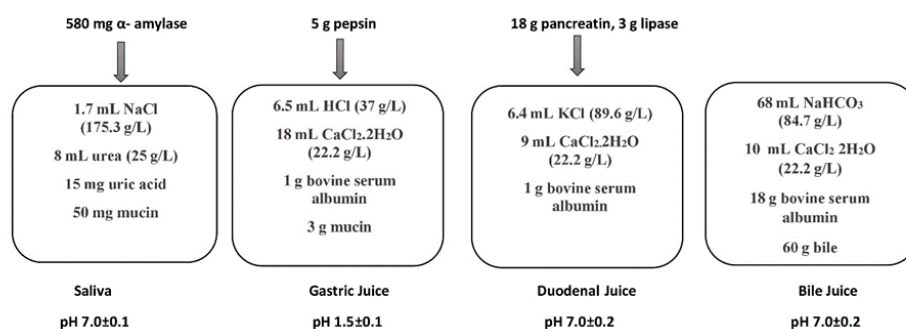


Figure 1. Saliva, gastric, duodenal, and bile juices used in the *in vitro* human digestion model.

1.5 g of each cracker test sample with herbal teas were mixed with 5 mL of saliva solution in a 100 mL beaker and incubated for 5 min at 37 °C in a shaking water bath. Then, 12 mL of gastric juice were added to the fluid obtained from the mouth phase and incubated for 1 h at 37 °C in a shaking water bath. After that, 5 mL of bile juice and 10 mL of duodenal juice were added to the sample obtained from the gastric phase. Then, this mixture was incubated for 2 h at 37 °C in a shaking water bath. After that, the final volume was diluted with deionized water to 50 mL. The samples were then centrifuged for 5 min at 8000 x g and filtered through a filter paper. This solution was used for the analysis of MGO. Bioaccessibility was calculated by dividing the concentration of v MGO in the digest by the MGO concentration in the original nondigested sample and expressed as a percentage.

2.4. HPLC determination of MGO.

The HPLC conditions for the determination of MGO described by Cengiz *et al.* (2020) were used. The HPLC system consisted of a Shimadzu LC 20AT pump with a Shimadzu SPD-20A UV/VIS detector (Shimadzu Corporation, Kyoto, Japan). The mobile phase has consisted of MeOH:water:ACN (42:56:2 v/v/v). The wavelength was set to 254 nm. An Inersil ODS-3 column was used with a flow rate of 1 mL/min, and the column oven temperature was set 30°C.

2.5. Statistical analysis.

The average value (n = 3) was given with a standard deviation. Significant differences were determined using ANOVA Tukey's test (p < 0.05).

3. Results and Discussion

The HPLC chromatogram of MGO in cracker 1 is shown in Figure 2.

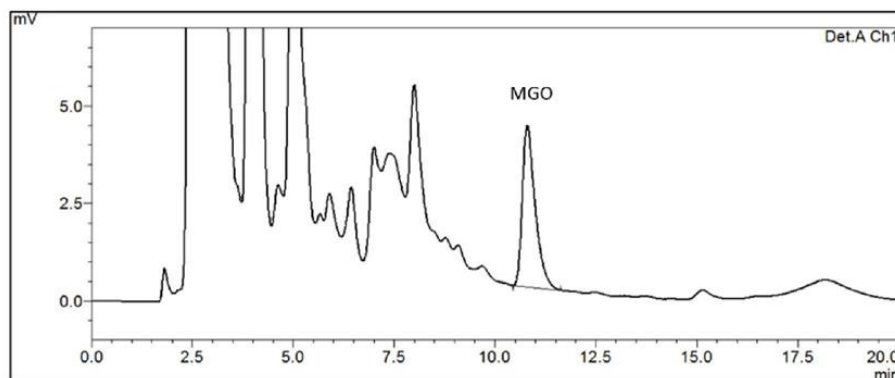


Figure 2 HPLC chromatogram of MGO in cracker 1.

The declared amount of macronutrients in cracker samples are given in Table 1.

As presented in Table 2, the amount of MGO in cracker and tea samples ranged between 51 and 104 µg/100 g, and 10 and 16.6 µg / 100 g, respectively. The highest MGO value was observed in cracker 4 and cracker 5 samples. However, MGO values were found very low (<17 µ/100 ml) in tea samples compared to crackers. The amounts of MGO in crackers and tea samples after *in vitro* gastrointestinal digestion were ranged from 274 to 408 µg / 100 g and 10 to 16.9 µg / 100 g, respectively. As seen, the MGO amounts in cracker samples were increased compared to initial values, and the increase rate was between 266 and 628%. Whereas the MGO amounts in tea samples were not increased compared to initial values (p >0.05).

Table 1. The declared amount of carbohydrate, sugar, protein, fat, fiber and salt in cracker samples.

Sample no	Energy (kcal)	Carb (g/100g)	Protein (g/100g)	Fat (g/100g)	Saturated Fat (g/100g)	Sugar (g/100g)	Fiber (g/100g)	Salt (g/100g)
Cracker 1, cheese	468	65.0	8.9	19.0	8.7	8.1	2.7	2.4
Cracker 2, spicy	413	71	8.5	13.3	6.8	7.6	3.1	2.8
Cracker 3, hot spicy	457	57.1	7.9	21.9	11.2	7.6	3.4	2.7
Cracker 4, plain	400	75.3	10	5.9	2.7	0	3.2	4.8
Cracker 5, sesame	463	61	10	19	7.3	6.3	4.9	1.8

As seen from Table 1, cracker samples contain a high amount of carbohydrate and fat and ranged from 57.1 to 75.3 and 5.9 to 21.9 g/100 g, respectively. The measured amount of MGO in crackers and teas is presented in Table 2.

Table 2. Sample type and main contents, amount of MGO before and after digestion, and increase rate.

Sample no	Sample type and main contents	Initial value MGO ($\mu\text{g}/100\text{ g}$)	After Digestion MGO ($\mu\text{g}/100\text{ g}$)	Increase Rate %
Cracker 1	Cracker, cheese	97 \pm 4	408 \pm 18	424 \pm 19
Cracker 2	Cracker, spicy	51 \pm 2	312 \pm 14	617 \pm 28
Cracker 3	Cracker, hot spicy	57 \pm 3	355 \pm 16	628 \pm 29
Cracker 4	Cracker, plain	102 \pm 5	299 \pm 14	296 \pm 13
Cracker 5	Cracker, sesame	104 \pm 5	274 \pm 12	266 \pm 12
Tea 1	Tea, black	14 \pm 1	15 \pm 1	107 \pm 4
Tea 2	Tea, green	10 \pm 0	10 \pm 1	100 \pm 3
Tea 3	Tea, turmeric	17 \pm 1	17 \pm 1	103 \pm 4
Tea 4	Tea, rosehip	14 \pm 1	14 \pm 1	100 \pm 3

Crackers are prone to α -DC formation due to rich carbohydrate, fat content, low moisture, and high-temperature cooking conditions [18]. Cengiz *et al.* measured MGO levels in crackers between 123-661 $\mu\text{g} / 100\text{ g}$ [19]. Similar to Cengiz *et al.*, in the present study high amount of MGO was detected in crackers. Differences in the amount of MGO between cracker samples may be attributed to shelf life and storage conditions. Carbohydrate content may contribute to MGO formation by sugar autoxidation or Maillard reaction [16]. Besides, lipid peroxidation can cause MGO formation in crackers. Unsaturated fats are at greater risk for lipid oxidation than saturated fats [20]. As seen in Table 1, all cracker samples contain about 50% unsaturated fat of total fat. This may have caused increased MGO formation in crackers. Lipid peroxidation increase with digestion due to prooxidant conditions in the gastrointestinal tract [11]. Therefore, MGO content was analyzed in crackers under *in vitro* gastrointestinal conditions, and as seen in Table 2 it was observed that MGO content increased up to 6 fold. The bioaccessibility of MGO was also studied by different researchers. Lugt *et al.* found that the presence of methylglyoxal-derived hydroimidazolone-1 in the gastrointestinal tract increased by more than 400% in ginger biscuits [21]. On the contrary, Degen *et al.* found that, After 8 hours of *in vitro* digestion, only 5–20% of the initial methylglyoxal was recovered in Manuka honey [22]. Daglia *et al.* also observed that after digestion, MGO concentration decreases in Manuka honey because MGO reacts with digestive enzymes by carbonylation their free amino groups [23]. The differences between results may be attributed to food composition or food processing techniques. *In vitro*, simulated digestion can reduce or strongly increase free α -DCs content depend on food content or reactions occurring during digestion [24].

Lipid peroxidation causes unfavorable effects on shelf life, nutrition quality, texture, storage time in foods and leads to the formation of ALEs in the body; therefore, it is important to reduce lipid peroxidation in foods [25, 26]. Antioxidants slow or prevent lipid oxidations in foods by scavenging free radicals, inactivating lipoxygenase, quenching singlet oxygen, and

chelating pro-oxidative metals [27]. Phenolic compounds have high antioxidant properties and prevent lipid oxidation through various mechanisms [28]. For this purpose, some herbal teas were added to crackers to reduce MGO content. Teas were also analyzed to evaluate the possible interactions between MGO content in teas and crackers. It was observed that the amount of MGO in the teas was low, and these amounts were not affected by *in vitro* gastrointestinal system conditions (Table 2). It was ensured that tea treatment would not affect MGO content in crackers. Bioaccessibility of MGO in cracker sample after different concentration tea samples are given in Table 3.

Table 3. Bioaccessibility of MGO in cracker sample after different concentration tea samples.

Sample Name	After Digestion MGO ¹ (µg/100 g)			MGO increase rate compared to initial value %			Reducing Rate %		
	2 ml	4 ml	6 ml	2 ml	4 ml	6 ml	2 ml	4 ml	6 ml
Cracker 1 + Tea 1	291±10 ^a	244±9 ^b	215±8 ^c	300±11	251±9	222±8	29±2	40±2	47±2
Cracker 1 + Tea 2	288±10 ^a	193±7 ^b	149±5 ^c	297±10	199±7	154±5	30±2	53±2	64±1
Cracker 1 + Tea 3	323±11 ^a	269±9 ^b	260±9 ^b	333±12	278±10	268±9	21±3	34±2	36±2
Cracker 1 + Tea 4	274±10 ^a	272±10 ^a	258±9 ^a	283±10	281±10	266±9	33±2	33±2	37±2

Values refer to the mean ± standard deviation (n = 3) for quantification of MGO in the reference material (cracker samples). ¹The different letters in the same row indicate that there are statistical differences between the applications (ANOVA p < 0.05, Tukey's test).

As seen from table 3, 4 four different tea samples with 3 different concentrations (2, 4, and 6 mL) were treated to cracker 1 (Table 2) in the simulated gastrointestinal system. When cracker1 was treated with different concentrations of tea samples, the increase rate of MGO (424%) was reduced by all tea samples with different concentrations. The highest decrease was observed for 6 ml of tea treatments, and the increase rate of MGO was decreased between 154 and 268 %. The addition of tea1, tea2, tea 3, and tea 4 samples to cracker 1 reduced the initial MGO value by 47, 64, 36, and 37%, in the simulated gastrointestinal system, respectively. Surprisingly, it was seen that 6 ml of tea added to the cracker corresponded to 1 portion of tea. In this regard, the optimal ratio was found in 1 portion. Therefore, in this study, the amount of tea added to crackers was accepted as 6 ml in other cracker samples.

As in the cracker 1 sample, the crackers 2, 3, 4, and 5 samples were treated with the tea samples. The amount of MGO in cracker 2, cracker 3, cracker 4, and cracker 5 was reduced by tea samples from 31 to 53%, 52 to 60%, 55 to 80%, and 21 to 80%, respectively (Table 4). It was observed that in this study, the most effective teas in reducing the amount of MGO were green tea for cracker 1 and cracker 2, rosehip tea for cracker 3, turmeric for cracker 4, and black tea for cracker 5. Generally, the reducing rate in cracker samples was between 31 and 81%.

Table 4. Bioaccessibility of MGO in cracker samples after tea treatments.

Sample no	After Digestion MGO ¹ (µg/100 g)				MGO increase rate (%)				Reducing Rate %			
	Tea 1	Tea 2	Tea 3	Tea 4	Tea 1	Tea 2	Tea 3	Tea 4	Tea 1	Tea 2	Tea 3	Tea 4
Cracker 2	160±7 ^a	147±7 ^a	217±10 ^b	164±7 ^a	313±14	287±13	426±19	321±15	49±2	53±2	31±3	48±2
Cracker 3	153±7 ^a	171±8 ^b	170±8 ^b	143±6 ^a	269±12	301±14	299±14	250±11	57±2	52±2	52±2	60±2
Cracker 4	90±4 ^a	136±6 ^b	58±3 ^c	104±5 ^d	89±4	134±6	57±3	102±5	70±1	55±2	81±1	65±2
Cracker 5	54±2 ^a	128±6 ^b	217±10 ^c	64±3 ^d	52±2	123±6	209±9	62±3	80±1	54±2	21±4	77±1

Values refer to the mean ± standard deviation (n = 3) for quantification of MGO in the reference material (cracker samples). ¹The different letters in the same row indicate that there are statistical differences between the applications (ANOVA p < 0.05, Tukey's test).

It is known that phenolic antioxidants reduce lipid peroxidation in foods. Lin *et al.* indicated in their study that green tea extract inhibits lipid peroxidation in pepperoni during

storage [29]. Khennouf *et al.* determined that phenolic compounds reduce lipid peroxidation by %42-51 [30]. Lorrain *et al.* showed that polyphenols inhibit lipid oxidation under gastric conditions [31]. In line with these studies, it was observed that green tea and black tea with phenolic properties reduce the amount of MGO up to %80, which is the potent lipid peroxidation precursor.

Turmeric has high antioxidant properties due to the phenolic components it contains. Therefore, it can be used in foods to prevent lipid oxidation. Kanani *et al.* showed that turmeric supplementation in heat-treated chickens significantly decreased the level of thiobarbituric acid (TBAR), which is a precursor of lipid peroxidation [32]. Van Hecke *et al.* tested the potential of herbs and spices to reduce lipid oxidation during gastrointestinal digestion in beef products. They found that turmeric was the most effective herb for reducing lipid peroxidation under gastrointestinal digestion [33]. The effects of turmeric on lowering lipid peroxidation had generally been studied on meats, but there is a need for studies focused on low moisture foods such as crackers. In this study, results showed that turmeric reduces MGO amount up to %81 in crackers under gastrointestinal conditions. D'souza *et al.* investigated the effects of turmeric on reducing MDA levels in fish. They found turmeric exhibited a significant reduction in lipid peroxides up to %28 [34].

Rosehip's potential to reduce lipid peroxidation has also been studied, but these studies have also been conducted on animal foods and have not been studied on low moisture foods. According to Özer, rosehip can be used in fermented meat products to inhibit lipid oxidation [35]. Varzaru *et al.* investigated the effects of rosehip on reducing lipid peroxidation in eggs. For this purpose, a rosehip supplement was given to laying hens. They found that rosehip supplementation reduced lipid peroxidation by up to 25% compared to control groups [36]. Similarly, in the present study, it was found that rosehip tea reduces MGO levels, these results also show that it has a lowering effect under the gastrointestinal system.

Prevention of lipid peroxidation in foods is crucial for both the food industry and human health. Inhibition of lipid peroxidation with antioxidants had been widely studied. These studies had been mostly focused on meat products. However, lipid peroxidation in low moisture foods is a serious problem due to their polyunsaturated fat content, but this issue has been poorly studied. In addition, most of the studies evaluate lipid peroxidation with MDA or TBAR. α -DC compounds are potential ALEs precursors that can be formed through lipid peroxidation. Therefore MGO analysis can be used as a precursor to evaluating lipid peroxidation. Moreover, lipid peroxidation increases with digestion; for this reason, it is important to evaluate MGO levels under gastrointestinal conditions. This study has a unique value in terms of investigating the effects of herbal teas on reducing MGO as a potential lipid peroxidation product under gastrointestinal conditions in low moisture foods. Findings showed that herbal teas significantly reduced MGO formation in crackers. The addition of these herbal teas as antioxidants in cracker formulations or consumption of herbal teas and low moisture foods may be recommended.

4. Conclusions

Briefly, in this study, it was demonstrated that MGO formation increases with digestion. For this reason, it is important to evaluate MGO levels under gastrointestinal conditions. The present study was also demonstrated that polyphenol-rich herbal teas significantly reduced MGO formation in crackers in the gastrointestinal systems. , The addition of these herbal teas as antioxidants in cracker formulations or consumption of herbal teas along with snack foods

may be recommended since this study had revealed that MGO in crackers under *in vitro* conditions, further studies are needed to investigate α -DCs formation in such foods extensively.

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Conflicts of Interest

The authors declare no conflict of interest.

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