separations

MDPI

Article

Advantageous Effects of Sumac Usage in Meatball Preparation on Various Quality Criteria and Formation of Heterocyclic Aromatic Amines

Adem Savaş [1], Elif Ekiz [1], Zeynep Elbir [1], Burcunur Demir Savaş [1], Charalampos Proestos [2], Tahra Elobeid [3], Mohammad Rizwan Khan [4] and Fatih Oz [1,*]

[1] Department of Food Engineering, Agriculture Faculty, Atatürk University, 25240 Erzurum, Türkiye
[2] Laboratory of Food Chemistry, Department of Chemistry, National and Kapodistrian University of Athens, Zografou, 15771 Athens, Greece
[3] Human Nutrition Department, College of Health Sciences, QU Health, Qatar University, Doha 2713, Qatar
[4] Department of Chemistry, College of Science, King Saud University, Riyadh 11451, Saudi Arabia
* Correspondence: fatihoz@atauni.edu.tr

Abstract: Heterocyclic aromatic amines (HAAs) are mutagenic/carcinogenic compounds that can be formed during the cooking process of proteinaceous foods such as meat. Therefore, it is needed to inhibit or reduce their formations in cooked meats. Hereby, the effects of sumac usage (0.5%, *w*/*w*) in beef meatball preparation on the formation of HAAs and some quality parameters (water, pH, cooking loss, and lipid oxidation values) of meatballs cooked at 150 and 250 °C were investigated. The sumac usage caused a reduction in pH ($p < 0.01$), cooking loss ($p < 0.05$), lipid oxidation level (TBARS, $p < 0.01$), and total HAA amount ($p < 0.05$) of the samples. In addition, increasing the cooking temperature significantly decreased the pH value ($p < 0.01$) and increased the cooking loss ($p < 0.05$) of the samples. Only one compound, 2-amino-3,8-dimethylimidazo [4,5-*f*]quinoxaline (MeIQx), from nine different HAAs studied in this study, could be determined, and the levels of the other HAAs studied were lower than their detection limits. On the other hand, MeIQx was not detected in the samples cooked at 150 °C, it was only determined in the control group samples cooked at 250 °C. The sumac usage completely inhibited MeIQx formation in the samples. Due to its positive effect on cooking loss value, lipid oxidation level, and MeIQx formation, it can be suggested to use sumac powder in meatball preparation.

Keywords: heterocyclic aromatic amines; sumac; meatball; lipid oxidation; cooking loss; mutagenic; carcinogenic; quality

Citation: Savaş, A.; Ekiz, E.; Elbir, Z.; Savaş, B.D.; Proestos, C.; Elobeid, T.; Khan, M.R.; Oz, F. Advantageous Effects of Sumac Usage in Meatball Preparation on Various Quality Criteria and Formation of Heterocyclic Aromatic Amines. *Separations* **2023**, *10*, 29. https://doi.org/10.3390/separations10010029

Academic Editor: Javier Saurina

Received: 13 December 2022
Revised: 25 December 2022
Accepted: 29 December 2022
Published: 3 January 2023

1. Introduction

Consumer awareness of the relationship between foods and diseases has been considerably expanded in recent years. Nutrition, which is a basic requirement of the human being, is supplied by food. Among the foods, meat has an important place in terms of nutrition due to some of its advantages, such as a high amount and quality protein, fat and fatty acid composition, and vitamin and mineral contents [1–4]. On the other hand, it is known that some heat treatment toxicants such as heterocyclic aromatic amines (HAAs) are formed in meat and meat products that are generally consumed after cooking [5–8]. Until today, nearly 30 types of HAAs have been identified in foods [9,10]. Many factors can affect the formation of these compounds in meats, such as high temperature, cooking conditions, amino acid content, meat type, creatine/creatinine, pH, water activity, surface area, and cooking time [11,12].

Epidemiological studies have shown that almost all of the HAAs are mutagenic and most of them are carcinogenic. Therefore, considering the risks associated with HAAs these days, their occurrence needs to be inhibited or reduced. For this aim, many studies have

been carried out in the literature to reduce the formation of HAA in foods. It has been reported that the most effective and easiest way to reduce the formation of these harmful compounds is to use spices in the preparation of foods [6,13–15]. It is declared that this inhibitory effect is attributed to the antioxidant activity of spices and their interference with some steps of HAA formation reactions [16]. Various studies have been conducted in the literature [3,12,17–22] to reduce the occurrence and exposure of HAAs. It has been determined that there are about 600 separate compounds and complex mixtures exhibiting antimutagenic/anticarcinogenic effects against HAAs [23]. Therefore, the use of natural and/or synthetic antioxidants in meat and products is increasing day by day. However, with the prohibition of synthetic antioxidants due to their carcinogenic potential, in some countries, the interest in the antioxidant properties of natural spices has increased [3,15].

Sumac (*Rhus coriaria* L.), which is one of the antioxidant spices belonging to the Anacardiaceae family, is in the genus Rhus [24,25]. Sumac is a rich source of tannins, phenolic compounds, anthocyanins, organic acids, fatty acids, vitamins, and minerals [26–28]. It is also stated that sumac fruit has antioxidant, antibacterial, antifungal, antilipidemic, hypoglycemic, and therapeutic effects [28–33]. Sumac is also used as a spice, food coloring, food preservative, and medicinal plant, as well as in the cosmetic and pharmaceutical industries [27,34,35].

In recent years, it is seen that the importance given to the safety of foodstuffs in terms of sensory, physical, and chemical properties and human health, as well as their nutritional value, has been increasing. Beef meatballs are one of the most popular foods consumed in the world. It is stated that this meat and its products, which are involved in the human diet, constitute an important source of HAAs [36]. As a matter of fact, HAAs can be significant in the formation of many diseases, especially cancer [37]. So far, many spices with high antioxidant activities have been used in meat products to reduce HAA formation. However, since spices with antioxidant activity can have prooxidant effects contingent on their usage rates, the popularity of these spices must be investigated [12,38]. Although there are many studies in the literature investigating the effect of spices with antioxidant properties on HAA formation, to the best of our knowledge, no report investigating the impact of sumac on HAA formation has been found in the literature review. Therefore, this study aimed to see how sumac usage (0.5%) in meatball preparation affected HAA formation and meat quality in beef meatballs cooked at 150 and 250 °C. In addition, the antioxidant activity of sumac was determined.

2. Materials and Methods

2.1. Materials

The raw materials used in the research were supplied from the Erzurum province. Beef muscle and intermuscular fat were purchased from the Erzurum Meat and Dairy Association Meat Combination, while sumac was purchased from a local herbalist selling spice products.

2.2. Chemicals

The HAA standards were purchased from Toronto Research Chemical (Downsview, ON, Canada): 2-amino-3-methylimidazo[4,5-*f*]quinoxaline (IQx), 2-amino-3-methylimidazo [4,5-*f*]quinoline (IQ), 2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (MeIQx), 2-amino-3,4-dimethylimidazo[4,5-*f*]quinoline (MeIQ), 2-amino-3,7,8-trimethylimidazo[4,5-*f*] quinoxaline (7,8-DiMeIQx), 2-amino-3,4,8-trimethylimidazo[4,5-*f*]quinoxaline (4,8-DiMeIQx), 2-amino-3,4,7,8-tetramethylimidazo[4.5-*f*]quinoxaline (4,7,8-DiMeIQx), 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP), 2-amino-9H-pyrido[2,3-b]indole (AαC), and 2-amino-3-methyl-9H-pyrido[2.3-b]indole (MeAαC). In HAA analysis, 4,7,8-TriMeIQx was used as an internal standard. All solvents and chemicals (analytical and HPLC-grade) including 2,2-diphenyl-1-picrylhydrazyl (DPPH), ascorbic acid, butylated hydroxyanisole (BHA), and butylated hydroxytoluene (BHT) were obtained from Sigma-Aldrich, Taufkirchen, Germany.

2.3. Methods

2.3.1. Production of Meatballs

The prepared meatball dough (with 15% fat) was divided into two parts. The first part consists of meatball dough without sumac, while the second part consists of meatball dough with sumac at the rate of 0.5%. Meatball dough with and without sumac was kept in the refrigerator for six hours and then it was shaped into meatballs (7 × 1 cm).

2.3.2. Cooking Conditions

Neither fat nor oil was used in the cooking process on the electric hot plate. After the surface temperature of the heating plate was adjusted to 150 and 200 °C using a laboratory thermometer (Testo, Lenzkirch, Germany), the cooking process was started. Meatballs were cooked for a total of 8 min.

2.3.3. Some Chemical and Physicochemical Analyses

Water, pH, and cooking loss values were determined according to the methods proposed by Ekiz and Oz [39]. The lipid oxidation level was determined according to the method of Kılıç and Richards [40]. Briefly, two grams of meat samples were homogenized (Ultra-Turrax, IKA Werk T 25, Staufen, Germany) for 30 s in 12 mL of trichloroacetic acid solution (7.5% TCA, 0.1% EDTA, 0.1% propyl gallat), and 3 mL of thiobarbituric acid solution (0.02 M) was applied to 3 mL of filtrate after straining through Whatman 1 filter paper. This mixture was kept in a 100 °C water bath for 40 min, then cooled down to room temperature. After centrifuging for 5 min at 2000 rpm, absorbance values against the blank sample at 530 nm were determined in the spectrophotometer (PG Instruments, T60V, Leicestershire, UK). 1,1,3,3- tetraethoxypropane (TEP) was used for the calculation of value. TBARS values were expressed in mg malondialdehyde (MDA)/kg. In addition, the value of vitamin C was determined according to Cemeroğlu [41]. Briefly, sumac (10 g) and oxalic acid (10 mL) were homogenized (Ultra-Turrax, IKA Werk T 25, Staufen, Germany) and filtered through Whatman 1. Oxalic acid (1:10 w/w, 2%) was added to the filtrate again, and the extraction was continued. The filtrate (5–25 mL) was titrated with 2,6-dichlorophenolindophenol solution (0.05%).

2.3.4. Antioxidant Extraction

The extract was prepared per Azizah et al. [42]. In summary, to determine 2.2-diphenyl-1-picrylhydrazil, an ethanol-water (9:1, v/v) mixture was first prepared. It was then mixed with 25 g of sample and 75 mL of ethanol–water in the dark using a magnetic stirrer. Finally, the obtained filtrate was evaporated at 50 °C and a stock solution was prepared with distilled water.

2.3.5. DPPH• Free Radical Scavenging Activity

Solutions prepared at different concentrations were transferred to tubes for DPPH• analysis. Then, 1 mL of the prepared DPPH• solution (1 mmol/L) was added to the samples and mixed thoroughly with the help of a vortex. Absorbance was measured at 517 nm. The samples were compared with the butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) standards [43,44].

2.3.6. Extraction and Determination of HAAs

In the research, HAA extraction of meatballs was determined according to the method of Savaş et al. [45]. In summary, the meatball sample and sodium hydroxide (1 N, 12 mL) were mixed for 1 h. Afterward, the packaging material (13 g, Extrelut NT, Sigma-Aldrich) was added and mixed. Extraction was passed through the cartridge (Oasis MCX, 3 cc, 60 mg, 30 µm, Waters) by adding different proportions of ethyl acetate (75 mL), hydrochloric acid (2 mL), and methanol (2 mL). The eluate (2 mL) was taken up with a mixture of 95:5% methanol:NH_3. The extracted samples were treated at −18 °C and the samples were dried at 45 °C before HPLC analysis. An internal standard containing 100 µL of methanol

(including the internal standard) was added to the dried vials. The HAA content of the samples was determined using a reverse-phase analytical column (AcclaimTM 120 C18, 3 µm, 4.6 × 150 mm, Tosoh Bioscience GmbH, Stuttgart, Germany) in HPLC (Thermo Ultimate 3000, Thermo Scientific, Waltham, MA, USA) equipment with a diode array detector (DAD-3000). The HAAs were separated in a column oven at 35 °C with a flow rate of 0.7 mL/min. The injection volume was 10 µL. Solvent A consists of methanol, acetonitrile, water, and glacial acetic acid (8/14/76/2, *v*/*v*/*v*/*v*). Furthermore, solvent B consists of acetonitrile (100%). For the method validation parameters, the limit of detection (LOD) and limit of quantification (LOQ), R^2, and recovery values were determined. LOD and LOQ values were calculated with signal-to-noise ratios of 3 and 10, respectively. R^2 and recovery rates for different HAAs in the samples were determined by the standard addition method [45].

2.3.7. Statistical Analysis

The present research was established according to the completely randomized design and carried out with two replicates (each replicate with two parallel). The data obtained were evaluated with the SPSS 25.0 program and the differences between the averages were evaluated with the Duncan multiple range test. Principal component analysis (PCA) was performed by SIMCA.14.1 software (UMETRICS, Umea, Sweden).

3. Results and Discussion

3.1. Some Physicochemical Analyzes of Raw Materials

The water, pH, and TBARS values of the raw materials used for the preparation of the meatballs are given in Table 1. It can be seen that the results of the analysis are consistent with the data in the literature [20,46,47]. In addition, the free radical scavenging activity ($DPPH^{\bullet}$) and ascorbic acid content of sumac were determined as 85.74% and 6.8 mg/100 g, respectively. Ozcan et al. [27] determined that the $DPPH^{\bullet}$ values of sumac were between 73.37% and 77%, while Morshedloo et al. [48] determined that $DPPH^{\bullet}$ values were between 35.66% and 82.73%. While Fereidoonfar et al. [49] determined that the ascorbic acid content of sumac was between 10 and 45 mg/kg, Kossah et al. [50]—in Chinese and Syrian sumac—found, in order, 13.90 to 38.91 mg/kg of ascorbic acid.

Table 1. Various analysis results of raw material.

	n	Water (%) ± SD	pH ± SD	TBARS (mg MDA/kg) ± SD
Meat	2	74.70 ± 0.18 ^{a}	5.46 ± 0.01 ^{b}	0.305 ± 0.035 ^{a}
Intermuscular fat	2	13.89 ± 0.16 ^{c}	6.47 ± 0.37 ^{a}	0.375 ± 0.134 ^{a}
Raw meatball	2	65.62 ± 0.8 ^{b}	5.63 ± 0.08 ^{b}	0.340 ± 0.070 ^{a}
Sign.		**	*	ns

Sign.: significance; ns: not significant ($p > 0.05$); SD: standard deviation; MDA: malondialdehyde; *: $p < 0.05$; **: $p < 0.01$. Different letters (a–c) in the same column are significantly different ($p < 0.05$).

3.2. Water Contents of the Cooked Meatballs

The effects of sumac addition and cooking temperature on water content are shown in Table 2. The addition of sumac had a significant impact on the water content of the meatballs ($p < 0.05$). It was determined that the water content of the samples increased with the addition of sumac. The increase in the water content of meatballs with the addition of sumac is thought to be due to the high dry matter content in the sumac powder used in this study. On the other hand, the cooking temperature did not significantly affect the samples ($p > 0.05$). Similar results are also found in the literature [20,51,52].

Table 2. Various analysis results of cooked meatballs (mean ± SD).

Sumac Concentration (SC)	Water (%)	pH	TBARS (mg MDA/kg)	Cooking Loss (%)	Total HAA (ng/g)
C (0%)	48.08 ± 4.65 ^{b}	5.83 ± 0.08 ^{a}	1.27 ± 0.11 ^{a}	43.81 ± 3.22 ^{a}	0.33 ± 0.43 ^{a}
0.5%	57.74 ± 2.24 ^{a}	5.48 ± 0.25 ^{b}	0.61 ± 0.05 ^{b}	38.72 ± 3.69 ^{b}	nd
Sign.	*	**	**	*	*
Cooking Temperature (CT)					
150 °C	51.68 ± 6.60 ^{a}	5.76 ± 0.07 ^{a}	0.94 ± 0.44 ^{a}	38.61 ± 3.26 ^{b}	nd
250 °C	54.13 ± 6.42 ^{a}	5.55 ± 0.32 ^{b}	0.95 ± 0.34 ^{a}	43.93 ± 3.42 ^{a}	0.33 ± 0.43 ^{a}
Sign.	ns	**	ns	*	*
Interactions SC × CT	ns	**	ns	ns	*

Sign.: significance; different letters (a, b) in the same column are significantly different ($p < 0.05$) Abbreviations: ns: not significant ($p > 0.05$); SD: standard deviation; **: $p < 0.01$, *: $p < 0.05$, nd: not detected, n = 4.

3.3. pH Values of Meatballs

Sumac addition had a significant effect on the pH values of the meatballs ($p < 0.01$). It was observed that the pH values of the samples decreased with the addition of sumac. This decrease is thought to be due to the acidic content of sumac (2.73). In their study, Langroodi et al. [53] determined that the pH values of the beef samples decreased compared with those of the control group as the addition of sumac extract and chitosan increased on the 0th day. On the other hand, as the cooking temperature increased, the values of the pH averages significantly decreased ($p < 0.01$). This result is different from the results found in the literature. This effect is thought to be caused by sumac, which has an acidic structure.

3.4. TBARS Values of Meatballs

The TBARS value is one of the most important indicators reflecting the degree of lipid oxidation [54]. It was determined that sumac addition significantly ($p < 0.01$) decreased the TBARS value. This decrease is thought to be due to the tannins, phenolic compounds, and antioxidant capacity of sumac [28,53]. On the other hand, the cooking temperature did not have a significant effect on the TBARS values of the meatballs ($p > 0.05$). Similar results have been found in the literature and have shown that cooking does not affect lipid oxidation as highly reactive compounds react with various compounds such as proteins and amino acids in meat [12,55,56].

3.5. Cooking Loss of Meatballs

Cooking time and losses affect various quality criteria of meat (color, flavor, juiciness, tenderness, and micronutrient content). During cooking, most of the meat is separated in the form of broth [56,57]. It was determined that the cooking loss values of the meatballs decreased with the addition of sumac. Khan et al. [58] found that the cooking losses of beef patties prepared using a mixture of thyme, sesame, and sumac varied between 39.84% and 48.18%. The addition of sumac and cooking temperature had a significant impact on the cooking loss values of the samples ($p < 0.05$). It was determined that as the cooking temperature increased, the cooking losses of the meatballs increased (Table 2). As a matter of fact, it is stated that the removal of the water in the meat during cooking is due to the denaturation and shrinkage of the protein structures due to the increase in temperature [57,59].

3.6. HAA Results of Cooked Meatballs

In the present research, the LOD and LOQ values of the analyzed cooked meatballs were determined separately for each HAA. LOD values were found between 0.025 and

0.004 ng/g, and LOQ values were between 0.085 and 0.013 ng/g. The coefficients of the regression line (R^2) for the standard curve are higher than 0.999 and the recovery values are between 55.63% and 87.16%. The method validation parameters are given in Table 3. When the HAA results were examined, only the MeIQx compound was detected among the nine HAA compounds in the analyzed meatballs.

Table 3. LOD, LOQ, R^2, and recovery values (n = 4).

HAA	LOD (ng/g)	LOQ (ng/g)	R^2	Recovery (%)
IQx	0.004	0.013	0.9999	75.65
IQ	0.009	0.029	0.9999	60.04
MeIQx	0.024	0.081	0.9999	78.48
MeIQ	0.014	0.047	0.9999	55.63
7,8-DiMeIQx	0.005	0.018	0.9999	75.87
4,8-DiMeIOx	0.008	0.025	0.9999	76.96
PhIP	0.025	0.085	0.9999	87.16
AαC	0.012	0.039	0.9999	79.71
MeAαC	0.010	0.035	0.9998	69.01

IQ was determined as below the detectable level in the samples. Similarly, Gibis [60] could not detect IQ in meatballs grilled at 230 °C for up to 4.5 min. In another study, non-IQ was detected in beef cutlet samples cooked up to 250 °C [61]. Korkmaz and Oz [21], Uzun and Oz [20], and Bingöl et al. [47] could not determine IQ in different meatball samples. Likewise, Oz [51] could not detect IQ in meatballs cooked in barbecue using different animal fats. There are also studies in the literature in which IQ was determined at different levels by other researchers. Balogh et al. [62] detected 2.8 ng/g IQ in beef patties cooked at 175–275 °C for 12 min. Oz and Kaya [15] reported IQ up to 5.46 ng/g, Oz et al. [61] determined IQ between nq–1.34 ng/g, and Lu et al. [6] determined IQ up to 11.29 ng/g. Keşkekoğlu and Üren [63] determined IQ up to 303.06 ng/g in beef patties that were cooked using different cooking methods. Gümüş and Kızıl [64] also reported that up to 0.82 ng/g IQ formed in beef samples marinated with blueberry and propolis extracts.

IQx could not be detected in the control and sumac-added meatball samples. There are many studies in the literature that support these findings. Gibis [60] did not detect IQx in beef patties cooked on the grill for up to 4.5 min at 230 °C. Likewise, Puangsombat et al. [65] did not detect IQx in meatball samples fried for 30 min up to 275 °C, nor did Uzun and Oz [20] and Bulan and Oz [66] in beef meatballs cooked up to 250 °C. On the contrary, Zeng et al. [67] determined nd–0.31 ng/g IQx in roast beef patties grilled at 225 °C. Oz et al. [61] reported that they detected nd–0.45 ng/g IQx in beef cutlet samples cooked at 250 °C. Korkmaz and Oz [21] determined 0.10 ng/g of IQx in meatballs cooked up to 250 °C. Similarly, Gümüş and Kızıl [64] reported that nd–0.17 ng/g IQx formed in beef samples marinated with blueberry and propolis extracts.

It is stated that one of the most common HAAs in meat products is MeIQ [68,69]. However, in this study, MeIQ was below the detectable level in the samples. Similarly, MeIQ was not detected in beef meatballs [60]. Oz et al. [61] reported that they could not detect MeIQ in beef cutlet samples cooked at 150 and 200 °C. Again, Khan et al. [70] could not detect MeIQ in goat meat patties cooked using different cooking methods at 175 °C, 195 °C, and 225 °C. On the contrary, Oz and Kaya [15] reported MeIQ at nd–2.66 ng/g in fried beef and chicken patties, Lu et al. [6] reported MeIQ at nd-18.09 ng/g in beef and chicken patties, Oz [51] reported MeIQ at 1.40–2.48 ng/g in beef meatballs, MeIQ was found at 2.31 ng/g by Kılıc et al. [12] in chicken meatballs cooked on a heating plate, and reported that nd–5.33 ng/g MeIQ was formed.

Meat products are an important part of our diet. Particularly in the cooking process applied to meat products, changes occur in the protein structure, appearance, taste, and chemical properties of meat. As a matter of fact, the cooking process makes the meat even more appetizing. However, with the cooking process, mutagenic and carcinogenic

compounds such as HAA can be formed [71]. In the study, MeIQx occurred at different levels in meatballs (up to 0.67 ng/g) (Table 4). Only MeIQx was determined in the control group cooked at 250 °C. In addition to the reaction of dialkylpyrazine free radicals and creatinine in the formation of MeIQx—one of the important HAAs compounds—, glycine and alanine amino acids also play a role [68,72]. On the other hand, sumac-inhibited MeIQx antioxidants are used in meat products to delay or prevent oxidative reactions. It is stated that antioxidants can effectively diminish the formation of MeIQx [13]. As a matter of fact, studies using apple peel powder, mallow extract, and onion powder have shown that the formation of MeIQx decreases [73–75]. Similarly, MeIQx (up to 18.23 ng/g) was determined by other researchers at different temperatures and in different meat samples (beef meatballs, beef cutlets, and goat meatballs) by other researchers [37,61,70,76]. Gümüş and Kızıl [64] reported that between nd and 0.39 ng/g MeIQx was formed in beef samples marinated with blueberry and propolis extracts. Nuray and Oz [18] and Korkmaz and Oz [21] reported that they did not determine MeIQx in samples cooked up to 250 °C. Again, Oz [51] reported that no MeIQx was detected in beef patties.

Table 4. HAA levels in the meatballs with and without sumac cooked at different temperatures (ng/g).

Sumac Concentration	Temperature	MeIQx	Total
C (0%)	150 °C	nd	nd
	250 °C	0.67	0.67
0.5%	150 °C	nd	nd
	250 °C	nd	nd

nd: not detected, n = 4.

7,8-DiMeIQx is below the detectable level in the samples. Similarly, Gibis [60] reported that they could not detect 7,8-DiMeIQx in beef patties cooked on the grill at 230 °C for up to 4.5 min. Oz et al. [46] could not detect 7,8-DiMeIQx in chitosan meatballs. Oz [51] reported that 7,8-DiMeIQx was not detected in beef patties. On the other hand, Uzun and Oz [20] could not detect 7,8-DiMeIQx in control and basil meatballs cooked on a heating plate at 150 °C and 200 °C, while nd−0.08 ng/g was determined in samples cooked at 250 °C. Oz et al. [61] reported that they detected 7,8-DiMeIOx at nd–0.15 ng/g in beef cutlet samples. Unal and the others determined [17] 7,8-DiMeIQx at 0.32 ng/g in their research. Again, Gümüş and Kızıl [64] reported that 7,8-DiMeIQx was formed between nd−1.74 ng/g in beef samples marinated in blueberry and propolis extracts.

4,8-DiMeIQx could not be detected in the control and sumac-added meatball samples. Jautz et al. [76] were unable to detect 4,8-DiMeIQx in beef patties grilled at 230 °C for up to 3 min. Likewise, for Bulan and Oz [66], control and tarragon meatballs did not exhibit 4.8-DiMeIQx. On the other hand, Oz and Kaya [15] found 4.8-DiMeIQx between nd–3.35 ng/g in meatballs fried up to 225 °C, and Gibis and Weiss [37] found nd to 1.27 ng/g 4,8-DiMeIQx in meatballs cooked on the grill at 230 °C for up to 4.5 min. Oz et al. [61] reported that they detected 4,8-DiMeIQx at nd–0.05 ng/g in beef cutlet samples. Zeng et al. [67] determined 0.02–0.19 ng/g 4,8-DiMeIQx in roast beef patties cooked at 225 °C. While Uzun and Oz [20] could not detect 4,8-DiMeIQx in control and basil patties cooked on the heating plate at 150 °C and 200 °C, it was determined at nd–0.08 ng/g in samples cooked at 250 °C. Oz [51] determined 0.44 ng/g in beef patties, Erdogan and Ocak [77] determined 4,8-DiMeIQx at 10.54 ng/g in beef patties cooked up to 250 °C using a pan and oven. Again, Erdogan and Ocak [78] determined 4,8-DiMeIQx at 0.49–5.71 ng/g in beef patties cooked in a pan and oven up to 250 °C using different extracts (propolis and carob extracts).

PhIP, one of the most studied HAAs in cooked meats, could not be identified in the current study. Similarly, no PhIP was detected in meatballs prepared using different animal fats (Oz, 2021). In contrast to Oz [51], PhIP was determined from nd to 31.80 ng/g by various researchers in beef patties, chicken patties, and veal chops [15,17,61,63,76,79–81]. PhIP was detected between 0.70–7.11 ng/g in roast beef patties cooked at 225 °C [67].

Erdoğan and Ocak [77] determined 1.08 ng/g PhIP in beef patties cooked up to 250 °C using a pan and oven.

AαC could not be determined in the samples. Gibis [60] stated that AαC could not be detected in beef meatballs cooked on the grill for up to 4.5 min at 230 °C. Again, in different studies on meatballs, AαC was not detected [20,51]. Contrary to the results found by other researchers, there are also studies where AαC was detected. AαC was determined at different levels in beef cutlet samples (nd−0.68 ng/g) cooked at 250 °C and beef samples marinated with blueberry and propolis extracts (nd–3.27 ng/g) [61,64].

MeAαC is below the detectable level in the samples. This compound could not be determined in meatballs cooked on the grill for up to 4.5 min at 230 °C by Gibis [60], in beef cutlet samples cooked up to 250 °C by Oz et al. [61], or in control and basil meatballs cooked on a hot plate by Uzun and Oz [20]. In a different study, MeAαC could not be detected in meatballs prepared using different animal fats and others [51]. On the contrary, MeAαC was determined between nd–0.05 ng/g in meatballs fried at 250 °C [82]. Xu et al. [83] determined that the total HAA (MeIQx, 7,8-DiMeIQx, Norharman, Harman, PhIP, and IFP) amounts of their samples (pan-fried pork patty, roasted pork patty, pan-fried beef patty, and roasted beef patty) were between 0.60 and 5.77 μg/kg. Herein, the total amount of HAA in meatball samples was determined as nd−0.67 ng/g depending on the addition of sumac and cooking temperature. When the results were examined, none of the HAAs were detected in all meatballs cooked at 150 °C. MeIQx formed especially in the control group meatballs (without sumac) cooked at 250 °C. It is rather difficult to directly compare the results of the current study with other studies. This is because HAA levels are highly variable due to the composition of the preparation and heating equipment as well as the precursors, this study is also the first study investigating the effect of sumac on HAA formation. Nuray and Oz [18] found 0.10 ng/g total HAA in meatball samples, 0.06 ng/g total HAA was identified by Bulan and Oz [66] in their meatball samples, and Puangsombat & Smith [84] found 11.82 ng/g total HAA in different meatball samples.

The obtained data show that an increase in cooking temperature will increase the formation of HAA. Findings are consistent with previous studies reported by Bula et al. [85], Kılıç et al. [12], and Ishak et al. [86]. Sumac addition reduced the total HAA formation of meatballs. Research results show that sumac can significantly reduce HAA formation. This decrease is thought to be due to the antioxidant contents/activity of sumac. This is due to sumac having 85.74% free radical scavenging activity. In fact, our TBARS data also support this result. It is also stated that sumac is rich in phenolic acids such as syringic, protocatetic, caffeic, quinic, and coumaric acids [30,48]. As a matter of fact, antioxidants, various spices, and plant extracts have been shown to reduce HAA formation and have an inhibitory effect [6,13–15,87].

3.7. Correlation Results of Samples and PCA Analysis

When the analysis results are examined in terms of the correlation between the analyzes (Figure 1), there is a negative relation between only water and TBARS ($r = -0.81$, $p < 0.05$). On the contrary, a positive relation between cooking loss with MeIQx was found ($r = 0.73$, $p < 0.05$). Total HAA showed a positive relation with cooking loss ($r = 0.73$, $p < 0.05$) and MeIQx ($r = 1.00$, $p < 0.01$).

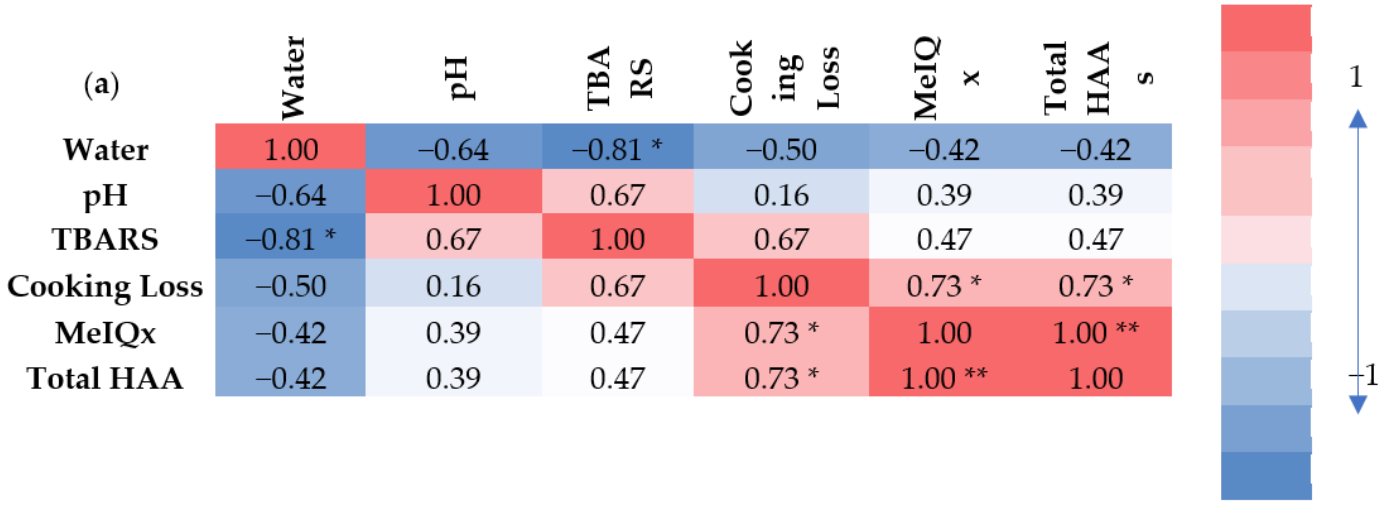

Figure 1. Correlation between water, pH, TBARS, cooking loss, and the formation of HAAs. *: $p < 0.05$; **: $p < 0.01$.

PCA analysis was performed to identify differences between samples. The score scatterplot, loading scatter plot, and biplot are shown in Figure 2A–C, it can be seen that two principal components accounted for 88.6% of the variance. Meatball samples were formed in two groups. The first group consists of control-150, S-0.5%-150, and S-0.5%-250, while the second group consists only of control-250 (Figure 2A). TBARS, pH, cooking loss, MeIQx, and total HAA were collected in the right region, while water was located on the left (Figure 2B). As seen in Figure 2C, total HAA has a positive correlation with MeIQx and cooking loss. In addition, it is seen that control-250 is directly related to the formation of total HAA (Figure 2C).

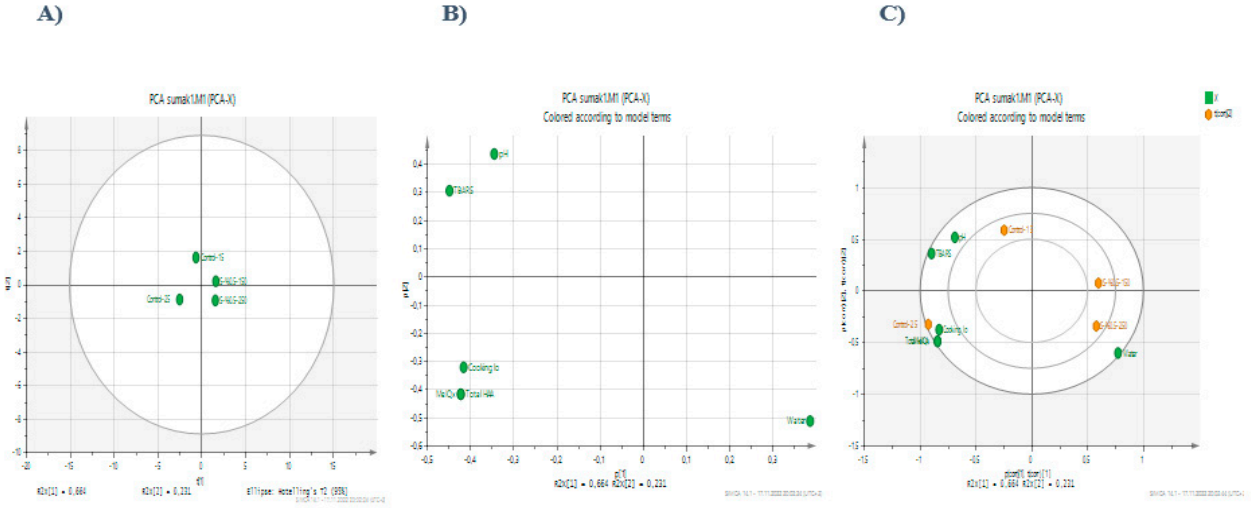

Figure 2. Score scatter plot (**A**), loading scatter plot (**B**), and biplot (**C**) of PCA analysis (PC1 versus PC2) for the components in the meatballs. C-150–250: control group meatballs cooked at 150, and 250 °C, respectively. S-0.5–150–250: meatballs formulated with 0.5% sumac and cooked at 150, and 250 °C, respectively.

4. Conclusions

In this study, the effect of sumac addition to meatballs on HAA formation was investigated. The results showed that the addition of 0.5% sumac prevented the formation of MeIQx in meatballs cooked at 250 °C and decreased lipid oxidation and cooking loss. As the cooking temperature increased, the pH values of the samples decreased, but the

cooking loss values increased. The use of 0.5% sumac in the production of meatballs is recommended as it reduces lipid oxidation, cooking loss, and formation of MeIQx in the samples.

Author Contributions: Conceptualization, A.S. and F.O.; methodology, A.S. and F.O.; validation, A.S. and F.O.; formal analysis, A.S. and F.O.; investigation, A.S. and F.O.; data curation, E.E., Z.E., B.D.S., C.P. and T.E.; writing—original draft preparation, A.S. and F.O.; writing—review and editing, E.E., Z.E., B.D.S., C.P., T.E., M.R.K. and F.O.; visualization, F.O.; supervision, F.O.; project administration, F.O. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Acknowledgments: The author Adem Savaş is supporting by the Council of Higher Education (CoHE, Yükseköğretim Kurulu, YÖK) with 100/2000 Ph.D. Scholarship in innovative food processing technologies and food biotechnology. The authors would like to thank the support provided by YÖK (Türkiye), Ataturk University (Türkiye), National and Kapodistrian University of Athens (Greece), Qatar University (Qatar), and the Researchers Supporting Project number (RSP2023R138), King Saud University (Riyadh, Saudi Arabia) for the preparation of this manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Biesalski, H.K. Meat as a component of a healthy diet–are there any risks or benefits if meat is avoided in the diet? *Meat Sci.* **2005**, *70*, 509–524. [CrossRef] [PubMed]
2. Oz, F. Effects of Water Extract of U rtica dioica L. on the Quality of Meatballs. *J. Food Process. Preserv.* **2014**, *38*, 1356–1363. [CrossRef]
3. Oz, E. Inhibitory effects of black cumin on the formation of heterocyclic aromatic amines in meatball. *PLoS ONE* **2019**, *14*, e0221680. [CrossRef] [PubMed]
4. Das, A.K.; Nanda, P.K.; Madane, P.; Biswas, S.; Das, A.; Zhang, W.; Lorenzo, J.M. A comprehensive review on antioxidant dietary fibre enriched meat-based functional foods. *Trends Food Sci. Tech.* **2020**, *99*, 323–336. [CrossRef]
5. Babaoglu, A.S.; Karakaya, M.; Oz, F. Formation of polycyclic aromatic hydrocarbons in beef and lamb kokorec: Effects of different animal fats. *Int. J. Food Prop.* **2017**, *20*, 1960–1970. [CrossRef]
6. Lu, F.; Kuhnle, G.K.; Cheng, Q. The effect of common spices and meat type on the formation of heterocyclic amines and polycyclic aromatic hydrocarbons in deep-fried meatballs. *Food Control* **2018**, *92*, 399–411. [CrossRef]
7. Elbir, Z.; Oz, F. The assessment of commercial beef and chicken bouillons in terms of heterocyclic aromatic amines and some of their precursors. *Int. J. Food Sci. Tech.* **2020**, *56*, 504–513. [CrossRef]
8. Cheng, Y.; Yu, Y.; Wang, C.; Zhu, Z.; Huang, M. Inhibitory effect of sugarcane (*Saccharum officinarum* L.) molasses extract on the formation of heterocyclic amines in deep-fried chicken wings. *Food Control* **2021**, *119*, 107490. [CrossRef]
9. Zamora, R.; Hidalgo, F.J. Formation of heterocyclic aromatic amines with the structure of aminoimidazoazarenes in food products. *Food Chem.* **2020**, *313*, 126128. [CrossRef]
10. Oz, E.; Oz, F. Mutagenic and/or carcinogenic compounds in meat and meat products: Heterocyclic aromatic amines perspective. *Theory Prac. Meat Proc.* **2022**, *7*, 112–117. [CrossRef]
11. Oz, E. Effects of smoke flavoring using different wood chips and barbecuing on the formation of polycyclic aromatic hydrocarbons and heterocyclic aromatic amines in salmon fillets. *PLoS ONE* **2020**, *15*, e0227508. [CrossRef] [PubMed]
12. Kilic, S.; Oz, E.; Oz, F. Effect of turmeric on the reduction of heterocyclic aromatic amines and quality of chicken meatballs. *Food Control* **2021**, *128*, 108189. [CrossRef]
13. Vitaglione, P.; Fogliano, V. Use of antioxidants to minimize the human health risk associated to mutagenic/carcinogenic heterocyclic amines in food. *J. Chromatogr. B* **2004**, *802*, 189–199. [CrossRef]
14. Janoszka, B. HPLC-fluorescence analysis of polycyclic aromatic hydrocarbons (PAHs) in pork meat and its gravy fried without additives and in the presence of onion and garlic. *Food Chem.* **2011**, *126*, 1344–1353. [CrossRef]
15. Oz, F.; Kaya, M. The inhibitory effect of black pepper on formation of heterocyclic aromatic amines in meatball. *Food Control* **2011**, *22*, 596–600. [CrossRef]
16. Lee, S.Y.; Yim, D.G.; Kim, O.Y.; Kang, H.J.; Kim, H.S.; Jang, A.; Park, T.S.; Jin, S.K.; Hur, S.J. Overview of the effect of natural products on reduction of potential carcinogenic substances in meat products. *Trends Food Sci. Tech.* **2020**, *99*, 568–579. [CrossRef]
17. Unal, K.; Karakaya, M.; Oz, F. The effects of different spices and fat types on the formation of heterocyclic aromatic amines in barbecued sucuk. *J. Sci. Food Agric.* **2018**, *98*, 719–725. [CrossRef] [PubMed]

18. Nuray, M.; Oz, F. The effect of using different types and rates of onion-water extract in meatball production on the formation of heterocyclic aromatic amines. *J. Sci. Food Agric.* **2019**, *99*, 3538–3547. [CrossRef]
19. Polak, T.; Došler, D.; Žlender, B.; Gašperlin, L. Heterocyclic amines in aged and thermally treated pork longissimus dorsi muscle of normal and PSE quality. *LWT-Food Sci. Technol.* **2009**, *42*, 504–513. [CrossRef]
20. Uzun, I.; Oz, F. Effect of basil use in meatball production on heterocyclic aromatic amine formation. *J. Food Sci. Technol.* **2021**, *58*, 3001–3009. [CrossRef]
21. Korkmaz, A.; Oz, F. Effect of the use of dry breadcrumb in meatball production on the formation of heterocyclic aromatic amines. *Brit. Food J.* **2020**, *122*, 2105–2119. [CrossRef]
22. Li, M.; Lin, S.; Wang, R.; Gao, D.; Bao, Z.; Chen, D.; Tang, Y.; Sun, N.; Zhang, S. Inhibitory effect and mechanism of various fruit extracts on the formation of heterocyclic aromatic amines and flavor changes in roast large yellow croaker (*Pseudosciaena crocea*). *Food Control* **2022**, *131*, 108410. [CrossRef]
23. Schwab, C.E.; Huber, W.W.; Parzefall, W.; Hietsch, G.; Kassie, F.; Schulte-Hermann, R.; Knasmüller, S. Search for compounds that inhibit the genotoxic and carcinogenic effects of heterocyclic aromatic amines. *Crit. Rev Toxic.* **2000**, *30*, 1–69. [CrossRef] [PubMed]
24. Başoğlu, F.; Cemeroğlu, B. Sumak'ın Kimyasal Bileşimi Üzerine Araştırma. *Gıda* **1984**, *9*, 167. Available online: https://dergipark.org.tr/en/pub/gida/issue/6911/92371#article_cite (accessed on 1 January 2023).
25. Tohma, H.; Altay, A.; Köksal, E.; Gören, A.C.; Gülçin, İ. Measurement of anticancer. antidiabetic and anticholinergic properties of sumac (*Rhus coriaria*): Analysis of its phenolic compounds by LC–MS/MS. *J. Food Meas. Charact.* **2019**, *13*, 1607–1619. [CrossRef]
26. Zargham, H.; Zargham, R. Tannin extracted from Sumac inhibits vascular smooth muscle cell migration. *MJM* **2008**, *11*, 119. Available online: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2582678/ (accessed on 1 January 2023). [CrossRef]
27. Ozcan, A.; Susluoglu, Z.; Nogay, G.; Ergun, M.; Sutyemez, M. Phytochemical characterization of some sumac (*Rhus coriaria* L.) genotypes from southern part of turkey. *Food Chem.* **2021**, *358*, 129779. [CrossRef]
28. Diler, Ö.; Özil, Ö.; Bayrak, H.; Yiğit, N.Ö.; Özmen, Ö.; Saygın, M.; Aslankoç, R. Effect of dietary supplementation of sumac fruit powder (*Rhus coriaria* L.) on growth performance, serum biochemistry, intestinal morphology and antioxidant capacity of rainbow trout (*Oncorhynchus mykiss*, Walbaum). *Anim. Feed Sci. Tech.* **2021**, *278*, 114993. [CrossRef]
29. Setorki, M.; Rafieian, M.; Heidarian, E.; Ghatreh, K.; Shahinfard, N.; Ansari, R.; Forouzandeh, Z. Effect of *Rhus coriaria* Consumption with High Cholesterol Food on Some Atherosclerosis Risk Factors in Rabbit. *J. Babol Univ. Med. Sci.* **2012**, *14*, 38–45. Available online: http://jbums.org/files/site1/user_files_a248ba/aaarchive-A-10-1370-784-f58b503.pdf (accessed on 1 January 2023).
30. Abu-Reidah, I.M.; Ali-Shtayeh, M.S.; Jamous, R.M.; Arráez-Román, D.; Segura-Carretero, A. HPLC–DAD–ESI-MS/MS screening of bioactive components from *Rhus coriaria* L. (Sumac) fruits. *Food Chem.* **2015**, *166*, 179–191. [CrossRef]
31. Ünder, D.; Saltan, F.Z. Sumak ve Önemli Biyolojik Etkileri. *Çukurova J. Agric. Food Sci.* **2019**, *34*, 69–78. Available online: https://dergipark.org.tr/en/download/article-file/765729 (accessed on 1 January 2023).
32. Sakhr, K.; El Khatib, S. Physiochemical properties and medicinal, nutritional and industrial applications of Lebanese Sumac (Syrian Sumac-Rhus coriaria): A review. *Heliyon* **2020**, *6*, e03207. [CrossRef] [PubMed]
33. Khalil, M.; Hayek, S.; Khalil, N.; Serale, N.; Vergani, L.; Calasso, M.; De Angelis, M.; Portincasa, P. Role of Sumac (*Rhus coriaria* L.) in the management of metabolic syndrome and related disorders: Focus on NAFLD-atherosclerosis interplay. *J. Funct. Foods* **2021**, *87*, 104811. [CrossRef]
34. Kizil, S.; Turk, M. Microelement contents and fatty acid compositions of *Rhus coriaria* L. and *Pistacia terebinthus* L. fruits spread commonly in the south eastern Anatolia region of Turkey. *Nat. Prod. Res.* **2010**, *24*, 92–98. [CrossRef] [PubMed]
35. Reidel, R.V.B.; Cioni, P.L.; Majo, L.; Pistelli, L. Evolution of volatile emission in Rhus coriaria organs during different stages of growth and evaluation of the essential oil composition. *Chem. Biodiv.* **2017**, *14*, e1700270. [CrossRef] [PubMed]
36. Fan, H.; Hu, H.; Li, C.; Xie, J.; Chen, J.; Zeng, M.; Shen, M.; Xie, M. Effects of cooking factors on the formation of heterocyclic aromatic amines in fried beef patties. *J. Food Process. Preserv.* **2022**, *46*, e16288. [CrossRef]
37. Gibis, M.; Weiss, J. Impact of precursors creatine creatinine and glucose on the formation of heterocyclic aromatic amines in grilled patties of various animal species. *J. Food Sci.* **2015**, *80*, C2430–C2439. [CrossRef]
38. Zeng, M.; Zhang, M.; He, Z.; Qin, F.; Tao, G.; Zhang, S.; Gao, Y.; Chen, J. Inhibitory profiles of chilli pepper and capsaicin on heterocyclic amine formation in roast beef patties. *Food Chem.* **2017**, *221*, 404–411. [CrossRef]
39. Ekiz, E.; Oz, F. The effects of different frying oils on the formation of heterocyclic aromatic amines in meatballs and the changes in fatty acid compositions of meatballs and frying oils. *J. Sci. Food Agric.* **2019**, *99*, 1509–1518. [CrossRef]
40. Kılıc, B.; Richards, M.P. Lipid oxidation in poultry döner kebab: Pro-oxidative and anti-oxidative factors. *J. Food Sci.* **2003**, *68*, 686–689 . [CrossRef]
41. Cemeroğlu, B. *Gıda Teknolojisi Derneği Yayın*; Gıda Analizleri: Ankara, Türkiye, 2010; p. 634.
42. Azizah, Z.; Yani, P.; Yetti, R.D. Antioxidant activity ethanol extract of garlic (*Allium sativum* L.) and black garlic. *Int. J. Res. Rev.* **2020**, *7*, 94–103.
43. Ozcelik, F.; Akan, E.; Kinik, O. Use of Cornelian cherry, hawthorn, red plum, roseship and pomegranate juices in the production of water kefir beverages. *Food Biosci.* **2021**, *42*, 101219. [CrossRef]
44. Binici, H.I.; Şat, İ.G.; Aoudeh, E. The effect of different drying methods on nutritional composition and antioxidantactivity of purslane (*Portulaca oleracea*). *Turk. J. Agric. For.* **2021**, *45*, 680–689. [CrossRef]

45. Savaş, A.; Oz, E.; Oz, F. Is oven bag really advantageous in terms of heterocyclic aromatic amines and bisphenol-A? Chicken meat perspective. *Food Chem.* **2021**, *355*, 129646. [CrossRef]
46. Oz, F.; Aksu, M.I.; Turan, M. The effects of different cooking methods on some quality criteria and mineral composition of beef steaks. *J. Food Process. Preserv.* **2017**, *41*, e13008. [CrossRef]
47. Bingol, M.; Brennan, C.; Zeng, M.; Oz, F. Effect of the fortification with astaxanthin on the quality parameters and heterocyclic amines content of meatballs. *Int. J. Food Sci. Tech.* **2022**, *57*, 7653–7665. [CrossRef]
48. Morshedloo, M.R.; Fereydouni, S.; Ahmadi, H.; Hassanpouraghdam, M.B.; Aghaee, A.; Mehrabani, L.V.; Maggi, F. Natural diversity in fatty acids profiles and antioxidant properties of sumac fruits (*Rhus coriaria* L.): Selection of preferable populations for food industries. *Food Chem.* **2022**, *374*, 131757. [CrossRef]
49. Fereidoonfar, H.; Salehi-Arjmand, H.; Khadivi, A.; Akramian, M.; Safdari, L. Chemical variation and antioxidant capacity of sumac (*Rhus coriaria* L.). *Ind. Crops Prod.* **2019**, *139*, 111518. [CrossRef]
50. Kossah, R.; Nsabimana, C.; Zhao, J.; Chen, H.; Tian, F.; Zhang, H.; Chen, W. Comparative study on the chemical composition of Syrian sumac (*Rhus coriaria* L.) and Chinese sumac (*Rhus typhina* L.) fruits. *Pak. J. Nut.* **2009**, *8*, 1570–1574. [CrossRef]
51. Oz, E. The presence of polycyclic aromatic hydrocarbons and heterocyclic aromatic amines in barbecued meatballs formulated with different animal fats. *Food Chem.* **2021**, *352*, 129378. [CrossRef]
52. Karadaş, Ö.; Yılmaz, İ.; Geçgel, Ü. Determination of physicochemical properties of irradiated sumac (*Rhus coriaria* L.) fruit oils. *Radiat. Phys. Chem.* **2022**, *198*, 110210. [CrossRef]
53. Langroodi, A.M.; Tajik, H.; Mehdizadeh, T.; Moradi, M.; Kia, E.M.; Mahmoudian, A. Effects of sumac extract dipping and chitosan coating enriched with Zataria multiflora Boiss oil on the shelf-life of meat in modified atmosphere packaging. *LWT* **2018**, *98*, 372–380. [CrossRef]
54. Zhang, J.; Zhang, Y.; Wang, Y.; Xing, L.; Zhang, W. Influences of ultrasonic-assisted frying on the flavor characteristics of fried meatballs. *Innov. Food Sci. Emerg.* **2020**, *62*, 102365. [CrossRef]
55. Alfaia, C.M.; Alves, S.P.; Lopes, A.F.; Fernandes, M.J.; Costa, A.S.; Fontes, C.M.; Castro, L.M.F.; Bessa, R.J.B.; Prates, J.A. Effect of cooking methods on fatty acids, conjugated isomers of linoleic acid and nutritional quality of beef intramuscular fat. *Meat Sci.* **2010**, *84*, 769–777. [CrossRef] [PubMed]
56. Modzelewska-Kapituła, M.; Dąbrowska, E.; Jankowska, B.; Kwiatkowska, A.; Cierach, M. The effect of muscle, cooking method and final internal temperature on quality parameters of beef roast. *Meat Sci.* **2012**, *91*, 195–202. [CrossRef] [PubMed]
57. Kondjoyan, A.; Oillic, S.; Portanguen, S.; Gros, J.B. Combined heat transfer and kinetic models to predict cooking loss during heat treatment of beef meat. *Meat Sci.* **2013**, *95*, 336–344. [CrossRef] [PubMed]
58. Khan, I.A.; Khan, A.; Zou, Y.; Zongshuai, Z.; Xu, W.; Wang, D.; Huang, M. Heterocyclic amines in cooked meat products shortcomings during evaluation factors influencing formation risk assessment and mitigation strategies. *Meat Sci.* **2022**, *184*, 108693. [CrossRef]
59. Tornberg, E.V.A. Effects of heat on meat proteins–Implications on structure and quality of meat products. *Meat Sci.* **2005**, *70*, 493–508. [CrossRef]
60. Gibis, M. Optimized HPLC method for analysis of polar and nonpolar heterocyclic amines in cooked meat products. *J. AOAC Int.* **2009**, *92*, 715–724. [CrossRef]
61. Oz, F.; Kızıl, M.; Zaman, A.; Turhan, S. The effects of direct addition of low and medium molecular weight chitosan on the formation of heterocyclic aromatic amines in beef chop. *LWT-Food Sci. Technol.* **2016**, *65*, 861–867. [CrossRef]
62. Balogh, Z.; Gray, J.I.; Gomaa, E.A.; Booren, A.M. Formation and inhibition of heterocyclic aromatic amines in fried ground beef patties. *Food Chem. Toxicol.* **2000**, *38*, 395–401. [CrossRef] [PubMed]
63. Keşkekoğlu, H.; Üren, A. Inhibitory effects of pomegranate seed extract on the formation of heterocyclic aromatic amines in beef and chicken meatballs after cooking by four different methods. *Meat Sci.* **2014**, *96*, 1446–1451. [CrossRef] [PubMed]
64. Gumus, D.; Kizil, M. Comparison of the reducing effects of blueberry and propolis extracts on heterocyclic aromatic amines formation in pan fried beef. *Meat Sci.* **2022**, *186*, 108746. [CrossRef] [PubMed]
65. Puangsombat, K.; Jirapakkul, W.; Smith, J.S. Inhibitory activity of Asian spices on heterocyclic amines formation in cooked beef patties. *J. Food Sci.* **2011**, *76*, T174–T180 . [CrossRef]
66. Bulan, R.; Oz, F. Impact of tarragon usage on lipid oxidation and heterocyclic aromatic amine formation in meatball. *Int. J. Food Sci. Tech.* **2022**, *57*, 942–950. [CrossRef]
67. Zeng, M.; Wang, J.; Zhang, M.; Chen, J.; He, Z.; Qin, F.; Xu, Z.; Cao, D.; Chen, J. Inhibitory effects of Sichuan pepper (Zanthoxylum bungeanum) and sanshoamide extract on heterocyclic amine formation in grilled ground beef patties. *Food Chem.* **2018**, *239*, 111–118. [CrossRef]
68. Skog, K.I.; Johansson, M.A.E.; Jägerstad, M.I. Carcinogenic heterocyclic amines in model systems and cooked foods: A review on formation, occurrence and intake. *Food Chem. Toxicol.* **1998**, *36*, 879–896. [CrossRef]
69. Gibis, M. Heterocyclic aromatic amines in cooked meat products: Causes formation occurrence and risk assessment. *Compr. Rev. Food Sci. Food Saf.* **2016**, *15*, 269–302. [CrossRef]
70. Khan, I.A.; Liu, D.; Yao, M.; Memon, A.; Huang, J.; Huang, M. Inhibitory effect of Chrysanthemum morifolium flower extract on the formation of heterocyclic amines in goat meat patties cooked by various cooking methods and temperatures. *Meat Sci.* **2019**, *147*, 70–81. [CrossRef]

71. Teng, H.; Deng, H.; Zhang, C.; Cao, H.; Huang, Q.; Chen, L. The role of flavonoids in mitigating food originated heterocyclic aromatic amines that concerns human wellness. *Food Sci. Hum. Wellness* **2023**, *12*, 975–985. [CrossRef]
72. Jägerstad, M.; Reuterswärd, A.L.; Öste, R.; Dahlqvist, A.; Grivas, S.; Olsson, K.; Nyhammar, T. Creatinine and Maillard reaction products as precursors of mutagenic compounds formed in fried beef. *Mail. React. Foods Nutr.* **1983**, *27*, 507–519. [CrossRef]
73. Gibis, M.; Weiss, J. Inhibitory effect of marinades with hibiscus extract on formation of heterocyclic aromatic amines and sensory quality of fried beef patties. *Meat Sci.* **2010**, *85*, 735–742. [CrossRef] [PubMed]
74. Natale, D.; Gibis, M.; Rodriguez-Estrada, M.T.; Weiss, J. Inhibitory effect of liposomal solutions of grape seed extract on the formation of heterocyclic aromatic amines. *J. Agric. Food Chem.* **2014**, *62*, 279–287. [CrossRef] [PubMed]
75. Sabally, K.; Sleno, L.; Jauffrit, J.A.; Iskandar, M.M.; Kubow, S. Inhibitory effects of apple peel polyphenol extract on the formation of heterocyclic amines in pan fried beef patties. *Meat Sci.* **2016**, *117*, 57–62. [CrossRef] [PubMed]
76. Jautz, U.; Gibis, M.; Morlock, G.E. Quantification of heterocyclic aromatic amines in fried meat by HPTLC/UV-FLD and HPLC/UV-FLD: A comparison of two methods. *J. Agric. Food Chem.* **2008**, *56*, 4311–4319. [CrossRef] [PubMed]
77. Erdoğan, B.; Özdestan-Ocak, Ö. Determination the effects of pumpkin and rosehip seed oils on heterocyclic aromatic amine formation in meatballs by high-performance liquid chromatography. *J. Food Process. Preserv.* **2022**, *46*, e16299. [CrossRef]
78. Erdoğan, B.; Özdestan-Ocak, Ö. Inhibitory effects of carob and propolis extracts on the formation of heterocyclic aromatic amines in beef meatballs cooked with different methods. *J. Food Process. Preserv.* **2022**, *46*, e16623. [CrossRef]
79. Shin, H.S.; Rodgers, W.J.; Gomaa, E.A.; Strasburg, G.M.; Gray, J.I. Inhibition of heterocyclic aromatic amine formation in fried ground beef patties by garlic and selected garlic-related sulfur compounds. *J. Food Prot.* **2002**, *65*, 1766–1770. [CrossRef] [PubMed]
80. Cheng, K.W.; Wu, Q.; Zheng, Z.P.; Peng, X.; Simon, J.E.; Chen, F.; Wang, M. Inhibitory effect of fruit extracts on the formation of heterocyclic amines. *J. Agric. Food Chem.* **2002**, *55*, 10359–10365. [CrossRef]
81. Oz, F.; Cakmak, I.H.; Zikirov, E.; Kizil, M.; Turhan, S. Heterocyclic aromatic amine contents of kavurma commercially cooked in steam and copper cauldron. *J. Food Process. Preserv.* **2015**, *39*, 583–590. [CrossRef]
82. Oz, F.; Cakmak, I.H. The effects of conjugated linoleic acid usage in meatball production on the formation of heterocyclic aromatic amines. *LWT-Food Sci. Technol.* **2016**, *65*, 1031–1037. [CrossRef]
83. Xu, Y.; Li, H.; Liang, J.; Ma, J.; Yang, J.; Zhao, X.; Zhao, W.; Bai, W.; Zeng, X.; Dong, H. High-throughput quantification of eighteen heterocyclic aromatic amines in roasted and pan-fried meat on the basis of high performance liquid chromatography-quadrupole-orbitrap high resolution mass spectrometry. *Food Chem.* **2021**, *361*, 130147. [CrossRef] [PubMed]
84. Puangsombat, K.; Smith, J.S. Inhibition of heterocyclic amine formation in beef patties by ethanolic extracts of rosemary. *J. Food Sci.* **2010**, *75*, T40–T47 . [CrossRef] [PubMed]
85. Buła, M.; Przybylski, W.; Jaworska, D.; Kajak-Siemaszko, K. Formation of heterocyclic aromatic amines in relation to pork quality and heat treatment parameters. *Food Chem.* **2019**, *276*, 511–519. [CrossRef] [PubMed]
86. Ishak, A.A.; Jinap, S.; Sukor, R.; Sulaiman, R.; Abdulmalek, E.; Hasyimah, A.K.N. Simultaneous kinetics formation of heterocyclic amines and polycyclic aromatic hydrocarbons in phenylalanine model system. *Food Chem.* **2022**, *384*, 132372. [CrossRef] [PubMed]
87. Dong, H.; Xian, Y.; Li, H.; Bai, W.; Zeng, X. Potential carcinogenic heterocyclic aromatic amines (HAAs) in foodstuffs: Formation, extraction, analytical methods, and mitigation strategies. *Compr. Rev. Food Sci.* **2020**, *19*, 365–404. [CrossRef] [PubMed]