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Article

Comparison of Minerals, Ferulic Acid, Antioxidant, and Anti-inflammatory Properties of Products from Raw Maize and Germinated Maize with Selenium

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ABSTRACT: In this research, maize kernels were hydrated with sodium selenite (50 mg/L), germinated for 48 h at 22 ± 1 °C, and subsequently subjected to a nixtamalization. In raw and germinated maize with and without Se, the mineral profiles of nixtamal, nejayote, and tortilla were analyzed by inductively coupled plasma mass spectrometry (ICP-MS) and free and bound ferulic acid (FA) contents were analyzed by high-performance liquid chromatography−ultraviolet (HPLC−UV). All samples were subjected to a simulated digestion to evaluate their cellular antioxidant activities (CAAs) and anti-inflammatory activities. The Se content in Se−tortilla and Se−germinated maize kernels was respectively 0.76 and 2.87 μg/g, dry weight (dw). Se−germinated maize kernels had 181% more bound FA content, 32% more CAA, and 43% more anti-inflammatory activity compared to germinated maize kernels. Nixtamal, nejayote, and tortilla from raw maize had the highest percentages of CAAs and anti-inflammatory activities of all samples. Zn, Ca, K, Mg, and Mn contents were similar in all tortilla treatments.

KEYWORDS: *tortilla, nixtamalization, antioxidant, maize, germination, selenium*

1. INTRODUCTION

The tortilla is the main form of maize consumption in Mexico; it has an important role in the diet of Mexicans. The annual *per capita* consumption of tortillas is close to 75 kg, equivalent to more than seven 1 oz. tortillas per day.[1]

The traditional process to elaborate tortillas consists in the nixtamalization of mature kernels. The lime cooking or nixtamalization scheme consists of first cooking kernels in food grade lime (calcium hydroxide) followed by steeping in the cooking liquor for about 12 h and finally washing the lime-cooked kernels or nixtamal in preparation for stone grinding. The wet grinding procedure yields a dough or masa that is further processed into baked tortillas or fried snacks (corn and tortilla chips).[2] The main disadvantage of this process is the generation of large amounts of wastewater high in pH and both insoluble and soluble solids commonly known as nejayote.

Nejayote is mainly composed of pericarp and soluble compounds such as proteins, polysaccharides, sugars, ferulic acid, and *p*-coumaric acid.[3] In maize, ferulic acid (FA) is the phenolic acid present in the highest concentration, forming ferulic acid dehydrodimers, -trimers, and -tetramers. This particular phenolic has been associated with various health benefits.[4] Due to its high content of phenolic compounds, bioactive peptides, and fiber, the solids of nejayote have been recovered and used as functional ingredients to improve the nutraceutical and antioxidant properties of foods.[5]

Tortillas are an important source of carbohydrates, proteins, and bioavailable calcium (Ca), which is considered one of the most relevant minerals in human nutrition.[2] Due to the high consumption of tortillas by the Mexican population, several approaches have been proposed for their enrichment such as the supplementation of macro- and micronutrients such as protein, fiber, vitamins (B1, B2, B3, folic acid), iron, zinc, and selenium (Se)[6] increasing the healthful properties of the tortilla and dietary intake of these nutrients.

In the case of Se-enriched foods, it has been well-documented that these foods enhance their antioxidant properties; for example rice,[7] soybean,[8] and chickpea kernels enriched with Se[9,10] have higher antioxidant, anti-inflammatory, and anti-cancer properties compared to kernels not enriched with Se. These findings have been related to a higher concentration of organic forms of Se, such as selenomethionine and selenocysteine, as well as the enhancement of the biosynthesis of phenolic compounds.

In humans, Se is key in the modulation of the enzymatic antioxidant system, mainly through glutathione peroxidase, which reduces the reactive oxygen species keeping under control the cellular oxidative stress.[11] The recommended daily intake of

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Se is 55 μg/day.[12] However, supranutritional doses (200 μg of Se/day) can reduce the risk of cancer.[13]

Due to its importance in health and the low levels of Se present in natural foods, enrichment with this mineral in staple foods, such as tortillas, is an excellent strategy to increase the consumption of dietary Se. In this regard, previously we documented a scalable, feasible, sustainable, and affordable process to produce high quality Se-enriched tortillas (0.651 μg of Se/g, dry weight (dw)) from maize kernels first soaked with an Na_2SeO_3 solution and then germinated for 2 days, when the germination time was selected based on the textural characteristic of force of the tortilla.[6] The germinated maize was nixtamalized following the steps of the traditional process. These tortillas showed good texture, flavor, and general acceptability. In addition, the lime cooking time was reduced from 39.15 to 8.42 min using germinated maize compared to ungerminated counterparts. This major difference in cooking requirements has a positive impact on energy use, making the process more sustainable. The study concluded that the consumption of 250 g of Se-enriched tortillas (0.651 μg of Se/g, dw) provided 100% of the recommended daily allowance (RDA) of this essential trace mineral.[6]

Now, in this study, we present the *in vitro* validation of the antioxidant and anti-inflammatory properties of tortilla from germinated maize with Se compared to tortilla from germinated maize without Se and tortilla from raw maize. In addition, we have included the characterization of raw and germinated kernels, nixtamal, and nejayote. The mineral profile and ferulic acid content were evaluated in all samples.

2. MATERIALS AND METHODS

2.1. Germination. White maize of the cultivar Blanco Sinaloa was harvested during January 2021 in Culiacan, Sinaloa, Mexico. Kernels were cleaned and disinfected in preparation for germination at a pilot scale level at a commercial plant (Alimentos Lee, Apodaca, Nuevo León, Mexico). Briefly, 3 kg of maize kernels was hydrated during 8 h with 0 or 50 mg of Na_2SeO_3/L dissolved in tap water. The kernels were germinated during 48 h at 22 ± 1 °C and 80% relative humidity. Immediately after germination, the germinated kernels were nixtamalized. The germinated maize without Se was denominated as GM, and the germinated with Se (50 mg Na_2SeO_3/L) was named GSe.

2.2. Nixtamalization and Tortilla Production Process. Nixtamalization of raw and germinated maize kernels with and without Se was made according to Guardado-Félix et al.[6] Three kilograms of sample raw maize or germinated kernels with and without Se were nixtamalized in a solution containing 9 L of water with 1% food grade lime (30 g of calcium hydroxide). The raw maize was cooked for 39.15 min, while germinated kernels with and without Se were cooked for for 8.42 min at 95 °C. After lime cooking, all treatments were steeped in the lime solution for 16 h to obtain nixtamal with approximately 50% moisture. All the nixtamal samples were washed three times with water to remove excess lime and pericarp. The cooking liquor and wash water were collected as nejayote.

Later, all nixtamal samples were stone-ground into doughs or masas and then continuously sheeted and formed into disks that were baked into tortillas following the methodology described by Guardado-Félix et al.[6] Tortillas from nixtamalized raw maize (RT), nixtamalized germinated kernels (GT), and nixtamalized germinated with Se kernels (GTSe) were obtained. For further analysis, nixtamal and tortilla samples were dried (Cabelas, Winnipeg, MB, Canada) at 55 °C for 12 h whereas nejayote samples were frozen at −80 °C and then freeze-dried during 72 h at −50 °C and 0.036 mbar (LABCONCO, Kansas City, MO). Dehydrated samples were milled in a coffee grinder (Hamilton Beach, Richmond, VA) and stored in plastic bags at −20 °C. The residual moisture was determined in all samples to express results in dry weight.

2.3. Mineral Determination. The contents of selected minerals in all samples were determined according to the method described by Guardado-Félix et al.[6] The contents of minerals were obtained by an Xseries 2 inductively coupled plasma mass spectrometer (ICP-MS; Thermo Scientific, Waltham, MA). The contents of sodium (Na), iron (Fe), zinc (Zn), potassium (K), calcium (Ca), magnesium (Mg), manganese (Mn), copper (Cu), chrome (Cr), nickel (Ni), cobalt (Co), mercury (Hg), lead (Pb), cadmium (Cd), and selenium (Se) were expressed as micrograms per gram of sample in dry weight.

2.4. Extraction of Free and Bound Phenolics. Free and bound phenolics were extracted following the method described by Adom and Liu with some modifications.[14] The free compounds were extracted from 1 g of dry ground sample mixed with 10 mL of ethanol:water (80:20 v/v) for 10 min in a shaker (MRC, Holon, Israel) at 250 rpm. Then, samples were centrifuged (Thermo Fisher Scientific SL 16R, Waltham, MA) at 3000*g* for 10 min at 4 °C to recover the supernatant with free phenolics. The pellet was stored to further extract bound phenolics. All extractions were repeated twice. The supernatants were evaporated at 40 °C for 7 h (Genevac Rocket, Warminster, PA) and stored at −20 °C.

Subsequently, the pellet was resuspended in 20 mL of 2 M NaOH to extract bound phenolics. Samples were hydrolyzed in constant agitation at 250 rpm for 60 min at 25 °C. Then, samples were acidified (pH 2) with HCl and centrifuged at 3000*g* for 10 min at 4 °C. The resulting pellet was discarded while the supernatant was collected and defatted with hexane (1:1 v/v). To remove hexane, samples were centrifuged at 3000*g* for 10 min at 4 °C. The defatted solution was mixed with 10 mL of ethyl acetate (1:2 v/v) and centrifuged at 3000*g* for 10 min at 4 °C to recover the supernatant. The extraction protocol was repeated four more times, and the supernatants were pooled. The pooled fractions were evaporated to dryness and stored at −20 °C.

2.5. Ferulic Acid Quantification by HPLC. Free and bound phenolic extracts were reconstituted in methanol:water (50:50 v/v) in preparation to quantify FA by HPLC−UV (Agilent 1100, Santa Clara, CA) equipped with a Zorbax SB-Aq 4.6 mm i.d. × 150 mm (3.5 μm) reverse column. Chromatograms were acquired at 320 nm and integrated by HP-Agilent Software (Chemstation for LC, Agilent Technologies, Santa Clara, CA). Peak identification of FA was based on the retention time of the FA standard (Sigma-Aldrich, St. Louis, MO). Results were expressed as milligrams of FA per 100 g, dry weight.

2.6. Simulated *In Vitro* Gastrointestinal Digestion (GID). A sample (5 g) was mixed with α-amylase solution (1500 U mL^{-1}) (Sigma-Aldrich, St. Louis, MO) for 1 min and incubated for 2 min at 37 °C with agitation (200 rpm). Later, the pH of the oral bolus was adjusted to 3.0 with 1 M HCl and mixed with porcine pepsin (25 000 U mL^{-1}) (Sigma-Aldrich, St. Louis, MO). The samples were incubated 2 h at 37 °C with agitation (200 rpm). Finally, to emulate the intestinal phase, the pepsin hydrolyzed bolus was mixed with 20 mL of gastric chyme containing pancreatin (3 mg/mL) (Sigma-Aldrich, St. Louis, MO) and bile salts (8 mg/mL) and incubated for 2 h at 37 °C with constant shaking (200 rpm). After the intestinal-simulated digestion, the samples were centrifuged at 4500*g* for 10 min at 4 °C to obtain the supernatant. Subsequently, the supernatants were frozen and freeze-dried for further analysis.

2.7. Cellular Antioxidant Activity (CAA). CAA assay was carried out as reported by Serrano-Sandoval et al.[9] The sample concentration was chosen according to a previous cytotoxic assay where the viability was above 95%. Freeze-dried extracts of the digested samples were evaluated at 100 μg/mL in Caco-2 cells to determine the CAA. Results were expressed as the percentage of CAA (%CAA).

2.8. Anti-inflammatory Activity. The anti-inflammatory potential was evaluated following the methodology described by López-Barrios et al.[15] Freeze-dried extracts of the digested samples were evaluated at 50 μg/mL in RAW 264.7 macrophage cells to determine nitrite concentration as an indicator of nitric oxide (NO) production. Results were expressed as the inhibition percentage (%) of NO production.

2.9. Statistical Analysis. The independent variables in this study were the germination process and Se concentration (0 and 50 mg of Na_2SeO_3/L (1:3 w/v)), while the dependent variables were the minerals, FA content, %CAA, and %NO inhibition. Data were

Table 1. Mineral Contents (μg/g of Sample, dw) of Raw and Germinated Maize with and without Se and Their Derived Nixtamalized Products: Nixtamal, Nejayote, and Tortilla[a]

treatment	minerals				
	Na	Fe	Zn	K	Ca
ungerminated maize					
raw maize	46.71 ± 1.8^{d}	14.70 ± 0.6^{b}	14.09 ± 0.7^{abcde}	3265 ± 142^{ab}	146.19 ± 3.4^{c}
nixtamal	29.87 ± 2.4^{d}	14.2 ± 0.3^{b}	17.5 ± 2^{abc}	2495.5 ± 93.3^{cdef}	2018.39 ± 35.3^{c}
nejayote	232.96 ± 0^{c}	19.1 ± 0^{b}	9.51 ± 0^{e}	1909 ± 0^{g}	70774.76 ± 0^{b}
tortilla	27.97 ± 0.6^{d}	14 ± 0.4^{b}	18.8 ± 1^{ab}	2512.17 ± 8.8^{cdef}	2389.3 ± 122^{c}
germination without Se					
germinated maize	152.48 ± 15.6^{cd}	22.8 ± 1.7^{b}	19.7 ± 1^{a}	3491.4 ± 141.2^{a}	412.31 ± 37.1^{c}
nixtamal	169.02 ± 7.3^{cd}	19.8 ± 0.1^{b}	15.5 ± 1^{abcd}	2887.5 ± 131^{bc}	2300.21 ± 173.1^{c}
nejayote	1898.12 ± 77.6^{a}	89.2 ± 15^{a}	12 ± 2^{cde}	2396.78 ± 61.3^{cdefg}	120191.86 ± 5288^{a}
tortilla	150.86 ± 10.6^{cd}	33.3 ± 0.6^{b}	15.7 ± 2^{abcd}	2852 ± 139.2^{bcd}	2258.47 ± 123.3^{c}
germination with Se					
germinated maize	118.52 ± 5^{cd}	17.9 ± 0^{b}	18.3 ± 1^{ab}	2233 ± 188.2^{efg}	367.75 ± 13.2^{c}
nixtamal	144.89 ± 4.2^{cd}	17 ± 2.1^{b}	13.7 ± 2^{bcde}	2356 ± 169^{defg}	2291.44 ± 161.5^{c}
nejayote	1679.42 ± 127.6^{b}	71.4 ± 11^{a}	10.5 ± 2de	2723.9 ± 85.3^{cde}	124098.32 ± 3464^{a}
tortilla	136.13 ± 0.2^{cd}	25.5 ± 1.1^{b}	13.6 ± 0^{bcde}	2156 ± 167^{fg}	2352.71 ± 6.2^{c}

treatment	minerals				
	Ni	Co	Hg	Pb	Cd
ungerminated maize					
raw maize	0.17 ± 0de	ND	0.1 ± 0^{c}	0.07 ± 0^{d}	ND
nixtamal	0.14 ± 0^{e}	ND	ND	0.06 ± 0^{d}	ND
nejayote	0.76 ± 0^{c}	ND	0.12 ± 0^{bc}	0.14 ± 0^{cd}	ND
tortilla	0.15 ± 0de	ND	0.16 ± 0^{abc}	0.08 ± 0^{d}	ND
germination without Se					
germinated maize	0.32 ± 0^{d}	ND	1.24 ± 1^{a}	0.25 ± 0^{bcd}	ND
nixtamal	0.23 ± 0.1^{de}	ND	0.21 ± 0^{abc}	1.65 ± 1.9^{bcd}	ND
nejayote	1.18 ± 0^{a}	0.13 ± 0^{a}	0.24 ± 0^{abc}	1.12 ± 0^{a}	ND
tortilla	0.7 ± 0.6^{de}	ND	0.54 ± 0^{ab}	0.46 ± 0.2^{bc}	ND
germination with Se					
germinated maize	0.23 ± 0de	ND	0.06 ± 0^{c}	0.08 ± 0^{d}	ND
nixtamal	0.1 ± 0^{e}	ND	0.06 ± 0^{c}	0.8 ± 0^{d}	ND
nejayote	0.99 ± 0^{b}	0.12 ± 0^{a}	0.09 ± 0^{c}	0.63 ± 0.1^{b}	ND
tortilla	0.15 ± 0de	ND	0.06 ± 4^{c}	0.35 ± 0.1^{bcd}	ND

treatment	minerals				
	Mg	Mn	Cu	Cr	Se
ungerminated maize					
raw maize	893.30 ± 34.9^{bc}	3.98 ± 1.7^{b}	1.18 ± 0^{c}	0.32 ± 0^{bc}	ND
nixtamal	926.95 ± 7.5^{bc}	4.13 ± 0.1^{b}	1.2 ± 0^{c}	0.28 ± 0^{cd}	ND
nejayote	495.32 ± 0^{c}	5.82 ± 0^{b}	2.86 ± 0^{c}	0.61 ± 0^{a}	ND
tortilla	923.81 ± 23^{bc}	4.01 ± 0^{b}	1.18 ± 0^{c}	0.31 ± 0^{c}	ND
germination without Se					
germinated maize	1098.86 ± 31.1^{b}	4.95 ± 0.1^{b}	2.28 ± 0^{c}	0.25 ± 0^{bc}	ND
nixtamal	1128.26 ± 34.8^{b}	4.41 ± 0.2^{b}	1.82 ± 0^{c}	0.31 ± 0^{c}	ND
nejayote	2333.23 ± 350.1^{a}	9.82 ± 1.3^{a}	17.4 ± 2^{a}	0.61 ± 0.1^{a}	0.4 ± 0^{c}
tortilla	941.69 ± 22.4^{bc}	3.92 ± 0.1^{b}	2.47 ± 0^{c}	0.56 ± 0.1^{ab}	ND
germination with Se					
germinated maize	1052.94 ± 17.2^{b}	4.71 ± 0.1^{b}	1.83 ± 0^{c}	0.05 ± 3.5^{d}	2.87 ± 0.3^{b}
nixtamal	1062.93 ± 120.3^{b}	4.07 ± 0.4^{b}	1.23 ± 0^{c}	0.06 ± 0^{d}	0.86 ± 0^{c}
nejayote	2430.05 ± 250^{a}	9.93 ± 1.7^{a}	11 ± 2^{b}	0.37 ± 0^{abc}	9.32 ± 1^{a}
tortilla	997.82 ± 4.3^{bc}	3.95 ± 0^{b}	1.6 ± 0^{c}	0.17 ± 0^{cd}	0.76 ± 0^{c}

[a]ND, not detected. Values are means ± SD of two replicates. Different letters within each column indicate significant differences ($p < 0.05$).

subjected to one-way analysis of variance (ANOVA) followed by a *post hoc* Tukey's test at 95% confidence, using the JMP 13 software from SAS institute (Cary, NC). Data were reported as means ± standard deviations (SDs) of three replicates.

3. RESULTS AND DISCUSSION

3.1. Minerals Content. The order of mineral abundance in raw maize was similar to that in germinated maize: K > Mg > Ca > Na > Fe > Zn > Mn > Cu > Cr > Ni > Hg > Pb. The mineral abundance in germinated maize with Se was K > Mg > Ca > Na > Zn > Fe > Mn > Se > Cu > Ni > Pb > Hg > Cr (Table 1).

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According to the total content of minerals, K was the most abundant mineral in raw maize and germinated maize kernels with and without Se (74.4, 95.3, and 58.5%, respectively). The second most abundant mineral was Mg with 20.3, 21.1, and 27.6% of the total mineral composition of raw maize and germinated maize with and without Se. The third most abundant mineral was Ca with about 3.3, 1.1, and 9.6% of the total minerals associated with raw maize and germinated maize with and without Se. In relation to germinated maize without and with Se, increases of Na (226 and 153.73%, respectively), Ca (182 and 151.5%, respectively), Fe (54.8 and 21.8%, respectively), Zn (39.9 and 29.5%, respectively), and Mg (23 and 17.8%, respectively) were observed when compared to raw maize kernels.

It has been documented that, after germination of flaxseeds, Fe increased up to 99.05%, Mn increased 37.27%, and Zn increased 50.53%.[16] In germinated green gram, Bengal gram, and horse gram, the Fe content increased 75.47, 34.24, and 21.21%, respectively, compared to ungerminated kernels. Mihafu et al. reported an increase of 50% of Fe in germinated maize after 72 h.[17] Also, the increase of Mg content in germinated kernels, such as barnyard and Kodo millets, of 11.5 and 11.2%, respectively, has been reported.[18] Chinma et al. reported that dry matter losses normally occur during germination, mainly attributed to degradation of carbohydrates and lipids, and that these losses increase the concentrations of minerals.[19]

Se in raw and germinated maize kernels was not detected, while in kernels soaked with 50 mg of Na_2SeO_3/L and subsequently germinated, the Se concentration reached the level of 2.87 μg/g (dw). Guardado-Félix et al. observed a Se content of 0.722 μg/g (dw) in germinated maize treated with 24 mg of Na_2SeO_3/L in soaking water at the laboratory scale. According to these results, it was observed that the preparation of soaking water with about twice the concentration of Na_2SeO_3 increased the accumulation of Se in the germinated kernels 3 times more.[6] It is reported that Se accumulates mainly in proteins because it is capable of intercalating with sulfur.[20] The amino acids selenomethionine and selenocysteine are the main organic forms identified in Se-fortified foods.[21]

It can be noticed that the nixtamalization process did not significantly affect the mineral content (Table 1). The orders of mineral abundance in nixtamal samples were K > Ca > Mg > Na > Zn > Fe > Mn > Cu > Cr in nixtamal from raw maize, K > Ca > Mg > Na > Fe > Zn > Mn > Cu > Pb in nixtamal from germinated maize, and K > Ca > Mg > Na > Fe > Zn > Mn > Cu > Se in nixtamal from germinated maize with Se. Ca was the second most abundant mineral in all nixtamal treatments, and the notorious increase is due to the use of calcium hydroxide during the nixtamalization process. The Ca content increased 13.8-, 5.6-, and 6.2-fold when nixtamal samples from raw maize, germinated maize, and germinated maize with Se were compared to raw kernels, respectively. These values represent 36.6, 35.2, and 38.8% of the total mineral content. Mora-Avilés et al. reported an increase of Ca content in quality protein maize and regular maize of 17- and 11-fold, respectively, after the lime cooking process.[22]

The 70% of the Se contained in the germinated maize enriched with Se leached into the nejayote or waste liquor. This effect could be attributed to the concentration of Na_2SeO_3 in the pericarp and germ tissues that are usually partially lost during lime cooking and nixtamal washing. Furthermore, the significant loss can be attributed to the solubilization of inorganic forms, such as selenite, and selenate in the cooking liquor, mainly the Se that was not bound to the maize protein structures.

Mineral abundances in nejayote solids were Ca > K > Mg > Na > Fe > Zn > Mn > Cu > Ni > Cr > Pb > Hg in the sample obtained after processing raw maize, Ca > K > Mg > Na > Fe > Cu > Zn > Mn > Cr > Ni > Pb > Se > Hg > Co in nejayote from germinated maize, and Ca > K > Mg > Na > Fe > Cu > Zn > Mn > Se > Ni > Pb > Cr > Co > Hg in the sample from germinated maize supplemented with Se. Nejayote contained high amounts of Ca ($p < 0.05$) compared to the other products, contributing 78.0, 94.6, and 79.7% of total mineral content in samples after processing of raw maize, germinated maize, and germinated maize with Se, respectively (Table 1). In addition, the Mg content in nejayote from both germinated treatments increased 4-fold compared to the sample obtained from raw maize. This indicates a greater solubilization of Mg in the nejayote obtained after lime cooking of germinated and other treatments. It has been reported that, during the germination of other seeds such as wheat, there is an increase in the metabolism, mobilization, and distribution of Mg.[23] Therefore, according to the results herein, it is possible that more soluble forms of Mg from germinated maize leached into the nejayote during nixtamalization. However, more studies should be carried out to prove this.

Additionally, significant amounts of Se were found in nejayote obtained after the nixtamalization of both germinated maize samples. However, the nejayote obtained from Se−germinated maize contained the highest concentration ($p < 0.05$) due to the Na_2SeO_3 supplemented during germination.

The orders of mineral abundance in tortilla samples were K > Ca > Mg > Na > Zn > Fe > Mn > Cu > Cr > Hg for the control tortillas, K > Ca > Mg > Na > Fe > Zn > Mn > Cu > Ni > Cr in those produced from germinated maize, and Ca > K > Mg > Na > Fe > Zn > Mn > Cu > Se > Pb in tortillas obtained from germinated kernels with Se. K, Ca, and Mg represented 42.6, 40.5, and 15.6% of the total mineral content in raw maize tortillas, whereas in tortillas from germinated maize they were 45.5, 36.07, and 15.04%, and in tortillas obtained from germinated maize with Se they represented 37.9, 41.3, and 17.5%. The Ca contents of all tortillas ranged from 2258.4 to 2389.3 μg/g dw. Mora-Avilés et al. reported similar Ca contents of 2990 and 2310 mg/kg in tortillas made with quality protein and regular maize.[22] For this reason, the tortilla is considered an excellent source of Ca in the Mexican diet.

There were no significant differences ($p > 0.05$) found in the mineral profiles of the three treatments of nixtamal, and their respective tortillas, which indicates that the cooking temperature of the tortilla did not negatively impact the mineral content. It was calculated that one tortilla enriched with Se (8 g, dw) contained 19.76 mg of Ca, 0.21 mg of Fe, 0.11 mg of Zn, and 6.4 μg of Se, and according to recommendations of the National Institutes of Health, seven tortillas can provide around 11.3% of Fe, 14% of Ca, 8% of Zn, 28% of Mg, and 82% of Se of the recommended daily allowances for adults.[12]

3.2. Free and Bound FA Contents. The FA content was evaluated in raw and germinated maize with and without Se and their respective products: nixtamal, nejayote, and tortilla (Table 2). Bound FA content was higher in all sample types analyzed with respect to free FA content. Approximately 80% of the total maize phenolics are linked or bound primarily to hemicellulose in the cell walls of the pericarp.[5]

The bound FA content in germinated maize with Se was 181.74 and 431.15% higher compared to germinated maize without Se and raw maize. Germination is an effective process to

Table 2. Ferulic Acid Contents (mg/100 g, dw) of Raw and Germinated Maize with and without Se and Their Derived Nixtamalized Products: Nixtamal, Nejayote, and Tortilla[a]

	ferulic acid (mg/100 g, dw)											
	raw or germinated maize			nixtamal			nejayote			tortilla		
treatment	free	bound	total	free	bound	total	free	bound	total	free	bound	total
ungerminated	0.34 ± 0.05^{c}	25.36 ± 5.2^{b}	25.7	15.56 ± 1^{a}	41.87 ± 1^{a}	57.43	185.69 ± 25^{a}	1337.42 ± 325^{a}	1523.11	13.47 ± 3^{a}	22.35 ± 5^{ab}	35.7
germinated maize	2.25 ± 0.13^{a}	47.81 ± 6^{b}	50.06	9.8 ± 0.17^{c}	10.63 ± 2^{c}	20.43	150.69 ± 26^{a}	1075.9 ± 82^{a}	1226	8.48 ± 0.9^{b}	30.36 ± 5^{a}	38.7
germinated maize with se	1.55 ± 0.13^{b}	134.7 ± 23^{a}	136.25	12.41 ± 0.6^{b}	28.04 ± 4^{b}	40.45	176.44 ± 18^{a}	1020.18 ± 115^{a}	1196	13.21 ± 0.4^{a}	11.82 ± 1^{b}	25

[a]The results are expressed as means ± SD; columns with different letters indicate statistical differences. The sum of free and bound FA represents the total FA content.

enhance the production of free and bound phenolic compounds in maize.[24] Likewise, Na_2SeO_3 caused salt stress during soaking of chickpeas and peanuts that provoked a significant activity increase ($p < 0.05$) of the enzyme phenylammoniolyase (PAL), which is key in the phenylpropanoid pathway, and derived an increase of phenolic content.[25,26] For that reason, germinated maize with Se can be used as a good source of phenolic compounds.

On the other hand, the total FA content in nixtamal from raw maize was 64.4 and 29.5% higher than the content in nixtamal from germinated maize and germinated maize with Se, respectively.

As can be observed in Table 2, there were no significant differences ($p > 0.05$) in free and bound FA contents between nejayotes. On the other hand, the contents of free FA and bound FA in all nejayotes were more than 500- and 53-fold compared to the free and bound FA contents quantified in raw maize and germinated maize with and without Se. These results are similar to those reported by Gutiérrez-Uribe et al.[27] It is reported that the alkaline cooking of maize releases phenolics due to fiber hydrolysis; consequently, the ratio of insoluble to soluble solids in lime cooking solution significantly increases, releasing bound phenolics in soluble forms.[28] The high concentrations of FA in nejayote make this byproduct attractive and with potential as a food ingredient. Acosta-Estrada et al. developed a food additive based on solids of nejayote (80%), and gluten (20%).[28] The authors made bread with 9% nejayote solids, resulting in 745 times more FA than the control bread.[28] In addition to providing nutraceutical properties, the use of nejayote could provide a solution to environmental problems related to its disposal.

In tortillas, the content of free FA was about 58% higher in the tortilla obtained from raw maize and the tortilla from germinated maize with Se, compared with the tortilla from germinated maize without Se. However, the bound FA was higher in the tortilla from germinated maize without Se, up to 61.07% more compared to the other two tortillas.

3.3. Cellular Antioxidant Activity. Raw maize, germinated maize with and without Se, and their respective products, nixtamal, tortilla, and nejayote, were subjected to *in vitro* gastrointestinal digestion to determine the %CAA (Figure 1). The products obtained from raw maize (nixtamal, nejayote, and tortilla) had the highest %CAA ($p < 0.05$) among all the products. In these samples the results are not related to their free and bound FA contents. Furthermore, the presence of other compounds, such as bioactive peptides, and free amino acids released during the digestion process could be contributing to their antioxidant properties.[29] Other investigations have shown the presence of antioxidant peptides in maize.[30,31] The effects of these peptides have been linked to amino acids with hydrophobic side chains and aromatic residues, which serve as hydrogen donors to disrupt the radical peroxidation chain reaction.[32]

On the other hand, it was notable that, in the kernels before the nixtamalization process, the %CAA was 53.8% higher in germinated maize with Se and 21.8% in germinated maize without Se compared to raw maize (Figure 1). These results may be due to the highest bound FA concentration in germinated maize with Se. Bound FA has a strong participation in the antioxidant properties of maize.[33] Although selenized peptides were not characterized in this study, selenized compounds could contribute to increased antioxidant activity. Guo et al.[34] demonstrated the presence of selenized peptides in Se-enriched maize that provided greater antioxidant properties. Besides, it

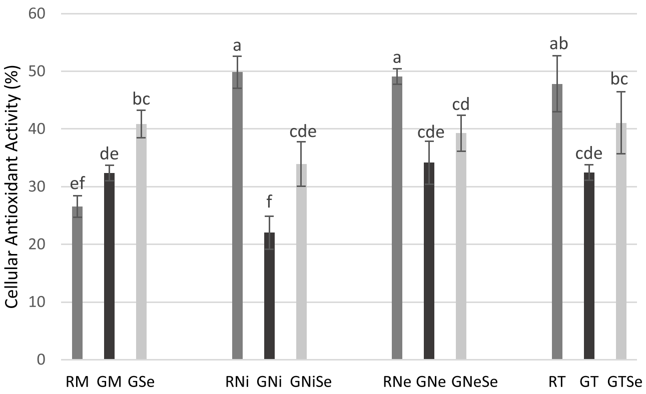

Figure 1. *In vitro* percentage cellular antioxidant activity (%CAA) of raw maize, germinated maize with and without Se, and their respective products, nixtamal, tortilla, and nejayote, subjected to *in vitro* gastrointestinal digestion. Raw maize (RM) and its respective products, nixtamal (RNi), nejayote (RNe), and tortilla (RT). Germinated maize (GM) and its respective products, nixtamal (GNi), nejayote (GNe), and tortilla (GT). Germinated maize with Se (GSe) and its respective products, nixtamal (GNiSe), nejayote (GNiSe), and tortilla (GTSe). Means with different letters are significantly different ($p < 0.05$).

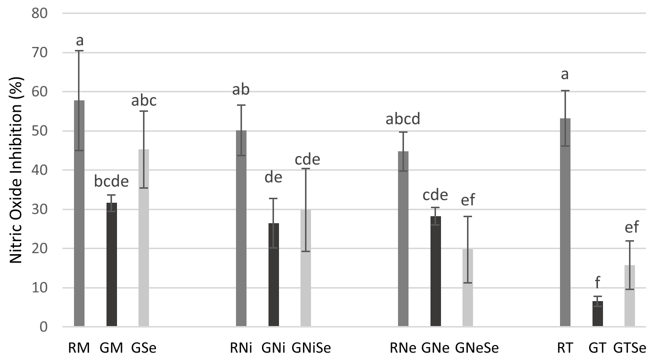

Figure 2. *In vitro* anti-inflammatory activity of raw maize, germinated maize with and without Se, and their respective products, nixtamal, tortilla, and nejayote, subjected to *in vitro* gastrointestinal digestion. Raw maize (RM) and its respective products, nixtamal (RNi), nejayote (RNe), and tortilla (RT). Germinated maize (GM), and its respective products, nixtamal (GNi), nejayote (GNe), and tortilla (GT). Germinated maize with Se (GSe) and its respective products, nixtamal (GNiSe), nejayote (GNeSe), and tortilla (GTSe). Means with different letters are significantly different ($p < 0.05$).

has been reported that selenized peptides from germinated chickpeas have higher antioxidant activities than those obtained from germinated chickpeas without Se.[9]

Also, in this study it was observed that, after the nixtamalization process, the %CAA was improved by around 90% in digested samples of nixtamal, nejayote, and tortilla obtained from raw kernel, compared with the antioxidant activity of raw maize without nixtamalization. So far, there are no other studies that relate an increase in antioxidant activity in nixtamal and tortilla due to the effect of nixtamalization, nor is there evidence on the comparison and characterization of antioxidant peptides before and after maize nixtamalization. It is known that nixtamalization does not have a significant impact on the protein content of the kernel.[35] However, it has been reported that nixtamalization increases the solubility of albumins, globulins, and prolamins.[36] It is important to carry out more studies on the profiles and specificities of peptides, as well as the impact of nixtamalization on their bioavailability and their bioactivities, to clarify these interesting results observed in this study.

According to the %CAA results, the nejayote from raw maize had the highest %CAA ($p < 0.05$), by 20% and 30.44% higher than nejayote from germinated maize with and without Se. It was observed that the FA content is not related to the %CAA. Therefore, it is necessary in future research to characterize the nejayote in terms of other components, for example peptides and protein−carbohydrate complexes, among others, which may be mainly responsible for the antioxidant response observed in this study.

With nixtamalization the antioxidant activity of germinated maize with Se decreased, due mainly to the loss of Se. Even so, the tortilla enriched with Se proved to be an excellent source of dietary Se and antioxidants, and it can be used as a strategy to reduce the risks of diseases related to oxidative stress in the Mexican population.

3.4. Anti-inflammatory Activity. The *in vitro* anti-inflammatory activities of raw and germinated maize with and without Se and their respective products, nixtamal, tortilla, and nejayote, subjected to *in vitro* gastrointestinal digestion are shown in Figure 2. Similar to the antioxidant response, raw maize and its derived products, nixtamal, nejayote, and tortilla, presented the highest anti-inflammatory activity. The %NO inhibition (57.74%) observed in raw maize was maintained after the nixtamalization process in nixtamal and tortilla. These results were not related to the content of free or bound forms of FA quantified in the samples. However, it is known that the *in vitro* anti-inflammatory activities of maize peptides have been associated with the regulation of several pro-inflammatory proteins such as nuclear factor kappa B (NF-κB) and TNF-α-induced pathways.[37] Liang et al. reported three sequences of maize peptides (PPYLSP, IIGGAL, and FLPPVTSMQ) that exerted significant *in vitro* anti-inflammatory properties through the inhibition of vascular cell adhesion molecule-1 (VCAM-1) by 54−38.9% and intercellular cell adhesion molecule-1 (ICAM-1) by 36.5−28.6%.[38]

Likewise, the nejayote obtained from the nixtamalization of raw maize had higher anti-inflammatory properties, with 36.8 and 55.8% higher NO inhibition than nejayotes obtained from germinated maize without Se and with Se, respectively. It has been reported that nejayote obtained from the nixtamalization of raw maize had the potential to inhibit NO production through hydroxycinnamic acids, mainly FA and *p*-coumaric acid, and other compounds such as dehydrodiferulic and dehydrotriferulic acids, *p*-dicoumaroylputrescine, and diferuloylputrescine.[39,40] Furthermore, during nixtamalization, protein complexes (<13 kDa) are released to the nejayote, which is known to interact with FA and exert significant anti-inflammatory activity.[41] Buitimea-Cantúa et al. used ultrafiltration to recover nejayote fractions and found two fractions with anti-inflammatory potential through NO inhibitions of 98.34 and 96.68%, which could be attributed to the synergistic effect of low molecular weight proteins and phenolic acids, mainly FA and *p*-coumaric acid.[41]

It was observed that the selenization of germinated maize kernels enhanced anti-inflammatory activity by 43% compared to counterparts germinated without Se. This was also observed in their lime-cooked tortillas. The tortilla obtained from germinated maize with Se exerts higher anti-inflammatory activity than the tortilla obtained from germinated maize without Se. Previous research reported that Se had anti-inflammatory properties due to the inhibition of NF-κB.[42]

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Another study reported the efficacy of an aqueous extract obtained from maize enriched with Se on the inhibition of pro-inflammatory genes in RAW264.7 cells.[43] Besides, Feng et al. found a relationship between Se content and anti-inflammatory activity of rice peptides.[44] They identified a Se-enriched brown rice peptide with the sequence ALLLQAVQSQYEEK with significant anti-inflammatory capacity through NO inhibition.[44]

In conclusion, results herein clearly indicated that the selenization of maize through germination with sodium selenite significantly increased the Se content, antioxidant activity, and bound FA content. In addition to being processed into nixtamalized tortillas, germinated maize with Se can be used in new processing methods to develop functional foods. It was also observed that the alkaline nixtamalization of germinated maize with and without Se reduced the antioxidant activities in their respective byproducts, tortilla, nixtamal, and nejayote, contrary to what was observed in the nixtamalization of raw maize. This was due to the loss of Se during nixtamalization and other compounds such as peptides and phenolic compounds, which should be characterized in future research. The anti-inflammatory activity did not show a relationship with the Se content or with the content of free or bound ferulic acid. This response may be more related to the digestion products of the samples. The nejayote obtained from the nixtamalization of raw maize and that obtained from germinated maize with and without Se are rich in antioxidant compounds, which can be recovered and used as functional ingredients. The mineral profiles are similar between the kernels, nejayotes, nixtamal, and tortillas of all the treatments. However, the Fe content was significantly higher in products obtained from germinated kernels, mainly due to a higher concentration due to loss of dry matter during germination. Finally, Se-enriched maize tortillas are a good option to supply the recommended dietary Se levels, with antioxidant properties similar to regular tortillas.

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