We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Flavonoid and Capsaicinoid Contents and Consumption of Mexican Chili Pepper (*Capsicum annuum* L.)

Landraces

Araceli M. Vera-Guzmán, Elia N. Aquino-Bolaños,
Elena Heredia-García, José C. Carrillo-Rodríguez,
Sanjuana Hernández-Delgado and
José L. Chávez-Servia

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/68076>

Abstract

There is insufficient evidence to identify the precise health effects of chili pepper consumption. However, there is evidence of their topical use as an analgesic to decrease pain from rheumatoid arthritis, osteoarthritis, neuralgias, neuropathic diabetes, neuronal dysfunctions and inflammation, among others. In this work, the diversity and variety of consumed forms of chilis in Mexico, flavonoid and capsaicinoid content in fruits, and their potential health uses are documented, based on various research results and bibliographic information. In Mexico, more than 150 landraces of wild and cultivated origins are consumed and preserved and are distributed throughout the country; the greatest diversity is concentrated in the central and south-southeastern regions. Consumption per capita in urban households is from 8 to 9 kg, and in rural communities, it varies from 14 to 17 kg. Chili peppers contain up to 23 flavonoids and 20 capsaicinoids, differing among landraces because of crop management, maturation of fruits, postharvest management and ecological-environmental influences. Flavonoids and capsaicinoids confer antioxidant, anticarcinogenic properties on the fruit and have lipolytic and preventative effects on chronic degenerative diseases. However, in vitro and in vivo experimental trials of capsaicinoids and flavonoids with beneficial effects must be conducted with regard to human health.

Keywords: *Capsicum annuum*, pepper landraces diversity, antioxidants, benefits of chili pepper consumption, flavonoids, capsaicinoids on health

1. Introduction

Chili pepper (*Capsicum* spp.) has been used in Mexico as food and a condiment for over eight centuries [1] and is an integral component of the diet and cultural identity of Mexico. Although various chili species grow wild and are cultivated in the United States of America, Mexico is the center of origin, domestication and diversification of *Capsicum annuum* L. [2, 3]. Wild variants continue diversifying (*C. annuum* var. *glabriusculum* [Dunal] Heiser & Pickersgill) and are distributed throughout the country [4, 5]. In this Mesoamerican biocultural context and using traditional management, farmers preserve and utilize a great diversity of chili landraces.

A total of slightly more than 150 landraces, occupying extensive planted surfaces and providing for great consumption, have been described in Mexico. The central and south-southeastern regions are more diverse and relevant for the in situ preservation of chilis. In these regions, approximately 80 landraces have been preserved. In Mexico, 153,565 ha are cultivated annually, resulting in an average production of 2.8 million tons of dry and fresh fruits. Annually, approximately 2 million tons of fresh and dry chilis are consumed, and in some years, imports range between 20,757 and 41,000 tons [6]. Consumption per capita in urban areas is from 8 to 9 kg, and in rural communities, it varies between 13 and 17 kg.

The health benefits of chili consumption and its active ingredients continue to be investigated using in vitro and in vitro biological models as well as theoretical and experimental models. Capsaicinoids and flavonoids are the determinant compounds of color, flavor, texture and aroma of food prepared with chilis. A common question among health specialists is whether chili consumption improves health or contributes to disease development. The chili fruit contains up to 15 or more capsaicinoid compounds. Among the majority are capsaicin, dihydrocapsaicin and nordihydrocapsaicin; in flavonoid content, quercetin, apigenin and luteolin are notable as well as some catechins and cyanidins. Thus, one does not only ingest vitamins B₁, B₂ and C, minerals, carotenoids and phenols by chili consumption.

Flavonoids contain phenolic hydroxyl groups in their chemical structure and possess excellent chelating properties of iron and other transition metals—characteristics that confer on chilis a high antioxidant capacity and anti-free-radical properties, generating protection against oxidative damage [7]. Flavonoids have positive effects on health although their mechanisms of action continue to be investigated because it is difficult to quantify daily intake and their direct effects on health. Thus far, flavonoids are associated with antisclerotic, anti-inflammatory, antitumoral, antithromobogenic, antiviral and antiosteoporotic effects and may function as a preventive agent in cancer, among other effects [8–10].

Capsaicinoids are synthesized in the placenta of the fruit and are genetically determined (*Pun1* allele of pungency) by the presence of the *Pun1* or *pun1* gene with EST- or AT3-type cofactors that induce a quantitative effect of the gene and variations in the pungency of the fruit. Therefore, not all chili peppers are spicy, and various consumers consider chili varieties that carry the *pun1* recessive gene to be sweet fruits [11]. In addition, genetic or genotypic factors, crop management, cultivation environments, maturity of the fruit upon cutting, postharvest management of fruit and forms of processing or cooking the fruit for consumption influence the level of pungency and flavor at the time of consumption [12].

In the last decade, hundreds of articles have been published on the potential adverse and beneficial effects of capsaicin (8-methyl-N-vainillyl-6-nonenamide) on human health. Experimental results are controversial and require testing in humans, not only biological models. Consumption of capsaicin in chilis stimulates neuronal networks and gastric secretions and stimulation; in addition, capsaicin is considered to be a preventative agent for cancer, has lipolytic action by increasing the hydrolysis of triacylglycerol in adipocytes and is associated with antioxidant action. Direct effects as a carcinogenic agent have not been demonstrated, and recent studies have demonstrated that there is no conclusive evidence that confirms the association between consumption of extremely spicy red chili peppers and mortality in the European and North American populations [13–18].

The role of diet in health is increasingly important and warrants further investigation. Several investigators have focused their studies on the documentation of macro- and micro-nutrients, vitamins, minerals, proteins, gastronomic aspects and, recently, the functional and nutraceutical character of various bioactive compounds. Chili peppers and other species are consumed universally because these fruits confer color, flavor, aroma and texture and help preserve foods. In this work, the diversity and variety of consumed forms of chilis in Mexico, flavonoid and capsaicinoid content in the fruits and their potential health benefits, are documented based on various study results and bibliographic information. Additionally, elements of the culinary culture associated with chili in Mexico, high levels of consumption and repercussions on human health with an emphasis on flavonoids and capsaicinoids are provided.

2. Diversity of chili pepper landraces in Mexico

Depending on the archaeobotanic, genetic and pre-Columbian sociocultural diversity, it has been established that chili peppers (*Capsicum annuum* L. and *C. frutescen* L.) have been collected, cultivated and consumed in Mexico for hundreds of years. For example, analysis of archaeological remains from the Tehuacán Valley in Mexico indicates that there were wild forms 8000 years ago, and different cultivation and domestication events of *C. annuum* occurred with evidence dating to 6000 years ago [19, 20]. Perry and Flannery [1], from excavations, collection and dating of archaeobotanic samples of the Silvia and Guila Naquitz's caves in Oaxaca, indicated that cultivated forms of *C. annuum* and *C. frutescens* have existed for nearly 8000 years. In Chiapas, Mexico, from a sample of ceramic residue, extensive culinary use of chili peppers was demonstrated [2]. In general, archaeobotanic, genetic and cultural linguistic evidence identifies the Mesoamerican region as the center of origin, domestication and diversification of *C. annuum* and *C. frutescens*, and those species continued to evolve under domestication or as wild forms [3].

In Mexico, wild species of *Capsicum* have certain characteristics in common, such as being small spicy fruits of round, elongated or conical forms that regularly ripen in red or yellow colors. The regularly erect fruits are easily separated from the calyx. They have small seeds, which form a portion of the diet of birds and facilitate the chilis' dispersal over long distances. Today, wild forms have a wide distribution from the southern United States of America to South America (Argentina). Among these cases, *C. annuum* var. *annuum* and *C. annuum* var. *glabriusculum* (Dunal) Heiser & Pickersgill are notable [5, 21–23].

During the domestication process, chili fruits and plants have undergone various genetic transformations in response to human and natural selection. Thus, by the processes of natural environmental and artificial selection, the forms, sizes, colors and flavors of the fruit began to change. Obtaining a larger fruit and greater productivity per plant is, even today, one of the goals of breeders and growers. In the domesticated or cultivated forms of chili, the fruits are hanging and remain on the plant upon ripening, and in some cases, the fruit is covered and hidden from birds; the plant is interdependent with man to survive. That is, domesticated or cultivated species do not survive in their wild state because the plants have lost various defense mechanisms against natural enemies, including their seed dispersion mechanisms. In commercial varieties, the fruits and seeds are generally larger (e.g., Bell types) compared with wild forms [3, 24]. One of the evident changes during the domestication syndrome was the increase in the germination rate of cultivated forms [4].

The domestication of chili peppers generated heritable genotypic changes, which are expressed in several known phenotypic variants. Environmental and human selection modified several morphological characteristics of the fruit and plant and continues to generate significant changes to adapt to different cultivation systems (e.g., greenhouse and high input use). Current cultivation and genetic improvement impose strong selection pressures to the point of dividing cultivated forms into highly pungent, intermediate and sweet or non-pungent groups. In all cases, sources of resistance or tolerance to disease and pests are sought but with high productive efficiency [25, 26]. Chili consumers seek a great diversity of fruits with varied grades of pungency, flavor, aroma, color and sizes of ripe, immature, fresh or dry fruits. In rural households, a few plants grown in the garden or backyard produce enough fruit to satisfy the needs of a family. Traditionally, small producers keep the produced seed from a small number of cultivated plants year after year; the seeds tend to be homogeneous or homozygotic because of regular self-pollination or crossing one another. All of these factors generate high differentiation among cultivated populations [23, 24, 27].

The extensive diversity of landraces of chili in Mexico and Mesoamerica is the product of the geographic convergence of wild and cultivated species. Among the cultivated endemic species, *C. annuum* and *C. frutescens* are notable, and species introduced from South America to Mexico are *C. chinense* Jacq. and *C. pubescens* R. & P. among *C. annuum*, *C. frutescens* and *C. chinense*, there is a strong crosslinking capacity, called the white flower *annuum-chinense-frutescens* species complex; this complex has a high likelihood of crossing with wild variants of *C. annuum* var. *glabriusculum*, particularly when the latter acts as a male parent [28, 29]. In this biogeographical context, diversity of landraces in Mexico is generated by crossing related species, genetic flow generated by the dispersal of seeds and the selection of cultivators, including the effects of genetic drift products from the low number of plants and geographic isolation [4, 5, 27, 30–32].

In addition to the high diversity of landraces, in the Mesoamerican region of Mexico, there is a large ethnolinguistic diversity, with the presence of 28 indigenous groups including Otomí, Mazahua, Náhuatl, Popolucas, Zapoteco, Mixteco, Mixe, Amuzgo, Triqui, Mazateco, Chinanteco, Mayas, Chontales, Huaves, Chatino, Cuicateco, Chontal, Tzeltal, Tzotzil, Purépecha, Totonaco, Ocuilteco and Matlazinca [33]. Pre-Columbian cultures represented by current indigenous groups exerted a strong selection pressure on chili cultivation to satisfy all food requirements

such as medicinal, cultural and ritual. Brown et al. [34] and Kraft et al. [3] studied paleobiolinguistic evidence of the domestication of *Capsicum* in Mexico. Among the primary findings was evidence of 17 words of proto-languages to designate the various cultivated and wild variants or populations of chili; among these terms are Uto-Aztecán, Otomanguean, Popolocan-Zapotecan, Chinantecan, Mixe-Zoquean, Zapotecan, Mayan, Chiapanec-Mangue, Sonoran, Tonacan, Otomapean, Mixtecan, Amuzgo-Mixtecan, Totozoquean and Popolocan, all related to the indigenous groups mentioned here. This renders it possible to distinguish relations between a high diversity of landraces and the extensive gastronomic diversity of dishes [35].

Based on the phenotypic and genetic diversity of chili peppers in Mexico, here, we use the concept of landraces as a combination of definitions proposed by Zeven [36] and Camacho-Villa et al. [37] and the dimensions of seed lots managed by growers proposed by Louette et al. [38]. Thus, a chili landrace is understood to be a dynamic population of cultivated plants in the backyard or crop plots with defined, highly variable or uniform evolutionary origins of the characteristics of the plant, strong similarity in the form of fruit, seed lots that are managed independently and high locally adapted genetic diversity, occasionally with a different name associated with traditional forms of consumption and cultivation. In various cases, the forms, flavors and aromas of the fruit are phenotypically distinguishable, and differentiation frequently obeys geographic-reproductive isolation and selection that farmers utilize. Nevertheless, from that diversity of landraces, numerous traditional and improved commercial varieties have been generated and continue to be generated.

2.1. Phenotypic and genetic diversity among landraces

The wild and cultivated chili of Mexico have been known since pre-Columbian times and are the result of genetic recombination between wild and cultivated forms, only cultivated forms or between primary and secondary gene pools. Today we know these gene pools as indigenous, traditional and regional varieties or landraces of high phenotypic variation in fruit and plant traits. However, these landraces have suffered genetic erosion as a result of habitat loss, changes in the use of soil from forests to cultivated or urban zones and displacement by improved varieties introduced and imposed by the demands of national or international markets [24].

There are marked phenotypic divergences among landraces, relative to sizes, forms, colors and pungency of the fruit. For example, Piquin has a fruit diameter of 2–20 mm compared with Chilaca, which has a cylindrical-elongated form that is 15–35 cm in length with a 2–6 cm diameter. Anchos are conical-triangular fruits that vary from 12 to 15 cm in length and from 8 to 10 cm in width [39]. Colors vary from coffee-reddish, yellow, light greens, dark greens, whitish and very light greens with purple anthocyaninic stains such as in the Pico Paloma and Tusta types of south-southeastern Mexican chili peppers (Table 1).

With regard to consumption, landraces can be classified as fresh or dry. The largest number of landraces are consumed fresh or dry; among the latter are Piquin, Guajillo or Mirasol, Costeño, Puya, Cascabel, Catarina, Canica, Chilhuacle, Ancho, Mulato, De árbol or Cola de Rata and Pasilla. A special case is the preparation of the Chipotle chili (a form of drying by smoking or by oven and pickled); Jalapeno variants are used before ripening, and the fruit is dehydrated and dried in an oven or smoked. In some cases, the fruit is dried in the sun or shade or by smoking [32, 39, 42].

Species and botanical varieties	Regionalization for cropping and on-farm conservation of landraces (local and regional names)
<i>C. annuum</i> var. <i>annuum</i> (Cultivated and wild forms)	Península de Yucatán: Pico de Paloma ^s , Xcat'ik ^m , Ya'ax ik ^m o Cha'hua ^m , Dulce, Jalapeño, Maax ^m , Canica, Sucurre, Kum ^m South-southeastern: Guajillo o Mirasol, Pasilla o Chilaca, Ancho o Poblano, Taviche, De Agua, Costeño, Miahuateco, Mulato, Gordo, Huacle o Chilhuacle, Jalapeño, Serrano, Loco, Coxle o Chicoxle ^c , Gallo-Gallina, De Árbol o Cola de Rata o Yahualica, Tabaquero, Taviche, Apaxtleco, Achilito, Nanche, Tusta, Piquín, Piquín de Simojovel, Chocolate, De Onza, Paradito o Escuchito, Lajoyero o Joyeño o Chilaquita, Parado de Zitlala, De Monte, Tecpín de Zitlala, Morrón, Garbanzo, Ojo de Cangrejo, Güero, Bojo, Blanco de Chiapas y Tabasco, Bandeño de Guerrero, Bolita de la Fraileasca, Siete Caldos, Morado, Serranito, De Gallo, Ardilla, Totic de Chiapas Central: Ancho o Poblano, Miahuateco, Mulato, De Chorro o Cristalino, Pasilla o Chilaca, Tecamatlán, Loco, Rayado, Jalapeño, Serrano, Criollo de Morelos, Soledad, Copi de Puebla, Guajillo o Mirasol, Tabaquero, Mirador o Chalinguero, Pico de Paloma, Piquín o Piquín Huasteco, Cascabel, Soltero, Morron, Morita, Güero, De Chorro, Comapeño de Veracruz, Catarino del Bajío, Chilacate de Jalisco, Pahueteco, Altamira Serrano de Guanajuato, Carricilo o Tornachile, Ozuluamero, Canica del Bajío Northwest: Ancho, Mulato, Pasilla o Chilaca, Guajillo o Mirasol, Puya, De Árbol o Cola de Rata o Yahualica, Cora, Piquín Northeast: Ancho, Mulato, De Árbol o Cola de Rata o Yahualica, Guajillo o Mirasol, Serrano, Puya, Cora, Piquín, Cascabel, De Chorro, Corazón de Durango, Caloro de Chihuahua, Guajón de Zacatecas, Sarta de Sonora, Negro de Chihuahua, Sinahuisa Serrano de Sonora, Vallero de Chihuahua
<i>C. annuum</i> var. <i>glabriusculum</i> (commonly as wild forms)	Península de Yucatán: Maax ^m o Mashito, Piquín South-southeastern: Mashito o Amashito, Amashito Grande, Ojo de Cangrejo, Garbanzo, Bolita, Chingolito Amarillo, Piquín de Tabasco, Piquín Amarillo de Chiapas, Güiña Shirunduu ^z , Chilpete de Jalisco Central: Piquín o Chiltepín Northwest: Piquín o Chiltepín Northeast: Piquín o Chiltepín
<i>C. frutescens</i> (cultivated a wild forms)	Península de Yucatán: Mashito ^m South-southeastern: Chilpaya, Tabasco, Mashito, Pico de Paloma, Bolita, Güiña Shuladi ^z , Mirasol de Oaxaca, Miraparriba, Tabasqueño de la Fraileasca Central: Pico de Paloma, Zacapaleño Northwest: Chilpaya

^mMaya, ^sEspañol, ^cCuicateco and ^zZapoteco (local languages).

Regions of distribution: (a) **Península de Yucatán** = Estados de Quintana Roo, Yucatán and Campeche, (b) **South-southern:** Include the south region from Veracruz, Tabasco, Chiapas, Oaxaca and Guerrero, (c) **Central:** Cover the states of Jalisco, Colima, Michoacán, Estado de México, Guanajuato, Querétaro, Hidalgo, Morelos, Tlaxcala, Puebla and Central region of Veracruz, (d) **Northwest:** Include Zacatecas Aguascalientes, Nayarit, Sinaloa, Durango Sonora, Chihuahua Baja California Norte and Baja California Sur, and (e) **Northeast:** From North of Zacatecas, San Luis Potosí, North of Veracruz, Tamaulipas, Nuevo León and Coahuila.

Sources: González-Jara et al. [4], Pozo-Campodonic et al. [39], Votava et al. [31], Aguilar-Meléndez et al. [32], Pérez-Castañeda et al. [29], Cazáres-Sánchez et al. [40], Castañón-Nájera et al. [41], Vela [42]; Aguilar-Rincón et al. [43], Narez-Jiménez et al. [44], Loaiza-Figueroa et al. [45].

Table 1. Regionalization of the diversity of *Capsicum annuum* landraces in Mexico.

With regard to the level of pungency or spiciness, chili peppers are classified as quite pungent, fairly pungent, sweet or without spiciness. Any consumer of chili in Mexico recognizes Habanero and Manzano as the most spicy chilis; both variants were introduced to the country and belong to the species *C. chinense* (150,000–325,000 Scoville units) and *C. pubescens* (30,000–60,000 Scoville units), respectively [42]. After these two, De Árbol, Serrano, Jalapeño and Piquín variants follow in order of pungency. Finally, there are the moderately pungent or sweet chilis such as Dulce (sweet) chili of the Yucatan Peninsula, De agua from Oaxaca, Poblano and Güero that are particularly notable. Pungent or spicy chilis are more often preferred for the preparation of numerous dishes (**Table 1**).

A total of slightly more than 150 landraces that are extensively planted and consumed have been described. The distribution of the diversity of chili landraces in Mexico can be divided into five regions. The Yucatan Peninsula includes the states of Quintana Roo, Yucatan and Campeche. Here, the Sucurre, Maax, Xcat'ik, Yaax ik and Dulce variants, among others, occur most frequently. Two regions are quite relevant to the in situ preservation of landraces: south-southeast and central, in which regionally, more than 80 local varieties are preserved (**Table 1**). In these regions, the greatest diversity of indigenous groups is also concentrated; therefore, current indigenous people preserve the great diversity of landraces. The landraces of northern Mexico (northeast and northwest) are less diverse than in central and south-southeastern areas.

Wild and cultivated forms of chilis of greater diversity, endemism and distribution in Mexico are *C. annuum* var. *annuum*, *C. annuum* var. *glabriusculum* and *C. frutescens*. Despite advances in the distribution, classification and quantification of the genetic diversity of *Capsicum*, interest-specific hybridizations in the *C. annuum*-*C. frutescens*-*C. chinense* complex that converges in Mexico remain unexplored, including the variability generated by hybridization between landraces and improved introduced varieties. Among landraces, strong genetic divergences have been documented by differences in regionally distributed populations. For example, by nine isoenzymatic systems, Loaiza-Figueroa et al. [45] determined high isoenzymatic diversity by the population description of 186 accessions.

The preservation of a large diversity of landraces is associated with a culture of exploitation of the species that originated in pre-Columbian times [1–3]. Among the aspects that continue to draw attention to gastronomic use are the variety of flavors, aromas and spicy characteristics, including variations in color in dishes and perceptions that are associated with compositions of the fruit in terms of capsaicinoids, flavonoids and polyphenols, among other compounds. In a traditional rural Mexican family, it is quite unlikely that the diet does not include chilis as a condiment, sauce or main dish.

Many authors have demonstrated that there is great genetic diversity among the populations of a landrace. With regard to diversity between and within landraces, Contreras-Toledo et al. [46] and Toledo-Aguilar et al. [47], using microsatellite markers, demonstrated great genetic diversity within the Ancho or Poblano, Piquín, Guajillo and Chilaca landraces. Kraft et al. [27] indicated that divergences among landraces are fundamentally a result of the form of selection of the seed and isolated management of the crop. This same pattern is observed among wild forms (e.g., Piquín), which grow spontaneously in backyards [4]. Pacheco-Olivera et al. [23], in evaluations of the genetic diversity of Mexican chili peppers by microsatellites,

observed that the diversity and genetic differentiation of three landraces were statistically similar to the evaluated pattern in seven commercial hybrids.

2.2. Regionalization of production and consumption of chili landraces

In Mexico, the cultivation and consumption of chili peppers have great economic and social importance. In 2015, 153,565 ha were cultivated, with an average production of 2.8 million tons of dried and fresh fruit. Of the total production, 22,143 and 793,501 tons of dry and fresh fruit were exported, respectively. National consumption neared 2 million tons, and in some years, imports of approximately 20,757–41,000 tons have been reported [6]. Consumption per capita in urban areas is from 8 to 9 kg, and in rural communities, it varies from 14 to 17 kg. Landraces and varieties of greater production and consumption are Jalapeño, Ancho, Serrano, Guajillo, Poblano and Mirasol, with more than 9000 hectares planted. The varieties of highest consumption dried are Ancho, Guajillo and Mirasol. Serrano, Jalapeño and Ancho are grown throughout in nearly all of Mexico (**Table 2**).

State of production origin ¹	Landraces, improved varieties and local populations of fresh and dry chili peppers
Aguascalientes	Guajillo, Poblano o Ancho
Baja California Norte	Serrano, Jalapeño, Anaheim, Bell
Baja California Sur	Bell, Anaheim, Caloro, Jalapeño, Serrano, Poblano,
Campeche	Habanero ^c , Jalapeño
Coahuila	Habanero ^c , Bell, Anaheim, Serrano, Poblano, Jalapeño
Colima	Habanero ^c , Jalapeño, Serrano
Chiapas	Habanero ^c , Serrano, Costeño
Chihuahua	Habanero ^c , Ancho, Colorado, De Árbol o Cola de Rata, Mirasol, Pasilla, Caloro, Cayenne, Chilaca, Jalapeño, Paprika, Poblano, Serrano,
Durango	Ancho, Puya, Jalapeño, Poblano, Anaheim, Bell
Guanajuato	Chilaca, Serrano, Jalapeño, Poblano, Bell, Anaheim
Guerrero	Ancho, Costeño, Puya, Chilaca, Guajillo, Mirasol, Serrano
Hidalgo	De Árbol o Cola de Rata, Jalapeño, Serrano, Bell, Anaheim
Jalisco	De Árbol o Cola de Rata, Tabaquero, Anaheim, Caloro, Chilaca, Jalapeño, Poblano, Serrano, Bell
México	Manzano ^p , Jalapeño, Serrano
Michoacan	Habanero ^c , Pasilla, Caloro, Chilaca, De Árbol o Cola de Rata, Jalapeño, Manzano o Peron ^p , Piquín, Poblano, Serrano, Bell, Anaheim
Morelos	Anaheim, Serrano, Jalapeño
Nayarit	Habane ^c , Cascabel, De Árbol o Cola de Rata, Caloro, Cristal, Jalapeño, Serrano, Anaheim, Bell

State of production origin ¹	Landraces, improved varieties and local populations of fresh and dry chili peppers
Nuevo Leon	Habanero ^c , Serrano, Jalapeño
Oaxaca	Habanero ^c , Ancho, Costeño, Pasilla, Tabaquero, De Agua, Jalapeño, Serrano, Soledad, Chilhuacle
Puebla	Ancho, Jalapeño, Serrano, Poblano, Miahuateco, Bell
Querétaro	Pasilla, Chilaca, Jalapeño, Serrano, Anaheim
Quintana Roo	Habanero ^c , Jalapeño, Dulce
San Luis Potosi	Habanero ^c , Ancho, Guajillo, Mirasol, Mulato, Pasilla, Puya, Chilaca, Jalapeño, Poblano, Serrano, Bell, Anaheim
Sinaloa	Habanero ^c , Anaheim, Bell, Caloro, Chilaca, De Agua, De Árbol o Cola de Rata, Hungaro, Jalapeño, Poblano, Serrano
Sonora	Habanero ^c , Anaheim, Bell, Jalapeño, Serrano
Tabasco	Habanero ^c , Costeño, Tabaquero, Jalapeño, Dulce
Tamaulipas	Habanero ^c , Jalapeño, Serrano, Piquín, Poblano, Bell, Anaheim
Tlaxcala	Serrano
Veracruz	Habanero ^c , Jalapeño, Manzano ^p , Serrano, Piquín, Soledad
Yucatan	Habanero ^c , Mulato, De Árbol o Cola de Rata, Xcat'ik, Bell, Anaheim
Zacatecas	Ancho, De Árbol o Cola de Rata, Guajillo, Mirasol, Mulato, Pasilla, Puya, Caloro, Poblano

¹SIAP [6]; Species: ^p*C. pubescens*, ^c*C. chinense* and without superscript are *C. annum*.

Table 2. Regionalization of landraces and improved varieties cropping by production origin.

According to the geography, altitude and climates of Mexico, there are six primary patterns of cultivation: (a) Habanero variants (*C. chinense*) are sown preponderantly in Yucatán, Quintana Roo and Campeche, although recently, Habanero was cultivated in Coahuila, Chihuahua, Colima, Nayarit and Michoacán, (b) diverse Manzano (*C. pubescens*) chilis are cultivated in Central Mexico in Michoacán, Estado de México, Puebla and Veracruz, (c) the commercial Morrón (sweet bell) varieties are preponderantly distributed in the north such as in Bell, Anaheim, California and Victoria, which are exported to the United States of America, (d) Ancho, Guajillo, Poblano and Pasilla variants are grown from Guanajuato to Zacatecas and Tamaulipas and finally, (e) varieties with regional distribution include Chilhuacle in Oaxaca and Guerrero, Tabaquero in Tabasco and Soledad in Veracruz and Oaxaca, among other patterns (**Table 2**).

Several references contrast the beneficial and harmful effects of capsaicinoids consumed by chilis. Despite advances in the demythification of harmful effects, studies nevertheless refer to capsaicin as a risk factor for cancer [14, 48]. Recent studies indicate a lack of direct association between chili peppers and capsaicinoid consumption and cancer or several other diseases.

Capsaicin is used as a topically applied analgesic to decrease pain in rheumatoid arthritis, osteoarthritis, neuralgias, neuropathic diabetes, neuronal inflammations and dysfunctions, among others [15, 17]. The use of capsaicinoids is controversial, and it is necessary to further investigate their effects on human health because among other aspects, it is not possible to extrapolate from biological studies of animals (e.g., rats) to humans [13, 17].

2.3. Chili peppers in Mexican gastronomy

The varied forms of chili consumption are characteristic of traditional Mexican cuisine and are ancestral and living cultural expressions of the community, a part of the Mexican national identity [49]. In Mexico, there is a great preference for spicy chili, whose consumption is more common in people who live in hot, tropical or subtropical climates than in people who live in temperate-to-cold regions [50]. The sensation of heat or sting is the result of the presence of various types of capsaicinoids such as capsaicin, dihydrocapsaicin, homodihydrocapsaicin, nordihydrocapsaicin and homocapsaicin, among others, which have vanillin, 8-methyl-N-Vanillyl-6-nonemide, as a base compound. During ingestion, chemo-static stimuli are generated that affect chemical stimulation of thermoreceptors, nociceptors and somatosensory receptors [51].

The populations of Mexico, Central and South America show evolutionary adaptations according to the food these people consumed. Culinary culture in Mexico is as diverse as differences in ethnicity, geography and ecology; the current cuisine is a combination of indigenous pre-Columbian, Spanish and French cuisines and, in some regions, Lebanese. Recent times have seen a marked influence of American culture, increasing Mexicans' consumption of carbohydrates. In Mexican families, food consumption practices are taught from childhood; mothers give chili to children from 1 to 3 years of age. This evidence of cultural reinforcement is primarily focused on distinguishing the flavonoid principles of food consumption. Common foods are bean broth, soups prepared with tomato (*Solanum lycopersicum* L.) and dishes flavored with chili; as the child grows, chili consumption increases. Consuming such foods helps to transmit identity from parents to children and implicitly strengthens the food culture [52].

In practical terms, the continued consumption of chili pepper through several generations has engendered genetic modifications in the population of Mexican consumers. Capsaicin tolerance is closely associated with AVI (alanine, valine and isoleucine) allelic variants of the TAS2R38 type 2 gene in the tongue and palate. Consequently, homozygotic carriers of the AVI haplotype of the taste receptor perceive only a slight "burning" sensation. This genetic variant is also associated with a low perception of a bitter flavor. That is, a lower perception of bitterness in other foods and a lower perception of the burning of chili are because of TAS2R38 [50, 53, 54].

The Mexican consumer of chili has an extensive variety of landraces that the consumer produces himself or can buy in local and regional markets, from the "sweet" types or types without spice to moderately spicy and extremely spicy, and all are widely used in regional cuisine and family diets. Chilies are consumed in whole, ground, sliced, diced, dried, roasted forms or can be acquired pickled in cans from nearly all landraces. Chilis are essential to Mexican gastronomy and played a decisive role in UNESCO's designating Mexican cuisine the "intangible cultural heritage of mankind" (Decision 5.COM 6.30, 2010) [55].

The variety of chili landraces is directly associated with a wide variety of processing forms for consumption. Among chili and forms of consumption are the following groups of peppers and preparation styles:

- (a) Group I. Sweet types such as Morrón (Anaheim, Bell and California), Ancho de Puebla, De Agua de Oaxaca or Dulce de Yucatán are eaten raw and used in salads, primarily the Morrón because that type ripens in red, green or yellow and adds color to dishes.
- (b) Group II. Unripe or ripe spicy green peppers such as the Serrano, Jalapeño, Rayado and Loco. Ya'ax ik, Criollos de Morelos, De Árbol Verde, Xcat'ik, Copi, Soledad, Cora, Tabaquero, Costeño Verde and others are regularly used to prepare traditional green salsas and green moles, typical dishes of Mexican cuisine.
- (c) Group III. Among chilis consumed, dried, powdered Piquín is notable, as are chilis used to prepare different types of regional moles: Ancho, Pasilla, Guajillo, Chilhuacle, Tavi-che, Costeño, Cascabel, De Onza, Mulato, Miahuateco, Cristalino, Gordo, Coxle, De Árbol Seco, Puya, Chawa, Tabaquero, Apaxtleco and others.

Mole is a typical Mexican national dish resulting from the fusion of Spanish and pre-Columbian indigenous cuisines. The word *mole* (in Spanish) comes from the indigenous language Nahuatl "*molli*", which means a mix of ingredients and flavors. Ingredients and forms of preparation vary from region to region or between states. For example, moles from Puebla, Oaxaca, Tlaxcala, Estado de México, Querétaro, Michoacán and Hidalgo are quite popular. The dish is a combination of different chili landraces (e.g., Ancho, Pasilla, Morita and others) and various fruits, seeds and bulbs, depending on the mole variant (**Table 3**). However, the essential ingredients, according to connoisseurs, are the chilis. In Oaxaca, seven types of moles are prepared, and the most popular are "negro (black mole) with Chilhuacle", "verde" (green mole) with Jalapeño or Serrano chilis, "coloradito" (reddish mole) with Ancho and Guajillo chilis, red mole with Ancho and Guajillo chilis and Amarillo (yellow mole) with Anchos, Guajillos and Costeños. Additionally, "chichilo" and "manchamantel" ("tablecloth-staining") moles are mentioned. For each type of mole, the complementary condiments vary [56].

Another common dish of Mexican cuisine is from spicy to extremely spicy salsas, which are prepared with fresh or dried chilis, cooked or uncooked, and are a traditional form of promoting spicy flavors (capsaicinoids), flavonoids, aromatic compounds and phenolic compounds. Occasionally, chilis are roasted and ground with green tomato (husk tomato, *Physalis ixocarpa* Brot.), red tomato (*S. lycopersicum*), garlic, onion, salt and water. In other cases, all of the ingredients are cooked and then ground (**Table 3**). From one region to another, the primary ingredients and forms of preparation vary. In this sense, Mexican guacamole is the addition of avocado to green salsa (e.g., Jalapeño or Serrano chilis cooked with green tomato, plus garlic and water) in which pieces of avocado are mashed slightly once the green salsa is ground, all of this in a "molcajete" (a rock with a hole) [57]. A group of Mexican dishes prepared with different local varieties of chilis is listed on **Table 3**. It is unlikely that the level of consumption of chilis in Mexico will decrease in the short term.

Typical dishes of the Mexican cuisine ¹	Landrace used or improved variety
Known molee: negro, coloradito, chichilo, rojo, verde, pipián, amarillo, poblano (turkey in deep-brown sauce), "estofado", "manchamantel", de caderas, de hongos, de frijol, relleno negro, almendrado	<p>(a) Blanck mole: Ancho, Chilhuacle</p> <p>(b) Red mole: Ancho and Guajillo</p> <p>(c) Green mole: Jalapeño, Rayado and Serrando</p>
Salsas (sauces) prepared with fresh and dry chilis: Borracha ("drunk"), verde, roja, de ancho, de guajillo	<p>(a) Freh: Commonly Jalapeño o Serrano buta ll high spiced chilis can be used.</p> <p>(b) Dry: Ancho, Pasilla, De árbol, Cascabel</p>
Chilaquiles: verdes (green), rojos (red), de mole (made with mole)	Jalapeño, Serrano, Ancho, Guajillo, Pasilla, Cascabel, De Árbol
Tamales de verdes (greenish) o rojos (red), de mole, de rajas de chile (with slices of chili)	Jalapeño, Serrano, Ancho, Pasilla
Traditional guacamole	Serrano, Jalapeño
Chiles rellenos (stuffed chili peppers)	Poblano, Ancho, De Agua, Güeros, Jalapeños
Tortas ahogadas and Pambazos	Pasilla, Guajillo
Elotes (cob) o frutas (tropical fruits) with powdery dry chili pepper	Chili Piquín milled with sal
Chile en chipotle (smoked peppers)	Jalapeño and Rayado
Chili in encurtidos (pickled peppers)	Usually Jalapeño and Serrano but all chili peppers can be used.
Roasted chili to slice o eat directly ("morder") o en rajas:	Regularly Serrano and Jalapeño
Immature peppers or green to mature but fresh to slice and combine with onion and lemon, regionally known as "gatos" or "pico de gallo"	<p>(a) Immature: Jalapeño, Serrano, De Agua</p> <p>(b) Muture: Habanero, Manzano, Bell, Anaheim o California</p>
Chileatole	Serrano
Chiles en nogada (dish name)	Ancho, Poblano, Miahuateco
Flautas ahogadas (dish name)	Jalapeño, Serrano
Mixiote verdes de pollo (dish name)	Jalapeño, Serrano

¹Sources: Urdaneta and Kanter [56] and Katz [57].

Table 3. Typical dishes of the Mexican cuisine where main ingredients are the diversity of landraces or improved varieties of chili pepper.

3. Flavonoid and capsaicinoid contents in fruits of chili pepper landraces

3.1. Flavonoids in *Capsicum*

In Mexico, there is a great diversity of phenotypic variants of chilis that are distinguished by color, flavor, spice, aroma, size and shape and are fundamental to and completely accepted in Mexican gastronomy. The species *C. annuum* originated in Mexico and is one of the most cultivated species in the world, with high genetic diversity [39, 43]. The organoleptic properties of each type of chilis are characterized by their chemical composition as a function of flavonoid

content, capsaicinoids, phenolic acids, vitamins, minerals and various volatile compounds [40, 58–61]. Flavonoids and capsaicinoids are molecules that, in addition to influencing the sensory characteristics of the fruit, contribute to the prevention of chronic degenerative diseases [62, 63].

Flavonoids are secondary metabolites of low molecular weight that share a common skeleton with diphenylpropanes (C6-C3-C6) and comprise two phenyl rings (A and B) joined through a C ring of pyran (heterocyclic). Flavonoids are classified according to oxidation state and degree of unsaturation of the central heterocyclic ring. The primary families are flavones, iso-flavones, flavanones, flavanols, antho-cyanidins and chalcones [64]. The structural diversity of flavonoids depends on the substitution of aromatic rings A and B by hydroxyl and methoxy groups and by extensive conjugations, including glucosides. In foods, flavonoids exist primarily as 3-O-glycoside and polymers [64, 65]. Flavonoids possess multiple properties for eliminating reactive oxygen species. Their activity as an antioxidant depends on the redox properties of their hydroxyphenolic groups and the structural relation between various components of the chemical structure [7]. Some of the characteristics that favor their antioxidant capacity are the ortho-hydroxylation of ring B, the number of free hydroxyl groups, a C2-C3 double bond at ring C and the presence of a 3-hydroxyl group [66].

In fruits and vegetables, it is estimated that more than 7000 flavonoids have been identified [64]. In chili fruit, the primary quantified flavonoids are quercetin, luteolin, kaempferol, catechin, epicatechin, rutin, luteolin, apigenin and myricetin [61, 67–76]. Variations in flavonoid concentrations are primarily the result of the diversity of genotypes, landraces, varieties and the ripening phase of the fruit; also implied are variations related to analytical laboratory parameters such as sample preparation, extraction method and quantification methods (**Table 4**).

In chili fruits, different flavonoids have been identified depending on morphotype, landrace, varietal group or variety. In sweet peppers (*C. annuum* L. cv. Vergasa), 23 flavonoids have been identified and quantified in the pericarp by high-performance liquid chromatography-diode array detection-electrospray ionization mass spectrometry (HPLC). These include O-glycosides of quercetin, luteolin and chrysoeriol and a large number of C-glycosyl flavones. The most abundant compounds were quercetin-3-O-rhamnoside and luteolin 7-O-(2-apiosyl-6-malonyl), which represented 41% of the total flavonoids [77]. Materska and Perucka [79] identified quercetin 3-O- α -L-rhamnopyranoside-7-O- β -D-glucopyranoside, luteolin 6-C- β -D-glucopyranoside-8-C- α -L-arabinopyranoside, apigenin 6-C- β -D-glucopyranoside-8-C- α -L-arabinopyranoside, luteolin 7-O-[2-(β -D-apiofuranosyl)- β -D-glucopyranoside], quercetin 3-O- α -L-rhamnopyranoside and luteolin 7-O-[2-(β -D-apiofuranosyl)-4-(β -D-glucopyranosyl)-6-malonyl]- β -D-glucopyranoside. These flavonoids are present in four varieties of *C. annuum*. In the “Italian sweet” (green), “Lamuyo” (yellow) and “California wonder” (red) varieties, 23 flavonoids and their glycoside derivatives were identified by high-performance liquid chromatography coupled with diode array and electrospray time-of-flight mass spectrometry detectors (HPLC), highlighting the group of flavonols known as glycosylated quercetin derivatives (rutin pentoside, quercetin 3,7-di-O- α -L-rhamnopyranoside and quercetin 3-O- α -L-rhamnoside) [79]. Various flavonoids continue to be identified in all species of *Capsicum*, and depending on advances, it is inferred that the task continues and the work is incipient in Mexican landraces.

Flavonoids ¹	Maturation stage	<i>C. annuum</i> landrace and variety groups							<i>C. frutescens</i>
		Jalapeño	Serrano	Ancho	Güero	Morron	Cayenne	Piquin	Tabasco
Quercetin	Immature	4.3.–151.2	9.30–159.8	276.0	42.4–210.2	4.76–276.0	6.0–22.9	ND	2.2
	Mature	ND	8.1	ND	23.9–64.4	3.29–448.0	3.7–24.7	ND	0.9
Kaempferol	Immature	5.9	2.1	ND	ND	ND	2.0–4.7	ND	ND
	Mature	1.4	ND	ND	ND	ND	6.3–6.4	ND	ND
Catechin	Immature	0.1	1.0	ND	ND	1.85–5.13	ND	ND	ND
	Mature	ND	ND	ND	ND	5.28–6.41	ND	ND	8.1
Epicatechin	Immature	0.1	1.2	ND	ND	3.70–7.35	ND	ND	ND
Rutin	Immature	0.2	2.0	ND	ND	0.38–1.90	ND	ND	ND
Luteolin	Immature	0.20–37.5	0.57–41.40	3.6	15.7–51.5	0.35–9.32	2.0–19.1	ND	43.6
	Mature	3.2	1.4	ND	5.96–16.8	0.36–11.0	7.1–17.3	ND	0.84–35.6
Myricetin	Immature	ND	ND	ND	ND	658.0	2.1.0–2.1	ND	ND
	Mature	ND	ND	ND	ND	171.0–244.0	5.9.0–7.2	ND	ND
Apigenin	Immature	ND	ND	ND	ND	272.0	ND	ND	ND
Total Flavonoids	Immature	10.2–332.0	11.4–441.0	309.6	58.1–309.0	5.4–31.7	10.0–48.8	97.40–544.6	45.8
	Mature	4.6	9.5	ND	29.9–81.3	3.6–892.0	42.1–44.3	50.1–425.0	36.5
References		[74, 76]	[74, 76]	[74]	[67, 74]	[67, 69, 71–73]	[67]	[61, 75]	[67, 73]

¹Quercetin, catechin or quercetin + luteolin equivalents (µg/g or g/g), ND = Not determined.
Sources: Vera-Guzmán et al. [61], Howard et al. [67], Miean and Mohamed [69], Kim et al. [71], Blanco-Ríos et al. [72], Zhuang et al. [73], Lee et al. [74], Rochín-Wong et al. [75], Álvarez-Parrilla et al. [76].

Table 4. Flavonoid contents in fruits of *Capsicum annuum* and *C. frustences*.

The structure of each flavonoid influences antioxidant capacity, which varies between species and genotypes of chili. Materska [80] isolated three glycosylated flavonoids (luteolin 6-C-glucoside, luteolin 6,8-di-C-glucoside and apigenin 6-C-glucoside-8-C-arabinoside) from the chili fruit (*C. annuum* var. Capel Hot) and determined their antioxidant activity using in vitro methods to generate radicals in hydrophilic (superoxide radical) and lipophilic (2,2-diphenyl-1-picrylhydrazyl—DPPH—and peroxide radicals) media. This study demonstrates that luteolin 6-C-glucoside and luteolin 6,8-di-C-glucoside have a greater ability to eliminate superoxide radicals generated in enzymatic and non-enzymatic systems and thus engender high antioxidant activity [80]. The high and effective antioxidant capacity confers functional and nutraceutical properties to the fruit for health.

Metabolism, biochemical synthesis and concentration of flavonoids in chili fruits depend on species, genotype, landrace or commercial varieties [61, 67–69, 81] interacting with agroecological characteristics and crop management [82]. Evidence indicates that the concentration of flavonoids is related to the degree of maturity of the fruit. Bhandari et al. [83] observed that fruits had a higher flavonoid content in the initial-to-intermediate phases (breaker stage) than in the phase immediately after maturity (green mature phase) and red ripe phase. Similarly, Howard et al. [67] observed that total flavonoid content was reduced in the immature-to-mature phase of the fruit (**Table 4**). This fact is consistent with other studies; green fruits (immature) reach four to five times the flavonoid content of mature fruits [67, 72, 77, 84]. In *C. chinense* Jacq. (Habanero), flavonoid content also decreases with ripening [85]. However, the behavior of Morrón peppers is different because the peppers ripen in different colors; for example, quercetin and luteolin flavonoid content was higher in red fruits than in green [68]. Differences in the composition of flavonoids and other compounds define the organoleptic characteristics of each chili fruit and are directly related to usage and consumption preferences [86].

Chili fruits are considered a natural source of antioxidants for their bioactive compounds [61, 77, 87]. Phenolic compounds increase the antioxidant activity of chili fruits and are related to the structure of their molecules. In the case of Caribe and Bell varieties (*C. annuum*), the major antioxidant activity was the result of the content of the flavonoids catechin, epicatechin and rutin, among other compounds [81]. In addition, high activity has been reported when quercetin 3-O α -L-rhamnopyranoside was identified; such activity was comparable with quercetin activity [78]. Quercetin is a highly antioxidative aglycone and is generated by enzymatic hydrolysis of the glycoside bond of rutin (quercetin 3-O-rhamnoglucoside) [66]. In evaluating the fruits of the landraces De Árbol, Chipotle, Guajillo and Morita (*C. annuum*), it was determined that there was greater bioaccessibility of polyphenols in the small intestine in a range of 72–77%. Therefore, these landraces are considered important sources of polyphenols and bioaccessible bioactive compounds in the intestine [88].

3.2. Capsaicinoids in chili pepper landraces

Capsaicinoids are compounds that confer pungency or spice to chili fruits and are synthesized by the condensation of vanillylamine with a branched short chain fatty acid. Their chemical structure comprises a phenolic nucleus joined by an amide bond to a fatty acid. The phenolic portion is vanillylamine and is synthesized from phenylalanine in the phenylpropanoid pathway. The fatty acid is generated from branched chain amino acids, valine or leucine [89]. Currently, more than 20 capsaicinoids are known [90], and differences in structures occur because of the nature of the side chain, which can vary between 8 and 10 carbons, and the number of double bonds. Capsaicinoids are classified into three groups of compounds: capsaicins possessing a methyl branched acyl residue with a carbon-carbon double bond, dihydrocapsaicins analogous to the previous class but being saturated compounds and N-vanillyl-n-acylamides comprising saturated, unbranched alkyl chains [91]. Capsaicin [(E)-N-(4-hydroxy-3-methoxybenzyl)-8-methyl-6-nonenamide] and its analogue 6,7-dihydrocapsaicin represents more than 90% of total capsaicinoids in chili fruits (**Table 2**), primarily accumulating in the placenta of the fruit [58]. Schweiggert et al. [91] identified and characterized

15 capsaicinoids in the red fruits of *C. frutescens*, primarily capsaicin, dihydrocapsaicin and nordihydrocapsaicin, with nornorcapsaicin, norcapsaicin, homocapsaicin I and II, nornordihydrocapsaicin, homodihydrocapsaicin isomers I and II, N-Vanillyl-octanamide, N-vanillyl-nonanamide and N-anillyl-decanamide as minor compounds (**Figure 1**).

Capsaicinoids are synthesized in the placenta of the fruit and are genetically determined (*Pun1* allele of pungency) by the presence of the *Pun1* or *pun1* gene with EST- or AT3-type cofactors that induce a quantitative effect of the gene and variations in the pungency of the fruit. In consequence, not all chili peppers are spicy, and various consumers consider chili varieties that carry the *pun1* recessive gene to be sweet fruits [11]. In practical terms, it is difficult to determine the exact content of capsaicinoids in chili fruits, and the estimates or patterns that are obtained vary enormously depending on genotypes, ecological-environmental conditions, crop systems, the maturity of the fruit and harvest season, among other aspects [61, 87, 92–95]. **Table 5** presents the estimates of the capsaicinoid content in fruits of different landraces and varietal groups. Various studies have demonstrated that capsaicinoid content is greater in mature fruits than in immature one [58, 73, 78]. Some of the landraces with notable concentrations of capsaicinoids are Piquín, De Árbol and Serrano, and those with lower concentrations are the Morrón group (California, Bell, Anaheim), Pasilla, Ancho and Guajillo, among others [59, 95, 96].

Ecological-environmental conditions are factors that influence the accumulation of capsaicinoids in fruits; among the primary climatic elements are temperature and precipitation or irrigation interacting with crop management. For example, González-Zamora et al. [95] observed that temperatures of 40–48°C reduce the concentrations of capsaicinoids from 32.5 to 61.5% and

Figure 1. Structures of major capsaicinoids identified in *Capsicum* species.

Landrace or varietal groups	Capsaicin (CAP) ¹		Dihydrocapsaicin (DIH)		Nordihydro-capsaicin		Homo-CAP and Homo-DIH	References
	Immature	Mature	Immature	Mature	Immature	Mat.	Immature	
Jalapeño	115.8–8000	169.0–373.5	54.0–9390	113.5–237.8	13.3–2480	24.4	160–970	[75, 95]
Serrano	47.5–1606	81.3–627.48	57.2–3540	87.7–399.7	22.3–530	27.8	640.0	[75, 95, 96]
Mulato	ND	29.5	ND	49.5	ND	ND	ND	[59]
Pasilla	1.0	49.2	ND	68.8	1.0	ND	ND	[96]
Guajillo	170.0	22.9	610.0	36.9	120.0	ND	560.0	[95, 96]
Ancho	0.3	42.8	0.8	0.4	0.3	ND	0.6	[96]
Poblano	0.6	ND	ND	ND	ND	ND	ND	[96]
Pasadox	ND	38.3	ND	58.4	ND	ND	ND	[96]
Puya	1180.0	53.9	2320.0	67.4	550.0	ND	68.0–80.0	[95, 96]
Tres Venas	ND	66.9	ND	77.1	ND	ND	ND	[96]
Mirasol	ND	353.8	ND	231.7	ND	ND	ND	[96]
Morita	ND	338.2	ND	334.9	ND	ND	ND	[96]
Chipotle	ND	163.8–883.0	ND	126.3–552.7	ND	ND	ND	[96]
De Árbol	138.5–4249	309.3–1293	146.4–6250	238.2–641.7	1070.0	ND	130.0–1290	[93, 95, 96]
Chiltepin	3790–15360	4170	13390	ND	2170.0	ND	220–690	[75, 86]
Piquin	ND	16.2–2657	ND	62.4–1031	ND	ND	ND	[61, 96]
Maax	640.0	750.0–3584	370.0	1707	ND	ND	ND	[40, 58]
Tusta	51.4	ND	33.5	ND	ND	ND	ND	[61]
Tabaquero	ND	6.7	ND	1.5	ND	ND	ND	[61]
Solterito	ND	142.0	ND	65.5	ND	ND	ND	[61]
Nanchita	ND	27.4	ND	13.2	ND	ND	ND	[61]

Landrace or varietal groups	Capsaicin (CAP) ¹		Dihydrocapsaicin (DIH)		Nordihydro-capsaicin		Homo-CAP and Homo-DIH	References
	Immature	Mature	Immature	Mature	Immature	Mat.	Immature	
Güero	44.5	ND	6.8	ND	ND	ND	ND	[61]
Costeño	ND	14.6	ND	4.0	ND	ND	ND	[61]
De agua	ND	4.9	ND	1.6	ND	ND	ND	[61]
Sucurre	26945	2930–18995	3652.0	4355–5043	ND	ND	ND	[40, 58]
Pico paloma	ND	2456.4	ND	1928	ND	ND	ND	[40]
Ya'x ik	ND	1777.6	ND	1811	ND	ND	ND	[40]
Chawa	12815	1415–11822	2175	1317–5555	ND	ND	ND	[40, 58]
Xcat ik	ND	748.4–3189	ND	831.3	ND	ND	ND	[40, 58]
Bobo	ND	204.7	ND	372.2	ND	ND	ND	[40]
Dulce	ND	42.4	ND	58.9	ND	ND	ND	[40]
Miahuateco	ND	63.6	ND	45.5	ND	ND	ND	[59]
Copi	ND	267.4	ND	167.7	ND	ND	ND	[59]
Tecomatlán	ND	54.6	ND	35.7	ND	ND	ND	[59]
Morrón	1.8–143.1	1.2–134.5	55.6–99.0	57.5–113.4	ND	ND	ND	[73, 84]
Cayenne	20.8–149.5	53.7–211.7	72.0	40.1–114.6	ND	ND	ND	[84]
Tabasco ²	ND	746.8	ND	496.1	ND	ND	ND	[73]

¹Content in µg/g of fresh or dry weight, ²*Capsicum frutescens*, ND = Not determined.

Sources: Cazáres-Sánchez et al. [40], Cisneros-Pineda et al. [58], Morán-Bañuelos et al. [59], Vera-Guzmán et al. [61], Kim et al. [71], Zhuang et al. [73], Rochín-Wong et al. [75], Álvarez-Parrilla et al. [76], Bae et al. [84], Othman et al. [93], González-Zamora et al. [95], Orellana-Escobedo et al. [96], Ornelas-Paz et al. [77].

Table 5. Capsaicinoid contents in fruits of chili landrace and varietal groups.

32.5% in Jalapeño and De Árbol chilis, respectively. By contrast, in Guajillos and Serranos, the identical temperature generated up to a three-fold increase; a similar effect was identified in Puya and Ancho but only 21 and 8.6% more, respectively. In a trial in three regions of Peru, the change in temperature from 19.4 to 26.8°C generated a decrease in capsaicinoid content [92].

3.3. The effect of traditional processing on flavonoid and capsaicinoid contents

Chili fruits are consumed fresh, dried or processed. The chili's condition or processing experience changes their chemical composition because of the effects of temperature changes, pH, solar radiation, smoking or other treatment. For example, the composition of Chiltepín chili fruits changes because of the effect of the pickling process (cooked in 1:1 water and vinegar). In this case, total flavonoids, capsaicin and antioxidant activity are reduced to less than 25%. However, no significant changes are shown as a result of sun drying (temperatures between 34 and 40°C for 32 h) [75]. Similarly, Álvarez-Parrilla et al. [76] identified reductions in capsaicinoids in Serrano and Jalapeño chilis from the pickling process. During the preparation of salsas with Chiltepín, losses in capsaicinoids were detected from changes in pH and the milling process; with pH 2.7, the reduction of capsaicin and dihydrocapsaicin was 90% [98].

Regarding processing for consumption, in Mexico, the preparation of mole paste (a traditional dish) prepared with Pasilla (landrace) chili generates a decrease in the content of flavonoids, phenols and antioxidant activity as a result of cooking and changes in pH, which induce degradation of these compounds [99]. Ornelas-Paz et al. [97] indicated that cooking in water at only 96°C or on the grill at 210°C generates moderate losses of 1.1 and 28.1% of the initial content in Poblano, Bell, Chilaca, Caribe, Jalapeño and Serrano landraces of *C. annuum*, Habanero (*C. chinense*) and Manzano (*C. pubescens*). In the particular case of the Jalapeño landrace, the decrease was 10.6–52.2%. The roasting process increased capsaicin content from 6.1 to 924.9%, dihydrocapsaicin from 2.6 to 57% and nordihydrocapsaicin from 6.6 to 206.8%, depending on genotype. Notably, the compounds are highly volatile, and the increase from heat treatment is attributed to dehydration of the fruit, cell breakdown and inactivation of enzymes that degrade capsaicinoids, such as peroxidases [100]. In this sense, Turkmen et al. [101] observed that cooking by boiling, vapor and microwaves produces increases from 2 to 26% of phenolic compounds and up to 30% in antioxidant activity in spicy chilis. In *C. frutescens* cv. Sina and *C. annuum* cv. Coduion, Shaimaa et al. [102] identified increases in phenolic compounds, flavonoids and antioxidant activity by boiling.

In Mexico, a smoked-drying or oven-drying method (65% of humidity and 75°C) is used with Jalapeño landraces, producing what is known as “chipotle chilis” (special preparation). This process increases the content of flavonoids and antioxidant capacity up to 10 times as a result of the combined liberation of phenolic compounds and flavonoids, including flavonoids generated by wood combustion. By contrast, there is a reduction in capsaicinoid content because of increase in temperature [103].

3.4. Flavonoids and capsaicinoids in health

Chili fruits, in addition to conferring sensory characteristics on foods, also provide nutritional advantages from their chemical composition of vitamins, minerals, carotenoids, flavonoids

and capsaicinoids, among others [40, 58, 59, 61]. Controversy remains regarding the beneficial and unfavorable health effects of chili consumption. Recently, Chopan and Littenberg [18] determined that there is no direct relation between high consumption of red chilis and mortality in various populations of North America and Europe. In these cases, adult consumers of red chilis showed a 13% lower risk of death than non-consumers. Lv et al. [104] also observed no direct relation between consumption of fresh or dried chilis and causes of mortality from cancer, diabetes, respiratory or cardiac diseases. Other reports argued that the bioactive or phytochemical compounds of *Capsicum* have anti-inflammatory, antidiabetic, antimicrobial, anticholesterolemic, anticoagulant and antioxidant properties [63].

Cancer is one of the primary causes of morbidity and mortality worldwide. Oxidative stress is implied in the etiology of this disease and results from imbalances in the production of reactive oxygen species (ROS) and the antioxidant defense system of cells. ROS deregulate redox homeostasis and promote formation of tumors by aberrant induction of signaling pathways that cause cancerous tumors [105]. ROS modulate different pathways of cell signaling, which are mediated by the transcription factors NF- κ B and STAT3, hypoxia-inducible factor, growth factors, kinases and other proteins and enzymes involved in the development of cancer [106]. In this carcinogenic process, it is argued that capsaicinoids (capsaicin and hydrocapsaicin) help eliminate reactive oxygen species and consequently demonstrate anticarcinogenic, antimutagenic and preventative properties [107, 108]. These properties help prevent the proliferation of cells, migration and induction of apoptosis [109]. In *in vivo* and *in vitro* trials, capsaicin inhibited the growth and proliferation of prostate cancer [110]. In addition, capsaicin stimulates the cascade of MAP protein kinase signaling, extracellular signal-regulated protein kinase (ERK) and c-Jun N-terminal kinase (JNK), which have antiproliferative effects [111]. Capsaicin also induces apoptosis of both androgen receptors AR-positive (LNCaP) and -negative (PC-3, Du-145) prostate cancer cell lines by increasing p53, p21 and Bax [112]. Other studies determined that capsaicin can regulate the increase in IL-6 by secretion of TNF- α and the signaling responsible for activation of Akt, ERK and PKC- α [110].

Capsaicin can prevent the growth of colorectal cancer cells by suppression of pathways dependent on β -catenin/TCF by proteosomal degradation of β -catenin and breakdown of β -catenin/TCF-4 interactions [113]. In addition, capsaicin induces apoptosis in gastric cancer cells and can serve as an antitumor agent in gastric cancer [114]. In other studies, capsaicin generates ROS through mitochondria and the depletion of intracellular antioxidants and generates mitochondrial damage and apoptosis in pancreatic cancer cells [115].

Dihydrocapsaicin showed strong antibacterial activity against *Helicobacter pylori*, the bacteria associated with gastric cancer [116]. In biological trials *in vivo*, oral administration of quercetin generated decreases in infection from *H. pylori* in gastric mucosa and reduced the inflammatory response and lipid peroxidation [62].

Flavonoids are molecules that not only act as conventional antioxidant hydrogen donors but also exert a modulatory action on the signaling of protein and lipid kinases of cells [117]. The apigenin flavonoid is an inhibitor of protein kinases and has an antiproliferative effect on breast cancer cells [118]. The aglycone of quercetin has a protective effect on DNA, which is induced by mitomycin C and antiproliferative activities in human lymphocytes [119]. This

molecule also contributes to the protective effect of nerve cells against neurotoxicity induced by oxidative stress, including in Alzheimer's [120].

Chili consumption can promote weight loss by the effect of capsaicin [121]. Capsaicin stimulates lipolysis, causing a reduction in intercellular lipids from the increase in the hydrolysis of triacylglycerol in adipocytes. This effect is mediated by the regulation of genes associated with the catabolic pathway of lipids, HSL and CPT-1a and genes involved in thermogenesis such as UCP2 [16]. Capsaicin promotes the removal of visceral fat and prevents obesity induced by diets high in fats. Capsaicin activates transient receptor potential cation channel sub-family V member 1 (TRPV1) channels, increases levels of Ca^{2+} ions mediated by connexin 43 (Cx43) and promotes lipolysis in adipocytes and fat reduction [122]. Capsaicinoids demonstrate hypocholesterolemic activity from stimulation of the conversion of cholesterol to bile acids by expression of the cholesterol 7-hydrolase gene and increased secretion of bile acids in feces [123].

4. Final considerations and conclusions

Chili peppers are used worldwide as food and spices. In Mexico, chilis have great economic, social and culinary importance with variations in consumption per capita from 8 to 17 kg, and approximately 2.8×10^6 tons are produced and consumed annually. Mexico is the center of origin, domestication and diversification of *C. annuum*, which has engendered more than 150 cultivated and wild *landraces* of wide distribution. Nearly every region in Mexico cultivates or consumes chilis. Indigenous groups and traditional producers are the primary actors responsible for in situ preservation of the diversity of chili landraces, particularly in the central and south-southeastern regions. The wild forms of *C. annuum* var. *glabriusculum* and *C. annuum* var. *annuum* are distributed throughout the country.

Daily consumption ranges from two to four times a week, and it is estimated that between 70 and 80% of the total Mexican rural population regularly consume spicy chilis. This high frequency of consumption has generated an adaptation to consumption of spicy and extremely spicy chilis, and among consumers, the TAS2R38 type 2 gene has been identified as being associated with tongue and palate receptors, which confer upon the chili consumer a higher capacity to not perceive or barely perceive the "burning" sensation of chilis. Into the diversity of landraces and improved varieties, there are non-pungent landraces, for example, Morrón, Dulce, Ancho and Chilaca and types of Morrón varieties such as California, Victoria and others.

Chili fruit contains up to 23 flavonoid compounds and 20 capsaicinoids, differing between landraces because of the effect of crop management, the state of maturation of the fruits and postharvest management and ecological-environmental influences. Capsaicinoids (capsaicin, dihydrocapsaicin, nordihydrocapsaicin, homodihydrocapsaicin, homocapsaicin, etc.) exert multiple physiological effects on human health, including their potential value in pain relief, cancer prevention and decreased bone loss and as antioxidant activity. Experimentally, anti-carcinogenic, antimutagenic and cancer preventative properties have been determined for capsaicin in addition to anti-lipid effects. However, these properties require direct evaluation

with regard to human health. The flavonoids quercetin and apigenin, present in chili fruits, have antiproliferative effects on breast cancer cells and exert a protective effect on neuronal cells against the neurotoxicity induced by oxidative stress in Alzheimer's.

Acknowledgements

The authors are grateful for the financial support provided by the National Polytechnic Institute (projects SIP-20160113 and SIP-20170781) and COFAA-IPN and EDI-IPN fellows.

Author details

Araceli M. Vera-Guzmán¹, Elia N. Aquino-Bolaños², Elena Heredia-García³, José C. Carrillo-Rodríguez⁴, Sanjuana Hernández-Delgado⁵ and José L. Chávez-Servia^{1*}

*Address all correspondence to: jchavez@ipn.mx

1 National Polytechnic Institute, CIIDIR-Oaxaca, Mexico

2 Basic Sciences Institute Universidad Veracruzana, Jalapa, Mexico

3 National Institute of Forest, Agricultural and Livestock Research (INIFAP), Experimental Station-El Bajío, Celaya, Mexico

4 Technologic Institute of the Oaxaca Valley, Oaxaca, Mexico

5 National Polytechnic Institute, Center of Genomic Biotechnology, Reynosa, Mexico

References

- [1] Perry L, Flannery KV. Precolumbian use of chili peppers in the valley of Oaxaca, Mexico. *Proceedings of National Academy of Science of the USA* 2007. **104**: 11905-11909. DOI: 10.1073/pnas.0704936104.
- [2] Powis TG, Gallaga-Murrieta E, Lesure R, Lopez-Bravo R, Grivetti L, Kucera H, Gaikwad NW. Prehispanic use of chili peppers in Chiapas, Mexico. *PLoS One* 2013. **8**(11): e79013. DOI: 10.1371/journal.pone.0079013.
- [3] Kraft KH, Brown CH, Nabhan GP, Luedeling E, Luna-Ruiz JJ, d'Eeckenbrugge GC, Hijmans RJ, Gepts P. Multiple lines of evidence for the origin of domesticated chili pepper, *Capsicum annuum*, in Mexico. *Proceedings of National Academy of Science of the USA* 2014. **111**: 6165-6170. DOI: 10.1073/pnas.1308933111.
- [4] González-Jara P, Moreno-Letelier A, Fraile A., Piñeiro D, García-Arenal F. Impact of human management of the genetic variation of wild pepper, *Capsicum annuum* var. *glabriusculum*. *PLoS One* 2011. **6**(12): e28715. DOI: 10.1371/journal.pone.0028715.

- [5] Hayano-Kanashiro C, Gámez-Meza N, Medina-Juárez LM. Wild pepper *Capsicum annuum* L. var. *glabriusculum*: Taxonomy, plant morphology, distribution, genetic diversity, genome sequencing and phytochemical compounds. *Crop Science* 2016. **56**: 1-11. DOI: 10.2135/cropsci2014.11.0789.
- [6] Servicio de Información Agroalimentaria y Pesquera (SIAP). Anuario Estadístico de la Producción Agrícola 2015. Servicio de Información Agroalimentaria y Pesquera, Secretaria de Agricultura, Ganadería, Desarrollo Rural, Pesca y Alimentación. México, DF. 2016. Available from: http://infosiap.siap.gob.mx/aagricola_siap_gb/identidad/index.jsp [Accessed: January 7, 2017].
- [7] Martínez-Flórez S, González-Gallegos J, Culebras JM, Tuñón MJ. Los flavonoides: Propiedades y acciones antioxidantes. *Nutrición Hospitalaria*. 2002. **7**: 271-278. http://www.bvs.sld.cu/revistas/ibi/vol22_1_03/ibi07103.pdf
- [8] Birt DE, Hendrich S, Wang W. Dietary agents in cancer prevention: Flavonoids and isoflavonoids. *Pharmacology and Therapeutics* 2001. **90**: 157-177. DOI: 10.1016/S0163-7258(01)00137-1.
- [9] Nijveldt RJ, van Nood E, van Hoorn EC, Boelens PG, van Norren K, van Leeuwen PAM. Flavonoids: A review of probable mechanism of action and potential applications. *American Journal of Clinical Nutrition* 2001. **74**: 418-425. <http://ajcn.nutrition.org/content/74/4/418.full.pdf+html>
- [10] Dixon RA, Pasinetti GM. Flavonoids and isoflavonoids: From plant biology to agriculture and neuroscience. *Plant Physiology* 2010. **154**: 453-457. DOI: 10.1104/pp.110.161430.
- [11] Stewart C, Kang B-C, Liu K, Mazourek M, Moore SL, Yoo EY, Kim B-D, Paran I, Jahn MM. The Pun1 gene for pungency in pepper encodes a putative acetyltransferase. *The Plant Journal* 2005. **42**: 675-688. DOI: 10.1111/j.1365-313X.2005.02410.x.
- [12] Ornelas-Paz JJ, Martínez-Burrola JM, Ruiz-Cruz S, Santana-Rodríguez V, Ibarra-Junquera V, Olivas GI, Pérez-Martínez JD. Effect of cooking on the capsaicinoids and phenolic contents of Mexican pepper. *Food Chemistry*. 2010 **119**: 1619-1625. DOI: 10.1016/j.foodchem.2009.09.054.
- [13] Surh Y-J, Lee SS. Capsaicin in hot chili pepper: Carcinogen, co-carcinogen or anticarcinogen? *Food and Chemical Toxicology* 1996. **34**: 313-316. DOI: 10.1016/0278-6915(95)00108-5.
- [14] Serra I, Yamamoto M, Calvo A, Cavada G, Báez S, Endoh K, Watanabe H, Tajima K. Association of chili pepper consumption, low socioeconomic status and longstanding gallstones with gallbladder cancer in a Chilean population. *International Journal of Cancer* 2002. **102**: 407-411. DOI: 10.1002/ijc.10716.
- [15] Surh Y-J. Anti-tumor promoting of selected spice ingredients with antioxidant and anti-inflammatory activities: A short review. *Food and Chemical Toxicology* 2002. **40**: 1091-1097. DOI: 10.1016/S0278-6915(02)00037-6.
- [16] Lee M-S, Kim C-T, Kim Y. Effect of capsaicin on lipid catabolism in 3T3-L1 adipocytes. *Phytotherapy Research* 2011. **25**: 935-939. DOI: 10.1002/ptr.3339.

- [17] Bode AM, Dong Z. The two face of capsaicin. *Cancer Research* 2011. **71**: 2809-2814. DOI: 10.1158/0008-5472.CAN-10-3756.
- [18] Chopan M, Littenberg B. The association of hot red chili pepper consumption and mortality: A large population-based cohort study. *PLoS ONE* 2017. **12**(1): e0169876. DOI: 10.1371/journal.pone.0169876.
- [19] Smith CE. Plant Remains. In: Byers DS, editor. *The Prehistory of the Tehuacan Valley, Vol. 1: Environment and Subsistence*. Austin: University of Texas Press. 1967. pp. 220-255.
- [20] Perry L, Dickau R, Zarrillo S, Holst I, Pearsall DM, Piperno DR, Berman MJ, Cooke RG, Rademaker K, Ranere AJ, Raymon JS, Sandweiss DH, Scaramelli F, Tarble K, Zeidler JA. Starch fossils and the domestication and dispersal of chili peppers (*Capsicum* spp. L.) in the Americas. *Science* 2007. **315**: 986-988. DOI: 10.1126/science.1136914.
- [21] Pickersgill B. Migrations of chili pepper, *Capsicum* spp, in the Americas. In: Stone D, editor. *Pre-Columbian Plant Migration*. Cambridge: Harvard University Press. 1984. pp. 105-124.
- [22] Pickersgill B. Domestication of plants in the Americas: Insights from Mendelian and molecular genetics. *Annals of Botany* 2007. **100**: 925-940. DOI: 10.1093/aob/mcm193.
- [23] Pacheco-Olivera A, Hernández-Verdugo S, Rocha-Ramírez V, González-Rodríguez A, Oyama K. Genetic diversity and structure of pepper (*Capsicum annuum* L.) from Northwestern Mexico analyzed by microsatellite markers. *Crop Science* 2012. **52**: 231-241. DOI: 10.2135/cropsci2011.06.0319.
- [24] Pickersgill B. Chile peppers (*Capsicum* spp.). In: Lira R, Casas A, Blancas J, editors. *Ethnobotany of Mexico: Interactions of the People and Plants in Mesoamerica*. New York: Springer Science+Business Media. 2016. pp. 417-437.
- [25] Pickersgill B. Genetic resources and breeding of *Capsicum* spp. *Euphytica* 1997. **96**: 129-133. DOI: 10.1023/A:1002913228101.
- [26] Paran I, Ben-Chaim A, Kang B-C, Jahn M. Capsicums. In: Kole C, editor. *Genome Mapping and Molecular Breeding in Plants, Vol. 5: Vegetables*. New York: Springer-Verlag Berlin Heidelberg; 2007. pp. 209-226.
- [27] Kraft KH, Luna-Ruiz JJ, Gepts P. Different seed selection and conservation practices for fresh market and dried chili farmers in Aguascalientes, Mexico. *Economic Botany* 2010. **64**: 318-328.
- [28] Pickersgill B. Relationships between weedy wild and cultivated forms in some species of chili pepper (genus *Capsicum*). *Evolution* 1971. **25**: 683-691. DOI: 10.2307/2406949.
- [29] Pérez-Castañeda LM, Castañón-Nájera G, Ramírez-Meraz M, Mayek-Pérez N. Avances y perspectivas sobre el estudio del origen y la diversidad genética de *Capsicum* spp. *Ecosistemas y Recursos Agropecuarios* 2015. **2**: 117-128. <http://148.236.18.64/era/index.php/rera/article/view/721/591>

- [30] Hernández-Verdugo S, Luna-Reyes R, Oyama K. Genetic structure and differentiation of wild and domesticated populations of *Capsicum annuum* (Solanaceae) from Mexico. *Plant Systematic and Evolution* 2001. **226**: 129-142. DOI: 10.1007/s006060170061.
- [31] Votava EJ, Baral JB, Bosland PW. Genetic diversity of chile (*Capsicum annuum* var. *annuum* L.) landraces from Northern New Mexico, Colorado and Mexico. *Economic Botany* 2005. **59**: 8-17. DOI: 10.1663/0013-0001(2005)059[0008:GDOCCA]2.0.CO.
- [32] Aguilar-Meléndez A, Morrel PL, Roose ML, Kim S-C. Genetic diversity and structure in semiwild and domesticated chiles (*Capsicum annuum*; Solanaceae) from Mexico. *American Journal of Botany* 2009. **96**: 1190-1202. DOI: 10.3732/ajb.0800155.
- [33] Boege E. El patrimonio biocultural de los pueblos indígenas de México. Hacia la conservación *in situ* de la biodiversidad y agrobiodiversidad en los territorios indígenas. Mexico, D.F: Instituto Nacional de Antropología e Historia y Comisión Nacional para el Desarrollo de los Pueblos Indígenas; 2010, 342 p.
- [34] Brown CH, Clement CR, Epps P, Ludeling E, Wichmann. The paleobiolinguistics of domesticated chili pepper (*Capsicum* spp.). *Ethnobiology Letters* 2013. **4**: 1-11. DOI: 10.14237/eb1.4.2013.2.
- [35] Long-Towell J. Los senderos prehispánicos del *Capsicum*. In: Long-Towell J, Attolini-Lecón A, editors. *Caminos y Mercados en México*. Mexico, D.F.: Universidad Nacional Autónoma de México e Instituto Nacional de Antropología e Historia; 2009. pp. 79-106.
- [36] Zeven AC. Traditional maintenance breeding of landraces: 2. Practical and theoretical considerations on maintenance of variation of landraces by farmers and gardeners. *Euphytica* 2002. **123**: 147-158. DOI: 10.1023/A:1014940623838.
- [37] Camacho-Villa TC, Maxted N, Scholten M, Ford-Lloyd B. Defining and identifying crop landraces. *Plant Genetic Resources* 2005. **3**: 373-384. DOI: 10.1079/PGR200591.
- [38] Louette D, Charrier A, Berthaud J. *In Situ* conservation of maize in Mexico: Genetic diversity and maize seed management in a traditional community. *Economic Botany* 1997. **51**: 20-38. DOI: 10.1007/BF02910401.
- [39] Pozo-Campodonic O, Montes-Hernández S, Redondo-Juárez E. Chile (*Capsicum* spp.). In: Ortega R, Palomino G, Castillo F, González VA, Livera M, editors. *Avances en el estudio de los recursos fitogenéticos de México*. Texcoco, México: SOMEFI, A. C., 1999. pp. 217-238.
- [40] Cazáres-Sánchez E, Ramírez-Vallejo P, Castillo-González F, Soto-Hernández RM, Rodríguez-González MT, Chávez-Servia JL. Capsaicinoides y preferencias de usos en diferentes morfotipos de chile (*Capsicum annuum* L.) del centro-oriente de Yucatán. *Agrociencia* 2005. **39**: 627-638. <http://www.colpos.mx/agrocien/Bimestral/2005/nov-dic/art-6.pdf>
- [41] Castañón-Nájera G, Latournerie-Moreno L, Mendoza-Elos M, Vargas-López A, Cárdenas-Morales H. Colección y caracterización de chile (*Capsicum* spp) en Tabasco, México. *Phyton, International Journal of Experimental Botany* 2008. **77**: 189-202. <http://www.revistaphyton.fund-romuloraggio.org.ar/vol77/CASTANION.pdf>

- [42] Vela E. Los chiles de México: Catálogo visual. *Arqueología Mexicana* 2009. 32: 39-77.
- [43] Aguilar-Rincón VH, Corona-Torres T, López-López P, Latournerie-Moreno L, Ramírez-Meraz M, Villalón-Mendoza H, Aguilar-Castillo JA. Los Chiles de México y su Distribución. Texcoco: SINAREFI, Colegio de Posgraduados, INIFAP, IT-Conkal, UANL y UAN; 2010, 114 p.
- [44] Náñez-Jiménez CA, de-la-Cruz-Lázaro E, Gómez-Vázquez A, Castañeda-Nájera G, Cruz-Hernández A, Márquez-Quiroz. La diversidad morfológica *in situ* de chiles silvestres (*Capsicum* spp.) en Tabasco, México. *Revista Fitotecnia Mexicana* 2014. 37: 209-215. <http://www.revistafitotecniamexicana.org/documentos/37-3/3a.pdf>
- [45] Loaiza-Figueroa F, Ritland K, Laborde-Cancino JA, Tanksley SD. Patterns of genetic variation of the genus *Capsicum* (*Solanaceae*) in Mexico. *Plant Systematic and Evolution* 1989. 15: 159-198. DOI: 10.1007/BF00936000.
- [46] Contreras-Toledo AR, López-Sánchez H, Santacruz-Varela A, Valadez-Moctezuma E, Aguilar-Rincón VH, Corona-Torres T, López PA. Diversidad genética en México de variedades nativas de chile 'Poblano' mediante microsatélites. *Revista Fitotecnia Mexicana* 2011. 34: 225-232. <http://www.revistafitotecniamexicana.org/documentos/34-4/1a.pdf>
- [47] Toledo-Aguilar R, López-Sánchez H, Santacruz-Varela A, Valadez-Moctezuma E, López PA, Aguilar-Rincón VH, González-Hernández VA, Vaquera-Huerta H. Characterization of genetic diversity of native 'Ancho' chili populations of Mexico using microsatellite markers. *Chilean Journal of Agricultural Research* 2016. 76: 18-26. DOI: 10.4067/S0718-58392016000100003.
- [48] López-Carrillo L, Fernández-Ortega MC, Costas-Dias R, Franco-Marina J, Alejandro-Badillo T. Creencias sobre el consumo de chile y la salud en la ciudad de México. *Salud Pública de México* 1995. 37: 339-343. <http://saludpublica.mx/index.php/spm/article/view/5854/6567>
- [49] Pilcher JM. Tamales or timbales: Cuisine and the formation of Mexican national identity, 1821-1911. *The Americas* 1996. 53: 193-196. DOI: 10.2307/1007616.
- [50] Nabhan GP. *Why Some Like it Hot: Food, Genes, and Cultural Diversity*. Washington DC: Island Press, 2004. 244 p.
- [51] Abdel-Salam OME. Preference for hot pepper: A complex interplay of personal, cultural and pharmacological effects. *Temperature* 2016. 3: 39-40. DOI: 10.1080/23328940.2015.1111289.
- [52] Mennella JA, Turnbull B, Ziegler PJ, Martinez H. Infant feeding practices and early flavor experiences in Mexican infants: An intra-cultural study. *Journal of the American Dietetic Association* 2005. 105: 908-915. DOI: 10.1016/j.jada.2005.03.008.
- [53] Hayes JE, Baroshuk LM, Kidd JR, Duffy VB. Supertasting and PROP bitterness depends on more than the TAS2R38 gene. *Chemical Senses* 2008. 33: 255-265. DOI: 10.1093/chemse/bjm084.

- [54] Román S, Ojeda-Granados C, Panduro A. Genética y evolución de la alimentación de la población en México. *Revista de Endocrinología y Nutrición* 2013. **21**: 42-51. <http://www.medigraphic.com/pdfs/endoc/er-2013/er131f.pdf>
- [55] United Nations Educational, Scientific and Cultural Organization (UNESCO). List of Intangible Cultural Heritage in Need of Urgent Safeguarding. Rome: United Nations Educational, Scientific and Cultural Organization; 2017. Available from: <http://www.unesco.org/culture/ich/en/lists> [Accessed: January 17, 2017].
- [56] Urdaneta ML, Kanter DF. *Deleites de la Cocina Mexicana: Healthy Mexican American Cooking*. Austin: University of Texas Press. 1996. 256 p.
- [57] Katz E. Chili pepper, from Mexico to Europe: Food, imaginary and cultural identity. In: Medina FX, Ávila R, De Garine I, editors. *Food, Imaginary and Cultural Frontiers*. Guadalajara: Universidad de Guadalajara; 2009, pp. 213-232.
- [58] Cisneros-Pineda O, Torres-Tapia LW, Gutiérrez-Pacheco LC, Contreras-Martín F, González-Estrada T, Peraza-Sánchez SR. Capsaicinoids quantification in chili peppers cultivated in the state of Yucatan, Mexico. *Food Chemistry* 2007. **104**: 1755-1760. DOI: 10.1016/j.foodchem.2006.10.076.
- [59] Morán-Bañuelos SH, Aguilar-Rincón VH, Corona-Torres T, Castillo-González F, Soto-Hernández RM, Miguel-Chávez S. Capsaicinoides en chiles nativos de Puebla, México. *Agrociencia* 2008. **42**: 807-816. Available from: <http://www.colpos.mx/agrocien/Bimestral/2008/oct-nov/art-7.pdf>
- [60] Eggink PM, Maliepaard C, Tikunov Y, Haanstra JPW, Bovy AG, Visser RGF. A taste of sweet pepper: Volatile and non-volatile chemical composition of fresh sweet pepper (*Capsicum annuum*) in relation to sensory evaluation of taste. *Food Chemistry* 2012. **132**: 301-310. DOI: 10.1016/j.foodchem.2011.10.081.
- [61] Vera-Guzmán AM, Chávez-Servia JL, Carrillo-Rodríguez JC, López MG. Phytochemical evaluation of wild and cultivated pepper (*Capsicum annuum* L. and *C. pubescens* Ruiz & Pav.) from Oaxaca, Mexico. *Chilean Journal of Agricultural Research* 2011. **71**: 578-585. http://www.chileanjar.cl/files/V71_I4_2011_ENG_AraceliMinervaVera-Guzman.pdf
- [62] González-Segovia R, Quintanar JL, Salinas E, Ceballos-Salazar R, Avilés-Jiménez F, Torres-López, J. Effect of the flavonoid quercetin on inflammation and lipid peroxidation induced by *Helicobacter pylori* in gastric mucosa of guinea pig. *Journal of Gastroenterology* 2008. **43**: 441-447. DOI: 10.1007/s00535-008-2184-7.
- [63] Chamikara MDM, Dissanayake DRRP, Ishan M, Sooriyapathirana SDSS. Dietary, anti-cancer and medicinal properties of the phytochemicals in chili pepper (*Capsicum* spp.). *Ceylon Journal of Science* 2016. **45**: 5-20. DOI: 10.4038/cjs.v45i3.7396.
- [64] de Villiers A, Venter P, Pasch H. Recent advances and trends in the liquid-chromatography-mass spectrometry analysis of flavonoids. *Journal of Chromatography A* 2016. **1430**: 16-78. DOI: 10.1016/j.chroma.2015.11.077.

- [65] Heim KE, Tagliaferro AR, Bobilya DJ. Flavonoid antioxidants: Chemistry, metabolism and structure-activity relationships. *The Journal of Nutritional Biochemistry* 2002. **13**: 572-584. DOI: 10.1016/S0955-2863(02)00208-5.
- [66] Burda S, Oleszek W. Antioxidant and antiradical activities of flavonoids. *Journal of Agricultural and Food Chemistry* 2001. **49**: 2774-2779. DOI: 10.1021/jf001413m.
- [67] Howard LR, Talcott ST, Brenes CH, Villalon B. Changes in phytochemical and antioxidant activity of selected pepper cultivars (*Capsicum* species) as influenced by maturity. *Journal of Agricultural and Food Chemistry* 2000. **48**: 1713-1720. DOI: 10.1021/jf990916t.
- [68] Sun T, Xu Z, Wu CT, Janes M, Prinyawiwatkul W, No HK. Antioxidant activities of different colored sweet bell peppers (*Capsicum annuum* L.). *Journal of Food Science* 2007. **72**: S98-S102. DOI: 10.1111/j.1750-3841.2006.00245.x.
- [69] Miean KH, Mohamed S. Flavonoid (myricetin, quercetin, kaempferol, luteolin, and apigenin) content of edible tropical plants. *Journal of Agricultural and Food Chemistry* 2001. **49**: 3106-3112. DOI: 10.1021/jf000892m.
- [70] Marinova D, Ribarova F, Atanassova M. Total phenolics and total flavonoids in Bulgarian fruits and vegetables. *Journal of the University of Chemical Technology and Metallurgy* 2005. **40**: 255-260. <http://dl.uctm.edu/journal/node/j2005-3/Marinova.pdf>
- [71] Kim JS, Ahn J, Lee SJ, Moon B, Ha TY, Kim S. Phytochemicals and antioxidant activity of fruits and leaves of paprika (*Capsicum annuum* L., var. Special) cultivated in Korea. *Journal of Food Science* 2011. **76**: C193-C198. DOI: 10.1111/j.1750-3841.2010.01891.x.
- [72] Blanco-Ríos AK, Medina-Juárez LÁ, González-Aguilar GA, Gámez-Meza N. Antioxidant activity of the phenolic and oily fractions of different sweet bell peppers. *Journal of the Mexican Chemical Society* 2013. **57**: 137-143. <http://www.jmcs.org.mx/PDFS/V57/2/11.-%20Blanco%20G3.pdf>
- [73] Zhuang Y, Chen L, Sun L, Cao J. Bioactive characteristics and antioxidant activities of nine peppers. *Journal of Functional Foods* 2012. **4**: 331-338. DOI: 10.1016/j.jff.2012.01.001
- [74] Lee Y, Howard LR, Villalon B. Flavonoids and antioxidant activity of fresh pepper (*Capsicum annuum*) cultivars. *Journal of Food Science* 1995. **60**: 473-476. DOI: 10.1111/j.1365-2621.1995.tb09806.x.
- [75] Rochín-Wong CS, Gámez-Meza N, Montoya-Ballesteros LC, Medina-Juárez LA. Efecto de los procesos de secado y encurtido sobre la capacidad antioxidante de los fitoquímicos del chiltepín (*Capsicum annuum* L. var. *glabriusculum*). *Revista Mexicana de Ingeniería Química* 2013. **12**: 227-239. <http://www.rmiq.org/iqfvp/Pdfs/Vol.%2012,%20No.%202/Bio1/Bio1.pdf>
- [76] Álvarez-Parrilla E, de la Rosa LA, Amarowicz R, Shahidi F. Antioxidant activity of fresh and processed Jalapeno and Serrano peppers. *Journal of Agricultural and Food Chemistry* 2011. **59**: 163-173. DOI: 10.1021/jf103434u.
- [77] Marín A, Ferreres F, Tomás-Barberán FA, Gil MI. Characterization and quantitation of antioxidant constituents of sweet pepper (*Capsicum annuum* L.). *Journal of Agricultural and Food Chemistry* 2004. **52**: 3861-3869. DOI: 10.1021/jf0497915.

- [78] Materska M, Perucka I. Antioxidant activity of the main phenolic compounds isolated from hot pepper fruit (*Capsicum annuum* L.). *Journal of Agricultural and Food Chemistry* 2005. **53**: 1750-1756. DOI: 10.1021/jf035331k.
- [79] Morales-Soto A, Gómez-Caravaca AM, García-Salas P, Segura-Carretero A, Fernández-Gutiérrez A. High-performance liquid chromatography coupled to diode array and electrospray time-of-flight mass spectrometry detectors for a comprehensive characterization of phenolic and other polar compounds in three pepper (*Capsicum annuum* L.) samples. *Food Research International* 2013. **51**: 977-984. DOI: 10.1016/j.foodres.2013.02.022.
- [80] Materska M. Flavone C-glycosides from *Capsicum annuum* L.: Relationships between antioxidant activity and lipophilicity. *European Food Research and Technology* 2015. **240**: 549-557. DOI: 10.1007/s00217-014-2353-2.
- [81] Medina-Juárez LÁ, Molina-Quijada DM, Del-Toro-Sánchez CL, González-Aguilar GA, Gámez-Meza N. Antioxidant activity of peppers (*Capsicum annuum* L.) extracts and characterization of their phenolic constituents. *Interciencia* 2012. **37**: 588-593. http://www.interciencia.org/v37_08/588.pdf
- [82] Lee JJ, Crosby KM, Pike LM, Yoo KS, Leskovar DI. Impact of genetic and environmental variation on development of flavonoids and carotenoids in pepper (*Capsicum* spp.). *Scientia Horticulturae* 2005. **106**(3), 341-352. DOI: 10.1016/j.scienta.2005.04.008.
- [83] Bhandari SR, Jung BD, Baek HY, Lee YS. Ripening-dependent changes in phytonutrients and antioxidant activity of red pepper (*Capsicum annuum* L.) fruits cultivated under open-field conditions. *HortScience* 2013. **48**: 1275-1282. <http://hortsci.ashspublications.org/content/48/10/1275.full.pdf+html>
- [84] Bae H, Jayaprakasha GK, Crosby K, Yoo KS, Leskovar DI, Jifon J, Patil BS. Ascorbic acid, capsaicinoid, and flavonoid aglycone concentrations as a function of fruit maturity stage in greenhouse-grown peppers. *Journal of Food Composition and Analysis* 2014. **33**(2): 195-202. DOI: 10.1016/j.jfca.2013.11.009.
- [85] Menichini F, Tundis R, Bonesi M, Loizzo MR, Conforti F, Statti G, De Cindio B, Houghton PJ, Menichini F. The influence of fruit ripening on the phytochemical content and biological activity of *Capsicum chinense* Jacq. cv Habanero. *Food Chemistry* 2009. **114**: 553-560. DOI: 10.1016/j.foodchem.2008.09.086.
- [86] Castellón-Martínez E., Chávez-Servia JL, Carrillo-Rodríguez JC, Vera-Guzmán AM. Preferencias de consumo de chiles (*Capsicum annuum* L.) nativos en los valles centrales de Oaxaca, México. *Revista Fitotecnia Mexicana* 2012. **35**: 27-35. http://www.revistafitotecniamexicana.org/documentos/35-3_Especial_5/5a.pdf
- [87] Deepa N, Kaur C, George B, Singh B, Kapoor HC. Antioxidant constituents in some sweet pepper (*Capsicum annuum* L.) genotypes during maturity. *LWT-Food Science and Technology*, 2007. **40**: 121-129. DOI: 10.1016/j.lwt.2005.09.016.
- [88] Hervert-Hernández D, Sáyago-Ayerdi SG, Goñi I. Bioactive compounds of four hot pepper varieties (*Capsicum annuum* L.), antioxidant capacity, and intestinal bioaccessibility. *Journal of Agricultural and Food Chemistry* 2010. **58**: 3399-3406. DOI: 10.1021/jf904220w.

- [89] Vázquez-Flota F, Miranda-Ham ML, Monforte-González M, Gutiérrez-Carbajal G, Velázquez-García C, Nieto-Pelayo Y. La biosíntesis de capsaicinoides, el principio picante del chile. *Revista Fitotecnia Mexicana* 2007. **30**: 353-360. <http://www.revistafitotecnia-mexicana.org/documentos/30-4/2a.pdf>
- [90] Thompson RQ, Phinney KW, Sander LC, Welch MJ. Reversed-phase liquid chromatography and argentation chromatography of the minor capsaicinoids. *Analytical and Bioanalytical Chemistry* 2005. **381**: 1432-1440. DOI: 10.1007/s00216-005-3098-3.
- [91] Schweiggert U, Carle R, Schieber A. Characterization of major and minor capsaicinoids and related compounds in chili pods (*Capsicum frutescens* L.) by high-performance liquid chromatography/atmospheric pressure chemical ionization mass spectrometry. *Analytica Chimica Acta* 2006. **557**: 236-244. DOI: 10.1016/j.aca.2005.10.032.
- [92] Meckelmann SW, Riegel DW, van Zonneveld M, Ríos L, Peña K, Mueller-Seitz E, Petz, M. Capsaicinoids, flavonoids, tocopherols, antioxidant capacity and color attributes in 23 native Peruvian chili peppers (*Capsicum* spp.) grown in three different locations. *European Food Research and Technology* 2015. **240**: 273-283. DOI: 10.1007/s00217-014-2325-6.
- [93] Othman ZAA, Ahmed YBH, Habila MA, Ghafar AA. Determination of capsaicin and dihydrocapsaicin in *Capsicum* fruit samples using high performance liquid chromatography. *Molecules* 2011. **16**: 8919-8929. DOI: 10.3390/molecules16108919.
- [94] Zewdie Y, Bosland PW. Evaluation of genotype, environment, and genotype-by-environment interaction for capsaicinoids in *Capsicum annuum* L. *Euphytica* 2000. **111**: 185-190. DOI: 10.1023/A:1003837314929.
- [95] González-Zamora A, Sierra-Campos E, Luna-Ortega JG, Pérez-Morales R, Ortiz JCR, García-Hernández JL. Characterization of different capsicum varieties by evaluation of their capsaicinoids content by high performance liquid chromatography, determination of pungency and effect of high temperature. *Molecules* 2013. **18**: 13471-13486. DOI: 10.3390/molecules181113471.
- [96] Orellana-Escobedo L, Garcia-Amezquita LE, Olivas GI, Ornelas-Paz JJ, Sepulveda DR. Capsaicinoids content and proximate composition of Mexican chili peppers (*Capsicum* spp.) cultivated in the state of Chihuahua. *CyTA-Journal of Food* 2013. **11**: 179-184. DOI: 10.1080/19476337.2012.716082.
- [97] Ornelas-Paz J, Martínez-Burrola JM, Ruiz-Cruz S, Santana-Rodríguez V, Ibarra-Junquera V, Olivas GI, Pérez-Martínez JD. Effect of cooking on the capsaicinoids and phenolics contents of Mexican peppers. *Food Chemistry* 2010. **119**: 1619-1625. DOI: 10.1016/j.foodchem.2009.09.054.
- [98] Montoya-Ballesteros LC, Gardea-Béjar A, Ayala-Chávez GM, Martínez-Núñez YY, Robles-Ozuna LE. Capsaicinoides y color en chiltepín (*Capsicum annuum* var. *aviculare*): Efecto del proceso sobre salsas y encurtidos. *Revista mexicana de Ingeniería Química* 2010. **9**: 197-207. http://www.rmiq.org/iqfvp/Pdfs/Vol9%20no%202/RMIQVol9No2_8.pdf

- [99] Álvarez-Parrilla E, Mercado-Mercado G, La Rosa LAD, Díaz JAL, Wall-Medrano A, González-Aguilar GA. Antioxidant activity and prevention of pork meat lipid oxidation using traditional Mexican condiments (pasilla dry pepper, achiote, and mole sauce). *Food Science and Technology* 2014. **34**(2): 371-378. DOI: 10.1590/fst.2014.0052.
- [100] Schweiggert U, Schieber A, Carle R. Effects of blanching and storage on capsaicinoid stability and peroxidase activity of hot chili peppers (*Capsicum frutescens* L.). *Innovative Food Science and Emerging Technologies* 2006. **7**: 217-224. DOI: 10.1016/j.ifset.2006.03.003.
- [101] Turkmen N, Sari F, Velioglu YS. The effect of cooking methods on total phenolics and antioxidant activity of selected green vegetables. *Food chemistry* 2005. **93**, 713-718. DOI: 10.1016/j.foodchem.2004.12.038.
- [102] Shaimaa GA, Mahmoud MS, Mohamed MR, Emam AA. Effect of heat treatment on phenolic and flavonoid compounds and antioxidant activities of some Egyptian sweet and chilli pepper. *Natural Products Chemistry and Research* 2016. **4** (2). DOI: 10.4172/2329-6836.1000218.
- [103] Moreno-Escamilla JO, Laura A, López-Díaz JA, Rodrigo-García J, Núñez-Gastélum JA, Alvarez-Parrilla E. Effect of the smoking process and firewood type in the phytochemical content and antioxidant capacity of red Jalapeño pepper during its transformation to chipotle pepper. *Food Research International* 2015. **76**: 654-660. DOI: 10.1016/j.foodres.2015.07.031.
- [104] Lv J, Qi L, Yu C, Yang L, Guo Y, Chen Y, Bian Z, Aun D, Du J, Ge P, Tang Z, Hou W, Li Y, Chen J, Chen Z, Li Z. Consumption of spicy foods and total and cause specific mortality: Population based cohort study. *BMJ* 2015. **351**: h3942. DOI: 10.1136/bmj.h3942.
- [105] Acharya A, Das I, Chandhok D, Saha T. Redox regulation in cancer: A double-edged sword with therapeutic potential. *Oxidative medicine and Cellular Longevity* 2010. **3**: 23-34. DOI: 10.4161/oxim.3.1.10095.
- [106] Prasad S, Gupta SC, Tyagi AK. Reactive oxygen species (ROS) and cancer: Role of antioxidative nutraceuticals. *Cancer Letters* 2017. **387**: 95-105. DOI: 10.1016/j.canlet.2016.03.042.
- [107] Cao S, Chen H, Xiang S, Hong J, Weng L, Zhu H, Liu Q. Anti-cancer effects and mechanisms of capsaicin in chili peppers. *American Journal of Plant Sciences* 2015. **6**: 3075. DOI: 10.4236/ajps.2015.619300.
- [108] Amruthraj NJ, Raj-Preetam JP, Saravanan S, Lebel-Antoine L. *In vitro* studies on anti-cancer activity of capsaicinoids from *Capsicum chinense* against human hepatocellular carcinoma cells. *International Journal of Pharmacy and Pharmaceutical Sciences* 2014. **6**: 254-558. <http://www.ijppsjournal.com/Vol6Issue4/8998.pdf>
- [109] Luo XJ, Peng J, Li YJ. Recent advances in the study on capsaicinoids and capsinoids. *European Journal of Pharmacology* 2011. **650**(1):1-7. DOI: 10.1016/j.ejphar.2010.09.074.

- [110] Venier, N.A., Yamamoto, T., Sugar, L.M., Adomat, H., Fleshner, N.E., Klotz, L.H. and Venkateswaran, V. Capsaicin reduces the metastatic burden in the transgenic adenocarcinoma of the mouse prostate model. *Prostate* 2015. **75**: 1300-1311. DOI: 10.1002/pros.23013.
- [111] Sánchez AM, Malagarie-Cazenave S, Olea N, Vara D, Chiloeches A, Díaz-Laviada I. Apoptosis induced by capsaicin in prostate PC-3 cells involves ceramide accumulation, neutral sphingomyelinase, and JNK activation. *Apoptosis* 2007. **12**: 2013-2024. DOI: 10.1007/s10495-007-0119-z.
- [112] Mori A, Lehmann S, O'Kelly J, Kumagai T, Desmond JC, Pervan M, McBride WH, Kizaki M, Koeffler HP. Capsaicin, a component of red peppers, inhibits the growth of androgen-independent, p53 mutant prostate cancer cells. *Cancer Research* 2006. **66**: 3222-3229. DOI: 10.1158/0008-5472.CAN-05-0087.
- [113] Lee SH, Richardson RL, Dashwood RH, Baek SJ. Capsaicin represses transcriptional activity of β -catenin in human colorectal cancer cells. *The Journal of Nutritional Biochemistry* 2012. **23**: 646-655. DOI: 10.1016/j.jnutbio.2011.03.009.
- [114] Park S-Y, Kim J-Y, Lee S-M, Jun C-H, Cho S-B, Park C-H, Joo Y-E, Kim H-S, Choi SK, Rew JS. Capsaicin induces apoptosis and modulates MAPK signaling in human gastric cancer cells. *Molecular Medicine Reports* 2014. **9**: 499-502. DOI: 10.3892/mmr.2013.1849.
- [115] Pramanik KC, Boreddy SR, & Srivastava SK (2011). Role of mitochondrial electron transport chain complexes in capsaicin mediated oxidative stress leading to apoptosis in pancreatic cancer cells. *PloS ONE* 2011. **6**(5), e20151. DOI: 10.1371/journal.pone.0020151.
- [116] Ochi T, Takaishi Y, Shibata H, Higuti T, Kataoka M. Chemical constituents of *Capsicum annuum* L var. *angulosum*, and anti *Helicobacter pylori* activity. *Natural Medicines* 2005. **59**: 76-84.
- [117] Williams RJ, Spenser JP, Rice-Evans C. Flavonoids: Antioxidants or signalling molecules? *Free Radical Biology and Medicine* 2004. **36**(7): 838-849. DOI: 10.1016/j.freeradbiomed.2004.01.001.
- [118] Way T, Kao M, Lin J. Apigenin induces apoptosis through proteosomal degradation of HER2/neu in HER2/neu-overexpressing breast cancer cells via the phosphatidylinositol 3-kinase/Akt-dependent pathway. *The Journal of Biological Chemistry* 2004. **279**: 4479-4489. DOI: 10.1074/jbc.M305529200.
- [119] Ündeger U, Aydin S, Basaran AA, Basaran N. The modulating effect of quercetin and rutin on the mitomycin C induced DNA damage. *Toxicology Letters* 2004. **151**: 143-149. DOI: 10.1016/j.toxlet.2003.12.071.
- [120] Heo HJ, Lee CY. Protective effects of quercetin and vitamin C against oxidative stress-induced neurodegeneration. *Journal of Agricultural and Food Chemistry* 2004. **52**: 7514-7517. DOI: 10.1021/jf049243r.

- [121] Varghese S, Kubatka P, Rodrigo L, Gazdikova K, Caprnda M, Fedotova J, Zulli A, Kruzliak P, Büsselberg D. Chili pepper as a body weight-loss food. *International Journal of Food Sciences and Nutrition* 2016. 1-10. DOI: 10.1080/09637486.2016.1258044.
- [122] Chen J, Li L, Li Y, Liang X, Sun Q, Yu H, Zhong J, Ni Y, Chen J, Zhao Z, Gao P, Wang B, Liu D, Zhu Z, Yan Z. Activation of TRPV1 channel by dietary capsaicin improves visceral fat remodeling through connexin43-mediated Ca²⁺ influx. *Cardiovascular Diabetology* 2015. **14**: 1-14. DOI: 10.1186/s12933-015-0183-6.
- [123] Zhang L, Zhou M, Fang G, Tang Y, Chen Z, Liu X. Hypocholesterolemic effect of capsaicinoids by increased bile acids excretion in ovariectomized rats. *Molecular Nutrition and Food Research* 2013. **57**: 1080-1088. DOI: 10.1039/c3fo30321g.