24 Mango Fruit Contribution to Human Nutrition and Health

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24.1 Introduction

Mango (*Mangifera indica* L.) is one of the most widely cultivated fruit crops in the world, comprising many commercial cultivars whose ripe fruit peel can be greenish, yellow or reddish and can be pigmented with purple, pink, orange, or red. In 2022, more than 100 countries grew and produced mangoes, with the main producers and consumers of the fruit being India, China, Thailand, Indonesia, the Philippines, Pakistan, and Mexico (FAOSTAT, 2022).

Mango fruit is characterized with high nutritional value, containing a variety of phytochemicals or bioactive compounds that confer properties beneficial for human nutrition and health (Maldonado-Celis *et al.*, 2019; Yahia *et al.*, 2023), although their content varies due to genotypic variation, climatic conditions and pre- and postharvest handling practices (Yahia *et al.*, 2006; Matheyambath *et al.*, 2016; Ghosh *et al.*, 2023). The main bioactive compounds in mango fruit include the most abundant phenolic acids, i.e., coumaric, ferulic and hydroxybenzoic acids, other polyphenols, i.e., quercetin, mangiferin, catechins, tannins, kaempferol, cyanins, gallic acid, ellagic acid, and so on, carotenoids (some are pro-vitamin A), as well as the vitamins ascorbic acid, thiamine, riboflavin and niacin (Burton-Freeman *et al.*, 2017; Lebaka *et al.*, 2021; Lenucci *et al.*, 2022). Several of these compounds are reported to have antioxidant activity (Madalageri *et al.*, 2015; Zapata-Londoño *et al.*, 2020) and help prevent cancer (Boateng *et al.*, 2007; Corrales-Bernal *et al.*, 2014; Yap *et al.*, 2021; Lozano-Casabianca *et al.*, 2022; Ahmad *et al.*, 2023; Yahia *et al.*, 2023), diabetes mellitus (DM) (Ediriweera *et al.*, 2017; Ahmad *et al.*, 2023; Zarasvand *et al.*, 2023), as well as cardiovascular diseases and inflammatory processes (Evans *et al.*, 2017; Rosas Jr. *et al.*, 2021; Castro *et al.*, 2023; Yahia *et al.*, 2023). These effects attribute to the activation of antioxidant signalling pathways that regulate gene expression and activate molecules that produce antioxidant, immunomodulatory, antiproliferative, and antidiabetic effects. The mechanisms of action that explain the bioactivity of several compounds present in mango fruit are based on *in vitro*, *in vivo* and clinical studies, although sometimes they are evaluated at concentrations higher than found in the fruit. However, the active ingredient or the interaction of multiple compounds in the extract can be overlooked, which may be necessary to produce a potent effect. Furthermore, the combination of bioactive compounds shows stronger responses than the effect of individual ingredients, which indicates that regular consumption of whole fruit, rather than individual bioactive compounds, is essential to combat the risk of chronic diseases (van Breda and de Kok, 2018; Yahia *et al.*, 2019a; Pezzuto and Vang, 2020; Samtiya *et al.*, 2021). Although some of the bioactive components are present in low quantities in these foods, they may still have beneficial effects. Consumption of formulations for phytotherapeutic purposes containing plant-based ingredients such as phenolic compounds, pigments, etc., could have negative health side effects, including alteration of glycaemia, lipid profile, hypertension, etc. compared with the positive effects produced by the consumption of whole fruits (Rasoanaivo *et al.*, 2011; Bondonno *et al.*, 2017).

This chapter presents a compilation of information on the nutritional composition of mango fruit, particularly their main phytochemical components that are useful for human nutrition and health. This knowledge should contribute to the understanding of how the regular consumption of this fruit contributes to the prevention of chronic non-communicable diseases, especially associated with unhealthy eating habits. The chapter discusses the nutritional content of mango fruit based on its macronutrients (carbohydrates, proteins and amino acids, lipids and fatty acids, organic acids) and micronutrients (minerals and vitamins). This is followed by the most relevant bioactive compounds identified in mango fruit (phenolic compounds, xanthones and pigments, i.e., chlorophylls and carotenoids). All these components are present in the edible portion of the fruit, but some are also present in the seed and skin, indicating that by-products of the mango fruit can also have benefits for human nutrition and health. A section about the bioaccessibility and bioavailability of bioactive compounds present in mango follows, with emphasis on carotenoids and phenolic compounds, to address and understand their impact on human health. Bioaccessibility refers to the amount and rate at which these compounds are released from the food matrix during digestion, while bioavailability relates to the effective

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absorption and utilization of these compounds by the body. The chapter also presents information on the mechanisms of action involved in the prevention and/or control of some chronic non-communicable diseases associated with the antioxidant, anti-inflammatory, antiproliferative, antidiabetic, antihypertensive effects, and the role of bioactive compounds present in mango fruit in digestive health, in order to understand their efficacy as functional food. Some preharvest and postharvest factors are discussed in relation to their effects on the bioactive components of mango fruit.

24.2 Nutritional Composition

Mango fruit is rich in nutrients such as carbohydrates, vitamins and minerals, low in lipids and proteins, and also rich in non-nutrient compounds such as organic acids, phenolic compounds, xanthones, pigments such as chlorophyll and carotenoids. The energy value per 100 g of fruit pulp ranges from 62 to 190 kcal (250–795 kJ) (Brecht and Yahia, 2009; Yahia *et al.*, 2011; Tharanathan *et al.*, 2016). The contents of these components vary according to cultivar and pre-harvest and postharvest factors and practices (Yahia *et al.*, 2011; Brecht and Yahia, 2017). Table 24.1 presents the nutritional composition reported by the United States Department of Agriculture (USDA, 2019) and the Colombian Institute of Family Welfare (Instituto Colombiano de Bienestar Familiar, ICBF, 2018) of ripe mango pulp of different cultivars.

24.2.1 Macronutrients

Carbohydrates

Mango fruit contain simple sugars such as glucose, fructose and sucrose and polysaccharides such as starch, pectins, cellulose and hemicellulose. The contents of these depend on the fruit cultivar, the stage of maturation and ripening as well as other handling practices before and after harvest (Yahia *et al.*, 2019b). Approximately 15% of the content of the ripe fruit pulp corresponds to simple sugars, which contribute mainly to the sweetness of the fruit, but have a lipogenic effect on human metabolism; therefore, high level intake of particular forms of mango such as juice or nectar may have negative repercussions on weight and displacement of essential foods in the diet, especially in children, although the consumption of fruit juices during childhood remains controversial. Some systematic reviews suggest that 100% fruit juice consumption may provide beneficial nutrients without contributing to paediatric obesity (Crowe-White *et al.*, 2016; Sakaki *et al.*, 2023). On the other hand, several studies have demonstrated pro-obesity effects of certain types of fruit attributed to the content of glucose and fructose, the main precursors of fatty acids induction through *de novo* hepatic lipogenesis, which may increase hepatic triglyceride levels, as well as circulating levels of low-density lipoproteins (LDL), thus leading to an increase in adipose tissue and obesity (Samuel, 2011).

Mango fruit also provide dietary fibre, defined by the American Association of Cereal Chemists (AACC, 2001) as the edible part of plants and analogues of carbohydrate that are resistant to digestion and absorption in the small intestine, with partial or total fermentation in the colon, including polysaccharides, oligosaccharides, lignin and associated plant substances. From a nutritional point of view, dietary fibres are based on the ability to generate hydration and gel formation with beneficial physiological effects on intestinal motility, weight and volume of the bolus, and intestinal transit time (Maldonado and Urango, 2017). Dietary fibre of mango fruit represents 1.6–3.9% of the edible portion of 'Tommy Atkins', 'Haden', 'Kent' and 'Keitt' (ICBF, 2018; USDA, 2019. Therefore, dietary fibre intake from mango fruit promotes weight control, improves blood glucose (Evans *et al.*, 2014) and reduces the absorption of bile acids and consequently the cholesterol levels in the blood, which have positive implications for chronic diseases such as systemic inflammation, cardiovascular diseases, diabetes and irritable bowel syndrome (Wollowski and Pool-Zobel, 2001; Asunción *et al.*, 2023).

Amino acids and proteins

As with most fruits and vegetables, the protein content in the edible portion of mango fruit is relatively low compared with other protein sources such as meat, dairy or legumes, varying between 0.5% and 5.5%, depending on the cultivar, ripening stage and conditions for fruit development (Yahia *et al.*, 2011; Saleem-Dar *et al.*, 2016). Table 24.2 presents the amino acids in the edible portion of mango fruit according to the US Department of Agriculture's Agricultural Research Service (ARS) (USDA, 2019). Mango fruit provide several essential amino acids. Amino acids alanine, arginine, glycine, isoleucine, leucine and serine are quantitatively important in the edible

Table 24.1. Proximal composition analysis of mango fruit pulp. Author's own table.

	Content (g/100 g DW)							
Cultivar	Water	Ashes	Lipids	Proteins	Carbohydrates	Dietary fibre	Energy (kcal)	Reference
Mangocriollo or naturalized	81.8	0.5	0.0	0.6	17.1	3.9	79	ICBF, 2018
'Tommy Atkins'	52.6	0.0	0.1	0.4	46.9	2.1	194	
'Tommy Atkins', 'Keitt', 'Kent', 'Haden'	83.5	0.36	0.38	0.82	15	1.6	60	USDA, 2019

DW, dry weight

Table 24.2. Amino acids content in the edible portion of mango fruit (adapted from USDA ARS, 2019; Yahia *et al*., 2006).

Amino acid	Content (g/100 g DW)
Essential	
Histidine	0–0.019
Isoleucine	0–0.029
Leucine	0–0.050
Lysine	0–0.066
Methionine	0–0.008
Phenylalanine	0–0.027
Threonine	0–0.031
Tryptophan	0–0.013
Valine	0–0.042
Nonessential	
Alanine	0–0.082
Arginine	0–0.031
Aspartic acid	0–0.068
Glutamic acid	0–0.096
Glycine	0–0.034
Proline	0–0.029
Serine	0–0.035
Tyrosine	0–0.016

DW, dry weight basis

portion of the fruit in the ripe stage, and other amino acids are present in trace quantities (Tharanathan *et al*., 2016). These amino acids are essential for protein synthesis in the human body and play an important role in various biological processes, such as muscle repair and growth, neurotransmitter synthesis and immune function. Therefore, although mango is not a significant source of protein, its consumption can contribute to the total dietary intake of essential amino acids.

Fatty acids and lipids

Lipids are nutrients present in small amounts in mango fruit pulp and fatty acids are the main constituents, representing between 0.8% and 1.36% in mango pulp (Table 24.3). During fruit ripening, an increase in unsaturated fatty acids is favoured (Desphande *et al*., 2017), mainly present as triacylglycerides, while monoglycerides and diglycerides are found in lower concentrations (Selvaraj *et al*., 1989).

From a nutritional point of view, the content of unsaturated fatty acids in mango pulp is important for human health because they are essential, cannot be synthesized (and, therefore, must be obtained through the diet) and contribute to vital functions such as cardiovascular health, nervous system, brain function and regulation of inflammations (Djuricic and Calder, 2021). The essential fatty acids linoleic and linolenic, omega-6 and omega-3, respectively, have diverse physiological effects in the prevention and treatment of cardiovascular diseases, atherosclerosis, thrombosis, dyslipidemia, hypertension, diabetes, arthritis and cancer (Uauy and Valenzuela, 2000).

On the other hand, the content of fatty acids is associated with the intensity of fruit aroma and flavour, particularly the ratio of palmitic acid to palmitoleic acid; if greater or less than 1, it indicates that the fruit has a mild or strong aroma and flavour, respectively. It has been proposed that fatty acids are precursors for the biosynthesis of lactones – molecules involved in determining the flavour of this food (Desphande *et al*., 2017).

Organic acids

Organic acids are weak acids, can be of high molecular weight such as humic acids with aromatic nuclei composed of carboxylic and phenolic groups, or of low molecular weight such as oxalic and citric acids (Richter *et al*., 2007). Organic acids in fruit are mostly derived from the tricarboxylic acid cycle and aerobic metabolism and they contribute to the organoleptic properties of the fruit; their content depends on the growing conditions and the handling practices for the tree and the fruit (Vallarino and Osorio, 2019). Among the organic acids present in mango fruit pulp are oxalic, succinic, malic and pyruvic acids as well as tartaric, muconic, galipic, glucuronic and galacturonic acids; however, the main organic acid present is citric acid, found at concentrations 0.13% - 0.71% fresh weight (FW) (Tharanathan *et al*., 2016).

The antioxidant capacity of citric acid contributes to the maintenance and preservation of fruit, a property that has been exploited in the food and chemical industry where citric acid is used as an additive for the preservation of juices, soft drinks, jams, cookies and other foods, because it is safe and has good solubility properties (Kumar *et al*., 2021; Zhang *et al*., 2023). Malic acid also shares this property with citric acid, but it has a higher relative acidity and produces a longer sour mouthfeel than citric acid (Kumar *et al*., 2021).

24.2.2 Micronutrients

Vitamins and minerals make up the micronutrients, because they are required in small but essential amounts, being essential substances for the maintenance of health, since the body is unable to synthesize and/or retain them adequately for the functioning of human metabolism. Micronutrients, especially those provided by mango fruit, do not have energetic functions, but have regulatory ones. Vitamins, in particular, are organic substances whose insufficient presence in the diet leads to the development of diseases.

Minerals

Minerals are constituents of the biosphere, varying widely in proportions according to the element and the geographical region. Some are so dispersed that their extraction is critical, others are soil micro-compounds, while many of them are biological constituents in proportions that vary from nanograms to milligrams, and therefore they are classified into macro and micro minerals (Albarracín, 2015). Macrominerals are found in the body composition in proportions that exceed 70 mg/kg of weight and include calcium (Ca), phosphorus (P), magnesium (Mg), sodium (Na), potassium (K), chlorine (Cl) and sulfur (S). On the other hand, microminerals are also called trace elements, and ten of them have been identified as

Table 24.3. Fatty acid content in mango fruit pulp (adapted from: Yahia *et al*., 2006; Jahurul *et al*., 2015; Leite Neta *et al*., 2018; Maldonado-Celis *et al*., 2019).

Carbon skeleton	Common name	Mango cultivar	Content
8:0[a]	Caprilic acid	'Espada'	0.50
12:0[a]	Lauric acid	'Espada'	2.61
14:0[b]	Myristic acid	'Alphonso'	174.29
16:0[a]	Palmitic acid	'Espada'	64.42
16:0[b]		'Alphonso'	1933.43
17:0[a]	Heptadecanoic acids	'Espada'	1.20
18:0[a]	Stearic acid	'Espada'	9-55
18:0[b]		'Alphonso'	75.63, 123.57
20:0[a]	Arachidic acid	'Espada'	0.63
20:0[b]		'Alphonso'	19.01, 29.21
22:0[b]	Behemic acid	'Alphonso'	24.90, 43.83
24:0[b]	Lignoceric acid	'Alphonso'	35.85, 86.16
16:1, n-7[a]	Palmitoleic acid	'Espada'	8.76
16:1, n-7[b]		'Alphonso'	2881.90
16:1, n-5[b]	11-Hexadecenoic acid	'Alphonso'	146.22,
17:1, n-7[b]	10-Heptadecenoic acid	'Alphonso'	11.82
18:1, n-9[a]	Oleic acid	'Espada'	9.01
18:1, n-9[b]		'Alphonso'	856.59
18:1, n-7[b]	11-Ocatdecenoic acid	'Alphonso'	646.48,
20:1, n-9[a]	11-Eicosenoic acid	'Espada'	0.85
20:1, n-9[b]		'Alphonso'	6.57, 10.01
16:2, n-4[b]	9,12-Hexadecadienoic acid	'Alphonso'	33.86
18:2, n-6[a]	Linoleic acid	'Espada'	8.03
18:2, n-6[b]		'Alphonso'	83.58, 422.83
18:2, n-3[b]	9,15-Octadecadienoic acid	'Alphonso'	61.58
7:2, n-3[b]	Hepta-2,4 (E,E)-dienoic acid	'Alphonso'	698.01,
18:3, n-3[b]	Linolenic acid	'Alphonso'	840.37

Content: a = %, b = μg/g tissue.

being essential, including iron (Fe), copper (Cu), cobalt (Co), manganese (Mn), iodine (I), zinc (Zn), selenium (Se), molybdenum (Mo), chromium (Cr) and fluorine (F). The essentiality of a mineral element implies the appearance of deficiency symptoms in its deficiency and the remission of these symptoms when the element is incorporated into the diet (Godswill *et al*., 2020).

Mango fruit contains several minerals that are distributed in different amounts in the pulp, peel and seed, such as Ca, Cu, Fe, Mg, Mn, P, K, Se, Na and Zn (Table 24.4). In mango fruit pulp, the presence of Fe, Ca and P suggests that the daily consumption of this fruit can contribute to the requirement of these micronutrients to help maintain a healthy nutritional status (Lebaka *et al*., 2021). The order of the contents of some of these minerals in the fruit pulp is as follow: Cu > Zn > Mn > Fe > Na > Mg > K > Ca, and significantly lower in the peel, with the following order: Ca > K > Mg > Na > Fe > Mn > Zn > Cu (Yahia *et al*., 2011; Njiru *et al*., 2014; Gupta *et al*., 2022).

Among the most relevant biological functions of these minerals are the generation of the adequate ionic medium for the development of metabolic reactions, maintaining homeostasis and acid–base balance, osmotic pressure and permeability of plasma membranes (such as Na, K, Cl, Ca, Mg and P), participation in enzymatic activity as cofactors (Zn, Se, Cu), formation of the structural part of compounds such as haemoglobin, myoglobin, cytochromes (Fe), neuro-motor functions (Ca, Mg, Na and K), control of the gene expression in the synthesis of

Table 24.4. Mineral contents in different parts of mango fruit (Adapted from: Yahia *et al*., 2006; USDA, 2019; Gupta *et al*., 2022).

Mineral (mg per 100 g)	Pulp	Peel	Seed kernel
Calcium	7–16	150	450
Iron	0.09–0.41	40.6	11.9
Magnesium	8–19	100	100
Phosphorus	10–18	–	140
Potassium	120–211	75	365
Sodium	0–3	50	150
Zinc	0.06–0.15	1.74	1.1
Copper	0.04–0.32	10.4	–
Manganese	0.03–0.12	–	–
Selenium	0–0.6	–	–

their own transport, storage and function of proteins (Fe, Zn and Cu) and contribution to the rigidity and hardness of structural components such as bones and teeth (Ca and P) (Albarracin, 2015; Godswill *et al*., 2020).

Vitamins

Vitamins are classified as water-soluble and fat-soluble, which is useful for the understanding of the processes of absorption, transport, storage, metabolism and excretion. Water-soluble vitamins do not usually have tissue reservoirs, with the exception of vitamin B12 in the liver, so they have the disadvantage of requiring a daily intake. Among the water-soluble vitamins present in mango fruit, vitamins C and B complex have been reported in 'Tommy Atkins', 'Kent', 'Haden' and 'Keitt' mangoes (Table 24.5).

On the other hand, fat-soluble vitamins are stored in tissues and provide reserves, mainly in the liver and the adipose tissue, but can cause disorders due to hypervitaminosis. Vitamin A is the predominant fat-soluble vitamin in mango pulp, with lesser amounts of vitamins K and E (Table 24.5). Regular consumption of mango can provide the daily requirement of vitamin A and C in people of all age groups (WHO/FAO, 2003).

VITAMIN C. Vitamin C content varies among mango cultivars, ranging from 9.8 to 186 mg per 100 g in the edible portion of fruit (USDA, 2019; Gupta *et al*., 2022). This variability is a result of the variation in pre- and postharvest conditions of the fruit that affect vitamin C biosynthesis and metabolism. In addition, fruit ripening processes affect the content of this vitamin, with its concentration being higher in the partially ripe stage of the fruit with respect to its fully ripe stage, a stage in which it decreases rapidly when the fruit is stored at room temperature for 5–7 weeks (Yahia, 2011; Ibarra-Garza *et al*., 2015; Matheyambath *et al*., 2016; Hu *et al*., 2018). The decrease in vitamin C content may be due to biosynthesis of tartrate, ethylene, or oxalate, as the vitamin acts as a coenzyme for the biosynthesis of these metabolites (Singh *et al*., 2011).

Because of its function as an antioxidant and its role in immune functions, vitamin C has been touted as a means to prevent and/or treat numerous health conditions (cancer, cardiovascular disease, age-related macular degeneration, cataracts and the common cold) (National Institutes of Health, 2021). In human metabolism, vitamin C participates in oxidation–reduction reactions, and is part of the electron transport along with the coenzyme NADP, glutathione and cytochromes. It is essential for the maintenance of connective tissue, since it participates in the biosynthesis of hydroxyproline and hydroxylysine of collagen for the formation and repair of collagen and is also a necessary vitamin for the formation of mucopolysaccharides that constitute the interfibrillar component of connective tissue; hence, its deficiency affects the formation of granulation in healing processes (Doseděl *et al*., 2021). Due to its reducing capacity, it participates in the absorption, transport and utilization of iron, as well as in the activity of folic acid (Khadim and Al-Fartusie, 2021). In addition, having iron and copper as cofactors, vitamin C participates in the metabolic pathways that have as precursors the amino acids tryptophan and tyrosine whose products are the neurotransmitters serotonin and noradrenaline, respectively, and participates in the metabolism of corticosteroids and in histamine detoxification reactions (Doseděl *et al*., 2021; National Institutes of Health, 2021).

Table 24.5. Vitamin contents in 100 g of mango fruit pulp (adapted from USDA, 2019; Yahia *et al*., 2023).

Vitamin	Value per 100 g
Ascorbic acid (Vitamin C)	13.2–92.8 mg
Thiamine (Vitamin B1)	0.01–0.04 mg
Riboflavin (Vitamin B2)	0.02–0.07 mg
Niacin (Vitamin B3)	0.2–1.31 mg
Panthotenic acid (Vitamin B5)	0.16–0.24 mg
Pyridoxin (Vitamin B6)	0.05–0.16 mg
Folate, total (Vitamin B9)	20–69 µg
Vitamin A	54 µg
Vitamin K	4.2 µg
Vitamin E (α-tocopherol)	0.79–1.02 mg

VITAMIN A. Vitamin A is a group of compounds with biological activity of trans-retinol, including its esters and oxidation products retinal and retinoic acid. Some carotenoids and carotenals are pro-vitamin A, which are precursors of retinol in humans. The nutritional functions of vitamin A can be summarized in two types: the first, in what refers to vision; and the second, in cell differentiation processes involving normal growth, reproduction and immune responses (D'Ambrosio *et al*., 2011), with benefits in the prevention of certain types of cancer and cardiovascular diseases (Yap *et al*., 2021; Lozano-Casabianca *et al*., 2022; Minniti *et al*., 2023).

Vitamin A participates in the mechanism of the rod photoreceptors of the retina, which are sensitive to low-intensity light. The cycle that elapses from light excitation and breaks down the rhodopsin of the rods into II-trans-retinal and opsin protein, subsequently conducts the electrical impulse that excites the optic nerve and that the brain interprets as vision. Subsequently, the rhodopsin is regenerated, but part of the retinal is irreversibly oxidized; hence the need for retinol intake to prevent the loss of night vision (D'Ambrosio *et al*., 2011; Albarracín, 2015). Its role in cell differentiation is linked to the presence of receptors in the nuclei for retinoic acid, regulators of the transcription of genes involved in the synthesis of proteins and mucopolysaccharides, in the maintenance of the structure of cellular and subcellular membranes through antioxidation mechanisms, being essential for the integrity of the epithelia (Albarracín, 2015).

Mango fruit are a rich source of the pro-vitamin A carotenoids, especially α- and β-carotenes, providing 300–1800 µg of retinol equivalents (RE) (Matheyambath *et al*., 2016), suggesting that this fruit is a good source of vitamin A, especially in vitamin A deficient regions, as 12 µg of β-carotene is equivalent to one RE (Muoki *et al*., 2009). Intake of ca. 300 g of fresh ripe mango fruit three times a day can provide >50% of the daily RE requirement, depending on the cultivar and ripening stage of the fruit. The recommended daily intake (RDI) of vitamin A for children aged 4–6 years, children aged 7–9 years and adult women and men aged 19–65 years is 450, 500 and 500–600 µg RE/day, respectively (WHO/FAO, 2003).

VITAMIN B COMPLEX. The complex of B vitamins is a group of eight water-soluble vitamins that perform functions in the metabolism as coenzymes or precursors of coenzymes that cannot be synthesized by humans; they participate in catabolic processes for the production of energy and in the biosynthesis of nucleotide bases for RNA and DNA. This group consists of the vitamins thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6), biotin (B7), folate (B9) and vitamin B12 (Boumenna *et al.*, 2021; Khadim and Al-Fartusie, 2021). B vitamins can be found in animal foods such as meat and dairy, but can also be synthesized in chloroplasts, mitochondria and cytoplasm of cells of green leafy plants, legumes and fruits (Smith *et al.*, 2007; Kennedy, 2014; Hanna *et al.*, 2022), with the exception of vitamin B12, which is synthesized by bacteria (Kennedy, 2014).

Vitamins B1, B2, B3, B5, B6 and B9 have been identified in mango pulp, whose concentrations can vary with the ripening stage of the fruit from 1.5 to 2.5 mg/100 g of fresh fruit pulp (Dar *et al.*, 2016). The average nutrient content per 100 g of mango pulp for these vitamins is presented in Table 24.5 (USDA, 2019).

24.2.3 Phytochemical (bioactive) compounds

The phytochemical compounds are the plant secondary metabolites with diverse biological activities and functions, including plant protection. They can be found in vegetables, fruit, aromatic plants and spices, cereals, legumes and nuts, and thousands of them have been identified. Among the most relevant are phenolic acids and many polyphenols, xanthones, pigments, e.g., chlorophylls and carotenoids, phytosterols, saponins, etc. These bioactive compounds have different biological activities in humans, i.e., antioxidant, anti-inflammatory, antiproliferative, antidiabetic, antihypertensive, immunomodulatory (Zapata-Londoño *et al.*, 2022; Yahia *et al.*, 2018a, 2019a). This has led to major interest in their applications, in their natural form or their extracts for the development of functional foods and nutraceuticals. This chapter presents the most relevant phytochemical compounds of mango fruit from the quantitative point of view and impact on human nutrition and health.

Phenolic compounds

Phenolic compounds are secondary plant metabolites that provide colour and several other functions to plants, and are found in a wide variety of human foods and beverages. These molecules are generally involved in protecting plants from different types of stress such as ultraviolet radiation, invasion by microorganisms, and reactive oxygen species (ROS), and can replicate these properties for human health when obtained from the diet (Maldonado-Celis *et al.*, 2019). Phenolic compounds are classified into different classes, including phenolic acids and other polyphenols, and their contents varies among types of plants, types of plant organs, cultivars, ripening stage, geographical location, environmental conditions, etc. (Burton-Freeman *et al.*, 2017). Some of the major phenolic compounds present in mango fruit are described below.

PHENOLIC ACIDS. Mango fruit contain hydroxybenzoic acid derivatives: gallic, p-hydroxybenzoic, protocatechuic, vanillic and syringic acids, as well as hydroxycinnamic acid derivatives: chlorogenic, p-coumaric caffeic and ferulic acids (Palafox-Carlos *et al.*, 2012a). The most abundant phenolic acids in mango fruit are ferulic (33.75 mg), chlorogenic (0.96–6.20 mg), gallic (0.93–2.98 mg), vanillic (0.57–1.63 mg), protocatechuic (0.77 mg) and caffeic (0.25–0.10 mg) per 100 g fresh fruit weight (Abbasi *et al.*, 2015), which can be found in free form or conjugated with glucose, quinoic acid or both (Mattila and Kumpulainen, 2002; Burton-Freeman *et al.*, 2017).

POLYPHENOLS. Polyphenols can be divided into ten general classes based on their chemical structure (number of carbon atoms and/or aromatic rings, structural elements that bind these rings to one another, association with carbohydrates and organic acids), and >8000 different compounds have been described (Manach *et al.*, 2005). The most abundant polyphenols in plants are the flavonoids (compounds with 15 carbon atoms in a structure of C6-C3-C6), accounting for about 60% of the dietary polyphenols (Ramos, 2007). Early interest in polyphenols was related to the 'anti-nutritional' effects of tannins for the decreasing absorption and digestibility of food because of their ability to bind proteins and minerals (Yang *et al.*, 2001). However, major current interests include antioxidant, anti-inflammatory, anti-carcinogenic activities of many phenolic compounds including flavonoids and tannins (Yahia *et al.*, 2023).

Flavonoids are the largest class of phenolic compounds, in which >9000 naturally occurring flavonoids have been described (Abou-Baker, 2022). Flavonoids share a common structure consisting of two aromatic rings (A and B) that are bound by three carbon atoms forming an oxygenated heterocycle (ring C). They can be divided into six subclasses (Fig. 24.1) based on the type of heterocycle involved: flavonols, flavones, isoflavones, flavanones, anthocyanidins, and flavanols (catechins, epicatechins and procyanidins) (Manach *et al.*, 2004).

Mango pulp (100 g) contains, in increasing order, apigenin (10 µg), delphinidin (20 µg), pelargonidin (20 µg), luteolin (20 µg), kaempferol (50 µg), myricetin (60 µg), cyanidin (100 µg) and (+)-catechin (1.72 mg) (Haytowitz *et al.*, 2018). Isoflavones, dimers, trimers and 4- to 6-dimer polymers of proanthocyanidins are found in 'Haden', 'Kent', 'Keitt' and 'Tommy Atkins' mangoes. Quercetin in free form and glycosides such as glucose, galactose, rhamnose, xylose and arabinose are found in mango pulp, the most prevalent being quercetin 3-galactoside (22.1 mg/kg), followed by quercetin 3-glucoside (16.0 mg/kg), quercetin 3-arabinoside (5.0 mg/kg), and quercetin aglycone (3.5 mg/kg), and traces of phistene, myricetin, rhamnetin and kaempferol (Matheyambath *et al.*, 2016; Ediriweera *et al.*, 2017). In terms of quantity as well as contribution to the antioxidant capacity of the pulp (100 g fresh weight), the main flavonoids include catechin (1.72 ± 1.57 mg), epicatechin (0.15 ± 0.0 mg), hydrolysable tannins, gallotannins and traces of their derivatives (2 mg) (Berardini *et al.*, 2005; Masibo and He, 2008).

Anthocyanins are water-soluble flavonoids that, among other functions, contribute to the red, blue or purple colours of plants (Ranganath *et al.*, 2018). The total anthocyanin concentration in

fully ripe mango fruit varies between 3600 and 5650 µg/g DW compared to 2030–3260 µg/g in less ripened yellow and green mangoes. However, in red 'Tommy Atkins' mango, the concentration of anthocyanins is low (0.21–3.71 µg/g DW) (Berardini *et al.*, 2005). Cyanidin, pelargonidin, delphinidin, malvidin, petunidin and peonidin are the main anthocyanins found in the peels of various coloured mango varieties (Gupta *et al.*, 2022).

A diet rich in flavonoids generally correlates with a lower risk of myocardial infarction, cardiovascular disease (CVD) and coronary heart disease (CHD) mortality, in addition to effects on overall vascular function (e.g., blood pressure), hyperlipidaemia, and glucose homeostasis (Yahia *et al.*, 2023). Neuroinflammation has similar underlying mechanisms as CVD and is considered to contribute to neurodegenerative diseases (Ockerman *et al.*, 2021) and colorectal cancer (Shi *et al.*, 2021a, b).

Xanthones

Xanthones, mainly found in nature in the form of glycosides, are characterized by having a C6-C3-C6 (A-B-C) ring structure (Fig. 24.2A); the A and B rings have hydroxyl, methoxyl and isoprene groups attached (Negi *et al.*, 2013). One of the main xanthones present in mango fruit (peel and pulp), as well as in the leaves and stem bark of the plant, is mangiferin (C 2-β-D- glucopyranosyl-1, 3, 6, 7-tetrahydroxyxyanthione) (Fig. 24.2B) with diversity of biological effects including antiviral, antitumour, immunomodulatory, analgesic and antioxidant activity (Benard and Chi, 2015; Matheyambath *et al.*, 2016; Ediriweera *et al.*, 2017; Imran *et al.*, 2017; Zapata-Londoño *et al.*, 2020). Six mangiferin derivatives have been identified: mangiferin, dimethyl mangiferin, homomangiferin, mangiferin gallate, isomangiferin and isomangiferin gallate (Matheyambath *et al.*, 2016). The amount of mangiferin and its derivatives may be higher in the peel than in the pulp as reported for 'Pica' (22.15 and 9.68 mg/100 g FW, respectively) and 'Tommy Atkins' (4.24 and 3.25 mg/100 g FW, respectively) mangoes (Ramirez *et al.*, 2014). In 'Azúcar' mango juice, mangiferin content has been reported to be 11.50 mg/l; however, after 16, 32 and 48 days of storage at 4°C, mangiferin levels were 9.21, 8.64 and 8.54 mg/l, respectively (Zapata-Londoño *et al.*, 2019).

The antioxidant capacity of mangiferin is comparable to that of ascorbic acid (vitamin C), and it contributes to preventing

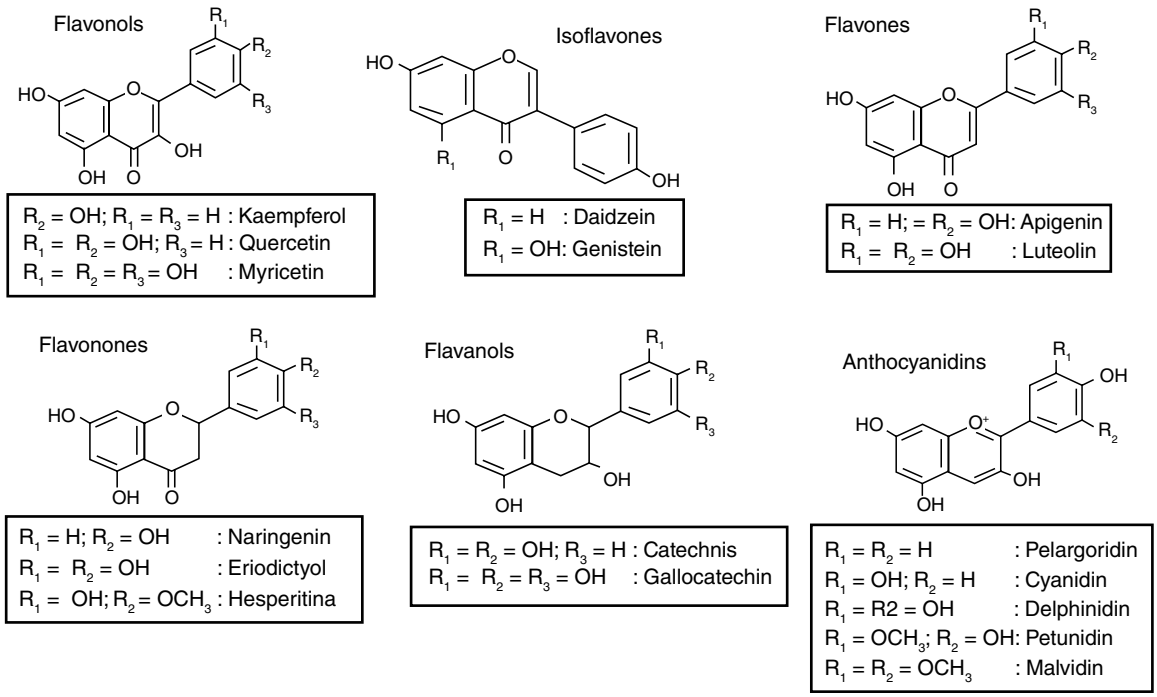

Fig. 24.1. Chemical structure of some classes of flavonoids. Author's own image

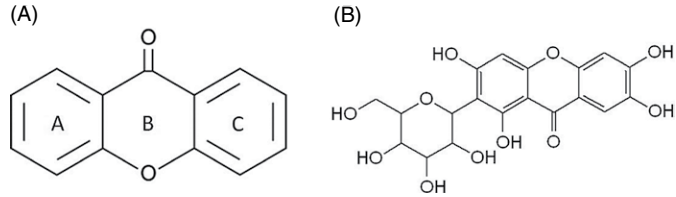

Fig. 24.2. Chemical structure of (A) xanthones and (B) mangiferin. (Author's own image)

the Fenton reaction and lipid peroxidation because its catechol motif forms a stable complex with Fe3+ (Benard and Chi, 2015). Mangiferin also has the ability to neutralize ROS such as peroxyl radical ($ROO^{\cdot}$), hydroxyl radical (OH^{-}), hydrogen peroxide (H_2O_2), and superoxide anion (O_2^{-}), and its activity is similar to ascorbic acid (Benard and Chi, 2015). It is also able to reduce oxidative stress induced in rat brains (Marquez *et al.*, 2012). Although mangiferin and its derivatives are present in very low amounts in mango fruit pulp, Zapata-Londoño *et al.* (2019, 2020) observed that healthy adults, after regular consumption of mango juice (without sweetener, preservatives) for 26 days, presented an increase in plasma mangiferin concentration between 7.05 ± 0.02 to 28.9 ± 0.87 mg/l, which was not detected before juice intake, as a result of the daily intake of juice. However, Hou *et al.* (2012) reported the maximum concentration in plasma of healthy adults after a single oral administration of mangiferin (0.9 g) was 38.64 ± 6.75 ng/ml. A wide range of plasma mangiferin concentration could be due to factors affecting bioavailability, such as CYP polymorphisms, gut microbiota, age and enzyme activity (D'Archivio *et al.*, 2010).

Pigments

Pigments in mango fruit are important as indicators of fruit maturation and ripening stages and fruit quality (Brecht and Yahia, 2009, 2017; Yahia, 2011; Chapter 23 in this volume). Although different mango cultivars have different skin colours during ripening, varying from green to yellow, orange and red, the colour of the pulp (mesocarp) of all mango cultivars is initially (at the immature stage) white and as the fruit matures and ripens the pulp becomes yellow to orange, due to the presence of carotenoids, depending on the ripening intensity (Yahia *et al.*, 2006; Brecht and Yahia, 2009; Yahia, 2011; Brecht and Yahia, 2017; Maldonado-Celis *et al.*, 2019). From a nutritional and health impact point of view, chlorophyll and carotenoid-type pigments, most commonly present in mango fruit, are known for their antioxidant properties and their ability to protect cells against damage caused by reactive oxygen species, which in turn contributes to reducing the risk of chronic non-communicable diseases associated with oxidative stress such as cardiovascular disease and cancer (Yahia and Ornelas-Paz, 2010; Yahia *et al.*, 2018a, 2019a, 2023).

Chlorophylls

Chlorophyll is a pigment that is widely distributed in plants and is found in chloroplasts (Fig. 24.3). It is attributed with preventive properties against certain types of cancer and diabetes (Manivasagan *et al.*, 2018; Pareek *et al.*, 2018); however, its nutritional value and benefit in human health have not been fully established (Yahia *et al.*, 2018a, 2019a, 2023).

Chlorophyll is the most important pigment that facilitates the process of photosynthesis (Pareek *et al.*, 2018; Yahia *et al.*, 2019c). It absorbs wavelengths in the red and blue-violet spectrum, converting light energy to chemical energy that is used to produce organic compounds and release oxygen (Yahia *et al.*, 2019c; Li *et al.*, 2024). Two types of chlorophyll that are commonly present in mango include one that provides a blue-green colour (chlorophyll a) and the other that confers a greenish-yellow colour (chlorophyll b) and they are commonly present in a 3:1 ratio (Lee and Schwartz, 2006; Pareek *et al.*, 2018; Yahia *et al.*, 2019c).

Chloroplasts are present in the peel and pulp of the developing mango fruit and contain chlorophyll, but this pigment decreases as the fruit ripens, promoting the increase in carotenoid content in the peel of some mango cultivars and in the pulp of all cultivars, due to the disintegration of the thylakoids in the chloroplasts. Therefore, colour changes from green to yellow or orange, depending on the cultivar and fruit maturity/ripening stage (Brecht and Yahia, 2009, 2017; Li *et al.*, 2024). Abiotic stress factors such as intense light, drought, high and low temperatures and ethylene lower chlorophyll content in the fruit by inducing changes in gene expression and activities of enzymes involved in chlorophyll biosynthesis and degradations (Pareek *et al.*, 2018; Yahia *et al.*, 2019c; Li *et al.*, 2024).

Carotenoids

These are fat-soluble pigments that confer yellow, orange and red colours, have an isoprenoid structure of 40 carbons (Fig. 24.4) and *trans* conjugated double bonds (Yahia and Ornelas-Paz,

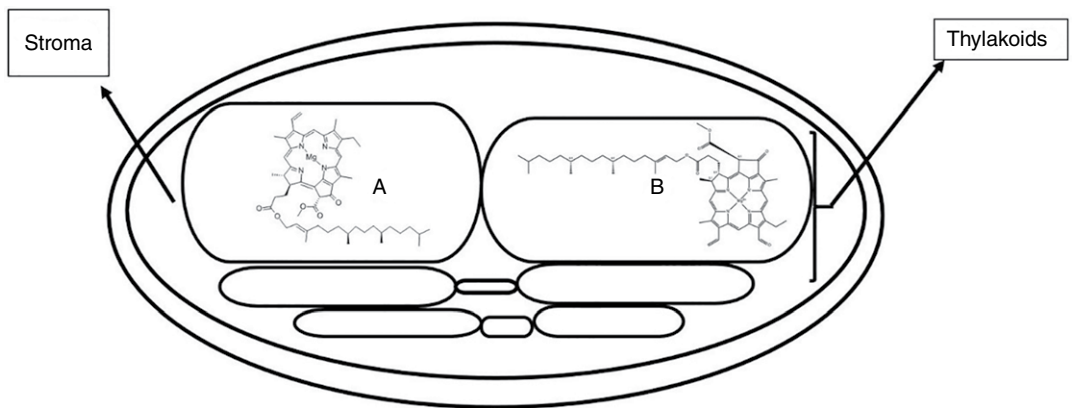

Fig. 24.3. Chemical structure of chlorophyll A and B inside the chloroplast. (Author's own image)

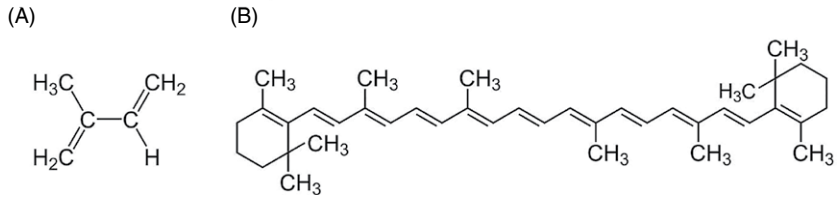

Fig. 24.4. Chemical structure of the isoprene unit (A) and β-carotene (B). (Author's own image)

2010; Yahia *et al*., 2018b). Some carotenoids are present in relatively large amounts in mango pulp (mesocarp) of all cultivars and in the peel of some cultivars (Yahia *et al*., 2006). β-Carotene accounts for up to 60% of the total carotenoid content in mango fruit, followed by violaxanthin (Masibo and He, 2008; Yahia, 2011). Carotenoids are classified in two groups: carotenes (such as α-carotene, β-carotene and lycopene) and xanthophylls (such as lutein, zeaxanthin, neoxanthin, violaxanthin and β-cryptoxanthin) (Milani *et al*., 2017; Yahia *et al*., 2018b). During the initial stages of mango fruit development, the pre-existing carotenoids (lutein, all-*trans* and *cis*- and neoxanthin, neochrome, luteoxanthin, zeaxanthin, anteraxanthin and auroxanthin) are masked by chlorophyll, but during maturation and ripening the chloroplasts are transformed into chromoplasts, starting with the synthesis of the carotenoid β-cryptoxanthin, while at later stages of maturation and ripening, α-, -β-, -ζ- and -γ-carotenes become abundant (Varakumar *et al*., 2011; Bramley, 2013; Ediriweera *et al*., 2017; Choo, 2019). Carotenoid concentration in mango fruit varies depending on cultivar, fruit developmental stage and ambient and other conditions during fruit growth and development, as well as preharvest and postharvest handling practices (Brecht and Yahia, 2009; Manthey and Perkins-Veazie, 2009; Yahia, 2011; Ranganath *et al*., 2018). Carotenoids possess antioxidant capacity, as they can trap free radicals through the donation of a hydrogen atom; this gives rise to a carotene radical, which at low oxygen concentrations can react with another peroxyl radical and give rise to non-radical carotene peroxides (Carranco Jáuregui *et al*., 2011; Yahia *et al*., 2018b).

24.3 Bioaccessibility and Bioavailability of Mango Bioactive Compounds

Bioaccessibility and bioavailability refer to the amount and rate at which ingested nutrients or phytochemical compounds are absorbed and utilized by the human body after ingestion. Bioaccessibility is the fraction of the nutrient that becomes available for absorption after the food has been digested and the nutrients have been released from its food structure. Bioavailability, on the other hand, is the amount of a nutrient that actually enters the blood circulation and becomes available for utilization (Cilla *et al*., 2018; Yahia *et al*., 2023). Therefore, bioaccessibility is the first step in achieving bioactivity of a specific compound or nutrient. The absorption efficiency of nutrients or phytochemicals depends on many factors, such as the molecular structure of the nutrient, the ripening state of the fruit, the presence of positive or negative absorption effectors (i.e., fats, fibre, proteins), interaction with other polyphenols of similar chemical structure, the concentration of the food, the amount introduced and the processing method (i.e., heat treatments, homogenization, freeze-drying, cooking method, storage method). All can also influence bioavailability, as well as intestinal factors such as enzyme activity, intestinal transit time and the microbiota (D'Archivio *et al*., 2010; Quirós-Sauceda *et al*., 2019; Yahia *et al*., 2023).

24.3.1 General digestion and absorption processes for phenolic compounds and carotenoids

The biological utilization of phenolic compounds and carotenoids from a food matrix requires digestion and subsequent absorption processes. Digestion comprises a set of mechanical processes such as chewing, peristaltic movements of the gastrointestinal tract, and chemical processes such as HCl secretion from the parietal cells of the stomach, pancreatic secretions, digestive enzyme activity of the mouth, pancreas, stomach and intestine, and of the microbiota that modifies the structures of these compounds with antioxidant properties and resulting metabolites conjugated with glucuronic acids or sulfates. All can influence the bioavailability and biological activity (Yahia *et al*., 2018a, 2023; Sensoy, 2021; Matsumura *et al*., 2023).

Subsequently, the modified phenolic compounds are absorbed into systemic circulation and distributed to different tissues of the body where they can exert their beneficial health effects or be further metabolized before excretion (Sensoy, 2021; Matsumura *et al*., 2023; Yahia *et al*., 2023). Intestinal absorption of phenolic compounds is influenced by various factors such as stereochemical structure, molecular weight, lipophilic or hydrophilic solubility, the presence of other dietary nutrients and the intestinal microbiota (Sensoy, 2021; Matsumura *et al*., 2023). Phenolic compounds are absorbed in the duodenum and jejunum (small intestine), comprising the formation and release of aglycones from the food matrix by the action of digestive enzymes such as the cytosolic β-glucosidase and the lactase-florizin hydrolase, which is found in the brush border of intestinal epithelial cells and has a broad specificity for flavonoids-O-β-glucosides. Subsequently, phenolic compounds can be taken up by passive diffusion or transporters such as P-glycoprotein and sodium-coupled glucose transporter type 1 (SGLT1) present in the membrane of enterocytes (Cosme *et al*., 2020).

With respect to carotenoids, the presence of food-derived fat in the aqueous medium of the stomach during digestion allows carotenoids to solubilize, forming lipid droplets that are reduced

in size in the duodenum due to the emulsifying effect of bile and favoured due to the action of pancreatic lipase that hydrolyses the tri-acylglycerides on the surface of the lipid droplets to form micelles that combine with bile salts, cholesterol and other products of lipid digestion in the gastrointestinal tract, thus incorporating the carotenoids into the micelles for absorption by enterocytes (Cervantes-Paz *et al*., 2016, 2017; Yahia *et al*., 2018a). The absorption of carotenoids can occur by passive diffusion, but it is a process that is saturated at high carotenoid concentrations; therefore, active transport is favoured by transporter proteins present in the membrane of intestinal brush border cells such as SR-BI, CD36 and NPC1L1. In the enterocyte cytoplasm, carotenoids are packaged into chylomicrons, a type of lipoprotein that forms in the intestinal cell and transports dietary triacylglycerides, cholesterol and amino acids; chylomicrons are dumped into the lymph and are transported by this route to the blood, so that they reach first the peripheral tissues and then the liver, after which the carotenoids can be exported from the liver to other tissues via LDL and VLDL lipoproteins (Yahia *et al*., 2018a, 2023).

24.3.2 Bioaccesibility and bioavailability of mango phenolic compounds

The release of phenolic compounds from mango fruit depends not only on their concentration but also on the ripening stage of the fruit, as reported in 'Ataulfo' mango (Quiros-Sauceda *et al*., 2019). In an *in vitro* gastrointestinal digestion model, the release of phenolic compounds is higher in the intestinal compartment (40–45%) with respect to the gastric (26–40%) (Quiros-Sauceda *et al*., 2019), and similar results have been observed in phenolic compounds from commercial mango juices and pulps of 'Hainan' and 'Shuixian' mangoes (Chen *et al*., 2014). The increase of phenolic compounds at the intestinal level is attributed to the effect of Na_2CO_3 on soluble pectins (Epriliati and Ginjom, 2012) and also to the hydrolysis of anthocyanins into phenolic compounds during digestion (Yahia *et al*., 2023).

After subjecting 'Osteen' mango pulp to *in vitro* oral digestion, Ordoñez-Díaz *et al*. (2020) found that the total polyphenol content increased significantly from 3.47 to 8.2 mmol/g DW, and the most affected compounds were those derived from phenolic acids and galloyl. Phenolic acids also increased significantly from 2169 to 7026 µmol/g DW, such as in the case of gallic acid (46–109 µmol/g DW), 4-O-methylgalic acid (69–132 µmol/g DW), the two hexoside isomers of hydroxybenzoic acid (1370–6078 µmol/g DW), methyl gallate (1–28 µmol/g DW), and the two ester isomers of methyl gallate (from 17.6 to 32.4 µmol/g DW); galloyl derivatives decreased from 1010 to 923 µmol/g DW, while flavan-3-ols, flavanones, hydroxycinnamic acids and xanthones were stable during the oral digestion (Ordoñez-Díaz *et al*., 2020).

In the gastric environment, pH favours the release of phenolic compounds from polyphenols such as gallotannins that hydrolyse to molecules ranging from 4-O-galloylglucose to 8-O-galloylglucose due to hydrolysis of m-depside and galloyl-glucosaglucose bonds due to the low pH and pepsin activity on polysaccharides covalently bound to the cell wall (Bohn, 2014; Barnes *et al*., 2016).

At the intestinal level, the pH and the action of the enzyme pancreatin and bile salts can favour the breakdown of the bonds between polyphenols and supramolecular structures of the food matrix (Ordoñez-Díaz *et al*., 2020). In the case of mango pulp, the most bioaccessible compounds are gallic acid, 3-O-methylgallic acid, the two hexosides of hydroxybenzoic acid, methyl gallate, 3,4-dihydroxybenzoic acid and benzoic acid,3-O-methylgallic acid, the two hexosides of hydroxybenzoic acid, methyl gallate, 3,4-dihydroxybenzoic acid and benzoic acid, which potentially cross the small intestine and reach the colon to be fermented by the resident microbiota (Ordoñez-Díaz *et al*., 2020).

A small amount of phenolic compounds (10–11.5%) released from mango pulp are bioaccessible, and can be absorbed by passive diffusion or active mechanisms in the stomach and intestine (Crozier *et al*., 2010; Cosme *et al*., 2020). Liu *et al*. (2016) reported that some phenolic compounds form micelles during digestion with bioaccessibility values of up to 1.5-fold compared with carotenoids. Ferulic, gallic, gentisic and protocatechuic acids have been detected in plasma after 2–4 post-ingestions of mango pulp and juice, reaching a maximum concentration of 7.9–8.7, 49.7–109.11, 8–12.2 and 30.8–34.5 ng/ml, respectively (Quiros-Sauceda *et al*., 2019). Chlorogenic, ferulic, gallic, sinapic, vanillic and p-coumaric acids and pyrogallol have been found in urinary excretion 8–24 h after mango consumption, as well as 4-O-methyl-galic acid, 4-O-methylgallic acid-3-O-sulfate, and pyrogallol derivatives such as pyrogallol-1-O-glucuronide, O-methylpyrogallol-O-sulfate, pyrogallol-O-sulfate deoxypyrogallol-O-sulfate, and O-methylpyrogallol-O-sulfate, 6 h after mango intake, of which the compounds 4-O-methylgallic acid and 4-O-methylgallic acid-3-O-sulfate 3-O-sulfate could be absorbed in the small intestine, while priogalol metabolites, which are absent in mango pulp can be produced from gallic acid by the action of carboxylase enzymes of the colon microbiota, where gallic acid can be absorbed and conjugated by liver and kidney enzymes (Barnes *et al*., 2016; Quiros-Sauceda *et al*., 2019). These compounds are the result of glucuronidation, methylation and sulfation reactions catalysed by phase I and II enzymes at the level of the small intestine and liver, some of which can be excreted in the intestine or reabsorbed with bile by enterohepatic circulation; however, the most important excretion pathway is renal (Burton-Freeman *et al*., 2017; Kim *et al*., 2021).

In the colon, microbiota transform dietary fibre and phenolic compounds from mango (mango pulp, juice or fruit bars) that are not absorbed in the small intestine into hydroxyphenolic acids, acetic acid, propionic and butyric acids (short-chain fatty acids, SCFA) through the action of tannase and gallic acid decarboxylase enzymes produced by intestinal microbiota, such as *Lactococcus plantarum*, *L. lactis* and *Clostridium butyrium* (Hernández-Maldonado *et al*., 2019; Ordoñez-Díaz *et al*., 2020).

Studies in lean and obese humans supplemented for 6 weeks with 400 g/day of 'Ataulfo' mango pulp showed increase of gallotannin metabolites in urine, increased levels of SCFA in faeces in lean participants, while in obese volunteers the population of *L. lactis* increased with decreased *Clostridium leptum*

and *Bacteroides thetaiotaomicron*, indicating the ability of mango pulp to positively modulate the intestinal microbiota to prevent dysbiosis and thus intestinal inflation that increases the risk of colorectal cancer (Kim *et al*., 2020).

24.3.3 Bioaccesibility and bioavailability of mango carotenoids

The absorption process of mango carotenoids begins with their release from the food matrix due to tissue disruption by oral and gastrointestinal digestion, the release of which is easier compared with tomato or carrot carotenoids that are present in crystalline form (Yahia *et al*., 2023). Oral bioavailability of each individual carotenoid may vary due to genetic polymorphisms in intestinal transport proteins, but also due to dietary patterns, dietary matrix composition or any gastrointestinal digestion process affecting the release of carotenoids from their matrix (Böhm *et al*., 2021).

Depending on the intensity of mango pulp chewing, the release of β-carotene and xanthophylls such as violaxanthin can be increased during the gastric and intestinal digestion. It has been reported that after chewing and gastric digestion of 'Kensington Pride' mango pulp, the release of 8–10% β-carotene and 5–18% xanthophyll can be achieved; at the intestinal level it can be 20–32% β-carotene and 35–55% xanthophyll (Low *et al*., 2015). In general, it has been observed from *in vitro* gastrointestinal digestion models of mango pulp or paste that xanthophylls are more readily released than carotenes.

During digestion, the micellarization of mango carotenoids depends on the concentration of β-carotene, fruit ripening stage and fruit fibre content, because the pectin present in the fibre reduces lipid emulsification and micelle formation by 10–14% with unripe mango, but increases with ripening by 3–28% due to fruit softening (Ornelas-Paz *et al*., 2008a, b; Yahia and Ornelas-Paz, 2010; Cervantes-Paz *et al*., 2016, 2017). The presence of fat and protein is necessary for carotenoid micellarization and absorption; therefore, the addition of milk can significantly increase the micellarization of β-carotene from mango pulp (Veda *et al*., 2007; Ornelas-Paz *et al*., 2008a; Yahia and Ornelas-Paz, 2010); however, not all types of fat favour this process. Emulsification of digested mango pulp with medium- or long-chain triacylglycerols increases the efficiency of micelle formation by 30–85% because the particle size is reduced at each stage of digestion (oral: 10 to 1 μm; gastric: to 0.2 μm; intestinal: to 0.13 μm), facilitating the action of lipases at each phase by 80–100% (Liu *et al*., 2016).

Mango by-products, such as peel and seeds, can represent up to 60% of the fruit and contain carotenoids, among other bioactive components (Jahurul *et al*., 2015). Total carotenoid content in mango peels ranges from 1.75 to 5.69 mg per 100 g dry weight (Lenucci *et al*., 2022). Although mango peel represents an important source of carotenoids, it limits the bioaccessibility of carotenoids due to the presence of dietary fibre, retaining these compounds in its structure, which has led to the use of methods to obtain carotenoid-enriched extracts to result in better bioaccessibility, but require proper storage to avoid considerable degradation, as they are sensitive to heat, light and oxygen (Chuyen *et al*., 2019). Therefore, microencapsulation strategies of carotenoids with a wall material such as maltodextrin, starch, inulin, alginate, gum Arabic and whey protein concentrate have been considered. This increases storage stability and improves bioaccessibility through controlled release during digestion (Eun *et al*., 2020).

Cabezas-Terán *et al*. (2023) evaluated the effect of two types of microencapsulation on the bioaccessibility of mango carotenoids, inulin and fructo-oligosaccharides, while β-carotene remained relatively stable during *in vitro* digestion because total recoveries were greater than 68%; inulin improved the bioaccessibility of β-carotene almost twofold compared with microparticles without prebiotics. In addition, the bioaccessibility of β-carotene increased proportionally with bile salt concentrations during digestion; however, when the bile salt concentration is >10 mM, it does not improve the bioaccessibility of β-carotene present in microparticles with prebiotics. These findings indicate that the use of microencapsulation could be a strategy that contributes to the development of functional foods with provitamin A activity.

24.4 Effects and Mechanisms of Mango Fruit Bioactive Compounds on Human Nutrition and Health

The bioactive compounds present in mango fruit have been shown to have several beneficial effects on human nutrition and health, acting through different mechanisms. The potent antioxidant activity of many of these bioactive compounds protects cells from damage caused by reactive oxygen species, which can prevent chronic non-transmissible diseases associated with oxidative stress (Yahia *et al*., 2023). In addition, mango fruit contain bioactive compounds with anti-inflammatory capacity, which helps regulate and modulate the expression and action of pro-inflammatory molecules. Another significant benefit is the antiproliferative action, which can inhibit the growth of cancer cells. Regarding their role in the regulation of human metabolism, mango fruit contain bioactive compounds that show antidiabetic effects by improving insulin sensitivity and regulating blood glucose levels. They also contribute to the reduction of blood pressure, offering antihypertensive effects beneficial to cardiovascular health. Mango consumption also supports digestive health, promoting efficient digestion and a balanced intestinal microbiome.

24.4.1 Antioxidant activity

Antioxidants reduce or inhibit the effects produced by reactive species and oxidizing agents. Several compounds present in mango fruit pulp and peel have antioxidant activity, including several carotenoids and phenolic compounds that benefit human health.

Many carotenoids possess direct antioxidant capacity because they can neutralize reactive species by donating a hydrogen atom; such a donation gives rise to a carotenoid radical, which at low oxygen concentrations can react with another

peroxyl radical and give rise to non-radical carotenoid peroxides such as 5,8-carotene endoperoxides (Chen *et al.*, 2011). The β-carotene is one of the most abundant carotenoids in mango, and can neutralize peroxyl radical (ROO·), hydroxyl radical (·OH), superoxide anion (O_2^-) and singlet oxygen ($^1O_2$) (Choe and Min, 2009).

Several carotenoids also activate indirect antioxidant mechanisms after forming a complex with Transcription Factor Nrf2 that binds to its Response Element (ARE) and induces the expression of genes for the enzymes glutathione S-transferase (GST), catalase, NAD(P)H:quinone oxidoreductase (NQO1) and thioredoxin (Tanaka *et al.*, 2012) as observed in male Wistar rats fed a 10% supplemented diet for 12 weeks that increased hepatic GST and catalase expression, reducing the cytotoxic effects induced by dimethylhydrazine in the group not supplemented with mango (Anilakumar *et al.*, 2003).

In vitro studies in FEK4 skin fibroblasts exposed to UV-A light show that the presence of β-carotene suppresses the expression of the gene for the enzyme haem oxygenase-1 (HO-1), a marker of oxidative stress in cells, and this effect occurrs at concentrations that have been observed in human plasma after dietary supplementation with β-carotene (Trekli *et al.*, 2003).

High concentrations of β-carotene (>10 μM) can induce oxidative stress and the formation of oxidative degradation products called β-apocarotenes, as well as NF-kB activation and increased expression of c-myc protein that in the context of leukaemic and colon adenocarcinoma cells inhibit their growth and induce apoptosis, a result reversible by N-acetylcysteine and α-tocopherol (Paolini *et al.*, 2001; Palozza *et al.*, 2003). High-dose β-carotene supplementation is not indicated for lung cancer chemoprevention in smokers, because β-apocarotene in plasma from this population induces increased c-Jun and c-Fos gene expression by three- to fourfold and increases lung squamous cell proliferation and metaplasia (Kordiak *et al.*, 2022). The transcription factors cc-Jun and c-Fos bind to the response element inducing the expression of genes involved in cell proliferation such as cyclin-D (Palozza *et al.*, 2010).

The most common phenolic compounds in mango fruit are chlorogenic acid, caffeic acid, gallic acid, ellagic acid, epicatechin gallate, epigallocatechin gallate, kaempferol and its conjugates, quercetin and its derivatives, rutin, mangiferin and procyanidins (Palafox-Carlos *et al.*, 2012a; Abbasi *et al.*, 2015; Maldonado-Celis *et al.*, 2019). Chlorogenic acid acts as a metal chelator, reduces lipid peroxidation and inhibits NAD(P)H oxidase enzyme activity (Clifford, 1999; Tajik *et al.*, 2017). The antioxidant effect was evaluated in diabetic rats with nephropathy that were supplemented with chlorogenic acid, and after 8 weeks of treatment it decreased lipid hydroxyperoxide, increased the reduced glutathione and decreased kidney damage through activation of Nrf2/HO-1, which interacts with inhibition of NF-κB (Bao *et al.*, 2018). Caffeic acid contributes to the reduction of oxidative stress, and in mouse hippocampus it decreased the levels of a biomarker of oxidative stress in hippocampus and microglia, 4-hydroxynonenal, in a dose-dependent manner at 30 mg/kg for 30 days (Koga *et al.*, 2019). Gallic acid also inhibits lipid peroxidation and neutralizes ROS as well as other oxidants such as H_2O_2 and HClO attributed to hydroxyl groups in the ortho position (Badhani *et al.*, 2015). Ellagic acid inhibits lipid peroxidation and SOD, catalase and glutathione peroxidase (GPx) activity in Chinese hamster lung fibroblasts (V79-4) after 48 h of treatment at 4, 20 and 100 μg/ml (Han *et al.*, 2006). The flavonoids catechin and epicatechin inhibit the Fenton reaction between Fe2+ and H_2O_2 (Masibo and He, 2008), and quercetin can scavenge O_2- and nitric oxide (NO-) due to the catechol motif in its B-ring and the hydroxyl group at position 3 of the C-ring (Boots *et al.*, 2008).

Mangiferin shares the antioxidant properties of the compounds above and its antioxidant capacity determined by DPPH, ABTS and ORAC antioxidant assays is comparable to that of vitamin C (Tang *et al.*, 2004; Malherbe *et al.*, 2014; Benard and Chi, 2015). *In vivo* studies with Wistar rats showed the preventive capacity of mangiferin (40 mg/kg body weight) on iron overload-induced lesions after 7 days. The treatment prevented serum iron overload, decreased lipid peroxidation in liver and serum, increased reduced glutathione levels and glutathione peroxidase (GPx) and SOD activity (Pardo-Andreu *et al.*, 2008). In adults (>65 years) supplemented with mangiferin (300 mg) for 60 days, SOD activity increased, lipid peroxidation and serum glutathione oxidase decreased (Pardo-Andreu *et al.*, 2006). In contrast, consumption of 200 ml of mango juice (cv. 'Azúcar') for 26 days by healthy adults with dietary habits that increase the risk of colorectal cancer did not significantly affect plasma antioxidant capacity and biomarkers of oxidative stress in plasma (lipid peroxidation, total glutathione and 8-hydroxy-guanosine (8-OHdG)). The differences between these last two studies can be attributed to the low consumption of fruit and vegetables in the participants of the study (Zapata-Londoño *et al.*, 2020), which is associated with higher levels of lipid peroxidation and oxidative DNA damage (Suwimol *et al.*, 2012), suggesting the protective importance against oxidative stress of these foods as a source of phenolic compounds. Robles-Sánchez *et al.* (2011) reported that consumption of 200 g of peeled and sliced 'Ataulfo' mango for 30 days by healthy individuals (20–50 years) significantly reduced serum triglyceride and VLDL levels, and increased plasma antioxidant capacity measured by ORAC and TEAC antioxidant assays.

24.4.2 Anti-inflammatory activity

Inflammation is an innate immune response that induces ROS and activates the transcription factor NF-kB by increasing the expression of pro-inflammatory cytokines, i.e., TNFα and interleukins (ILs) and Il-1β that affect the activation of the mitogen-dependent kinase (MAPK) pathway, including extracellular signal-regulated kinases (ERK1/2), JNK (1, 2 and 3) and p38; in addition that NF-kB induces the synthesis of adhesion molecules that facilitate phagocyte infiltration (Kang and Kim, 2023).

One of the critical roles of bioactive compounds in the immune response is to maintain a balance between proinflammatory and anti-inflammatory signals to avoid overreaction leading to tissue damage and disease (Kominsky *et al.*, 2010). *In vitro* studies have shown the ability of β-carotene to significantly reduce ROS production and inactivate NF-kB in *Helicobacter pylori*-infected AGS cells by inactivating p-38 and

ERK pathways (Jang *et al*., 2009), decreasing the expression of the inducible enzymes nitric oxide synthetase (iNOS) and cyclooxygenase-2 (COX-2), and the synthesis of protaglandin-E2 (PGE2), which has immunosuppressive and mitogenic effect during carcinogenesis (Palozza *et al*., 2003; Wang and Dubois, 2006; Jang *et al*., 2009). BALB/c mice injected with azoxymethane (AOM) to induce colorectal carcinogenesis, and receiving mango ('Sugar') juice for 8 weeks, had reduced serum PGE2 levels compared with the control group, a result correlated with the decrease of aberrant crypt foci (ACF) in the colon mucosa, indicating that regular consumption of mango may contribute to the control of colorectal carcinogenesis (Corrales-Bernal *et al*., 2016).

Proinflammatory cytokines are considered tumour-promoting factors because they increase the production of ROS and the expression of chemokines, small proteins that guide the migration of immune cells to sites of infection, inflammation, or tissue damage, as well as during development and tissue homeostasis (chemotaxis). Therefore, the administration of carotenoid-containing foods to reduce biomarkers of inflammation has been of interest. IL-1β levels in BALB/c mice injected with AOM decreased significantly after consumption of 0.3% w/v mango juice for 8 weeks with respect to the control group, while IL-6 levels did not change in both groups, and TNFα was not detected (Corrales-Bernal *et al*., 2016). However, supplementation with 0.5% β-carotene in Wistar rats injected with AOM for 33 weeks did not significantly reduce COX-2 expression and PGE2 levels (Choi *et al*., 2006). Vaisman *et al*. (2006a) showed that in patients with parenteral nutrition enriched with low doses of carotenoids (3 mg/15,500 kcal) for 3 months as the only food, normalized serum carotenoid levels decreased the active form of NF-kB as an indicator of oxidative stress, but no significant changes in serum lipid peroxides were observed with respect to the control group.

Watzl *et al*. (2005) demonstrated that intake of two to eight servings/day of carotenoid-rich fruits and vegetables for 4 weeks did not affect the immune response biomarkers, but did affect the inflammatory processes as indicated by a significant reduction in plasma C-reactive protein. Therefore, the hypothesis that a single bioactive dietary component such as β-carotene reduces the risk of developing chronic disease is questionable, and despite the promising results in *in vitro* and *in vivo* studies of individual bioactive compounds, it is clear that these compounds alone do not explain the health benefit conferred by regular consumption of fruit, vegetables and whole grains (Liu, 2013).

It was demonstrated in human colon myofibroblast CCD-18Co cells exposed to lipopolysaccharide (LPS) that 10 mg GAE/l of the phenolic compounds gallic acid and gallotannins from 'Keitt' mango pulp extract significantly reduced the expression of the proinflammatory cytokines TNF-α, IL-1β and iNOS and of the proteins PI3K, AKT and mTOR, while miR-126 increased following treatment with the extract (Kim *et al*., 2016). These results indicate that mango polyphenols attenuated the inflammatory response by decreasing the expression of NF-kB, PI3K, HIF-1α, RPS6 proteins through modulation of the PI3K/AKT/mTOR pathway (Kim *et al*., 2016). Therefore, mango polyphenols may prevent agents in ulcerative colitis.

Kim *et al*. (2020) demonstrated that adjunctive therapy in patients with inflammatory bowel disease (IBD) who received 200–400 g of 'Keitt' mango pulp for 8 weeks significantly improved the Simple Colitis Clinical Activity Index (SCCAI) with reduction of IL-8, growth-regulated oncogene (GRO) and granulocyte-macrophage colony-stimulating factor (GM-CSF), which are involved in neutrophil-induced inflammation. In addition, daily intake of mango pulp significantly increased the microbiota of *Lactobacillus* spp., *Lactobacillus plantarum*, *Lactobacillus reuteri* and *Lactobacillus lactis*, and butyric acid production in faeces. These results demonstrate that regular consumption of mango or other gallotannin-rich foods in combination with conventional drugs for the treatment of IBD may be an alternative adjuvant therapy that reduces biomarkers of inflammation and modulates the intestinal microbiota (Kim *et al*., 2020).

Reduction of proinflammatory biomarkers was also observed in an *in vitro* model of MCF-12 and MDA-MB231 breast cancer cells treated with TNF-α and a polyphenol-rich 'Keitt' pulp extract (cv. 'Keitt') (Arbizu-Berrocal *et al*., 2019), suggesting the potential use of mango pulp in the prevention and/or treatment against breast cancer without affecting non-cancerous cells.

Inflammation is an event that is also associated with obesity. Gomes Natal *et al*. (2016, 2017) determined the effect of 'Ubá' mango juice (35 ml/day) prepared from the pulp with and without peel and administered to obese Wistar rats for 7 days. Both types of juice reduced total body weight, visceral fat, adiposity index and the expression of the transcription factor PPAR-γ that activates the transcription of adipogenic genes such as the enzyme fatty acid synthase (FAS) and TNF-α (Gomes Natal *et al*., 2016), as well as serum resistin levels and hepatic steatosis (Gomes Natal *et al*., 2017).

24.4.3 Antiproliferative action

Carcinogenesis is a multistage process including tumour initiation, promotion and progression. Initiation is a rapid process involving initial uptake or exposure to a carcinogenic agent that is genotoxic. Tumour promotion involves epigenetic mechanisms; it is a relatively long and reversible process leading to the accumulation of premalignant cells that divide abnormally; and progression is where invasion and metastasis occur, which is generally irreversible (Manson, 2003).

Phytochemicals present in a diet rich in fruit and vegetables can block the initiation phase of carcinogenesis or suppress the proliferative capacity of preneoplastic lesions in the phases of tumour promotion and progression (Surh, 2003). Phenolic compounds have been described as blocking agents because they protect DNA from the genotoxic effects of reactive nitrogen species and ROS (Bub *et al*., 2003). Flavonoids also act as blocking agents by altering the metabolism of procarcinogens through induction of cytochrome P450 and Phase II enzymes that facilitate their elimination or their intermediates (Zhang *et al*., 2023). Polyphenols can induce cancer cell suppressor or elimination mechanisms, modulation of signal transduction pathways, and transcriptional regulation, inhibition

of COX-2 enzyme, suppression of oncogenes, induction of apoptosis, cell cycle blockade (Surh, 2003), and inhibition of arachidonic acid biosynthesis which produces proinflammatory and/or mitogenic metabolites such as PGE2 and ROS (Corrales-Bernal *et al.*, 2016).

In vitro and murine studies have demonstrated the chemopreventive capacity of mango against certain types of cancer. HL-60 acute promyelocytic leukaemia cells exposed to mango juice and mango juice fractions arrested the cell cycle in G0/G1 phase, and dose-dependent neoplastic transformation of BALB/3T3 cells was inhibited (Percival *et al.*, 2006). Similar proliferation inhibition results were obtained with ethanolic extracts of mango peel (125–1000 µg/ml) in human gastric cancer AGS, human cervical cancer HeLa and human hepatocarcinoma HepG2 cells in a dose-dependent manner (Kim *et al.*, 2010).

The antiproliferative capacity of mangiferin has been evaluated in different *in vitro* cancer models. In prostate cancer PC3 cells, mangiferin decreased their viability in a dose (10, 20 and 40 µM) and time (0, 24, 24, 48 and 72 h) dependent manner by inducing apoptosis, caspase-3 and decreased Bcl-2 expression (Li *et al.*, 2016). These effects have been observed in CNE2 nasopharyngeal carcinoma cells exposed to different concentrations of mangiferin (12.5, 25, 50, 50, 100, 150 and 200 µM) for 72 h via G2/M cell cycle blockade, and decreased the Bcl-2/Bax protein ratio (Pan *et al.*, 2014). In rhabdomyosarcoma (RD) cells, the cytotoxic effect of mangiferin (IC50 = 70 µM) resulted in loss of lactate dehydrogenase and nitric oxide, and increased intracellular calcium concentration, ROS with decreased mitochondrial membrane potential in these cells (Pan *et al.*, 2014).

Preclinical studies in a murine model to study the chemopreventive capacity of mango or its components such as the ovarian adenocarcinoma xenograft model – cell line (OVCAR3), in female BALB/c mice treated with mangiferin (10, 50 and 100 mg/kg body weight) for 14 days, showed a significant decrease in tumour volume (Zou *et al.*, 2017). When mice received a combined treatment of mangiferin (50 mg/kg body weight) plus cisplatin (10 mg/kg body weight) for 14 days, it increased the sensitivity of OVCAR3 cells involving apoptosis as a mechanism of action (Zou *et al.*, 2017).

Noratto *et al.* (2010) demonstrated that a pulp extract enriched with polyphenolic compounds from 'Ataulfo' mango inhibited the growth of colon adenocarcinoma cells SW480 5 mg GAE/l for 48 h of treatment without affecting colon myofibroblast cells (CCD-18Co) (non-malignant) under the same conditions. The antiproliferative effect of the extract involved activation of caspase-8 and increased expression of pro-apoptotic genes Bax and Bim with respect to untreated cells. When the concentration of the extract was 10 mg GAE/l, the SW480 cell cycle was arrested in the G2/M phase after 24 h of treatment and was associated with increased PKKMYT1 expression (Noratto *et al.*, 2010). The encoded protein is a membrane-associated kinase that negatively regulates the G2/M transition of the cell cycle by phosphorylating and inactivating cyclin-dependent kinase 1. Corrales-Bernal *et al.* (2014) evaluated the antiproliferative capacity of a complete aqueous extract of 'Sugar' mango pulp in SW480 cells, as well as its primary chemopreventive effect in the preclinical model of AOM-induced colorectal carcinogenesis in female BALB/c mice. Mango aqueous extract (200 µg/ml) inhibited SW480 growth up to 22.3% after 72 h of treatment (Corrales-Bernal *et al.*, 2014). In the preclinical model, mice that received 0.3% w/v aqueous mango extract for 10 weeks reduced 60% of FCA with respect to the control group that received water (Corrales-Bernal *et al.*, 2014). Boateng *et al.* (2007) also demonstrated the antiproliferative effect (83%) of mango juice (20%) administered for 9 weeks in Fisher 344 rats injected with AOM. These results indicate that mango contains bioactive compounds that are capable of controlling colorectal carcinogenesis.

The antiproliferative effect of 'Yulima' mango pulp aqueous extract on SW480 cells and their metastatic SW620 derivatives treated with 43 and 29 mg/ml, respectively, for 48 h, induced increased intracellular ROS production, cell cycle arrest in G2/M phase and apoptosis without Blc-2/Bax mitochondrial depolarization (Lozano-Casabianca *et al.*, 2022, 2023). The intracellular pro-oxidant condition of the extract can cause DNA damage leading to cell cycle arrest and apoptosis in SW480 and SW620 cells (Shi *et al.*, 2021b). Aqueous mango extracts have a differential effect on both cell lines. It increased the expression of TRAIL-DR4, Fas and TNF-R1 cell death receptors that activate extrinsic apoptosis, along with caspase-3 activation and DNA fragmentation in SW480 cells, while in SW620 cells, the aqueous mango extract induced cell death rather than apoptosis (Lozano-Casabianca *et al.*, 2023). Although both cell lines were isolated from the same individual, they differed in their response to apoptosis induction; SW480 is susceptible to cell death by the anti-Fas monoclonal antibody CH11 and TRAIL whereas SW620 cells are resistant (Hewitt *et al.*, 2000; Maldonado-Celis *et al.*, 2009). In addition, the extract reduced the presence of autophagic SW480 and SW620 cells in culture; an important result because autophagy cell death protects malignant cells against oxidative and metabolic stress conditions (Galati *et al.*, 2019). Considering that SW480 and SW620 are models to study colorectal cancer progression *in vitro* (Hewitt *et al.*, 2000), the ability of mango aqueous extracts to modulate cell invasion processes or the expression of key metalloproteins (MMPs) in tumour invasion in colorectal cancer, MMP-7 and MMP-9, was evaluated (Siddhartha and Garg, 2021). The extract did not affect the expression of MMPs or cell invasion processes in SW480 and SW620 (Lozano-Casabianca *et al.*, 2023).

24.4.4 Antidiabetic effects

Diabetes is the seventh leading cause of death worldwide, affecting 463 million globally in 2019, with type 2 diabetes mellitus (T2DM) being the most common form, characterized by insulin resistance and insufficient insulin production (Saeedi *et al.*, 2019). Hyperglycaemia contributes to the development of microvascular and macrovascular complications that influence diabetes-associated morbidity and mortality (Chawla *et al.*, 2016). Strategies for the control and treatment of the disease include lifestyle changes (healthy eating, physical activity) and treatment of T2DM with oral medications such as meglitinides, thiazolidinediones, sulfonylureas, biguanides, α-glucosidase

inhibitors and dipeptidyl peptidase 4 inhibitors (Chaudhhury *et al.*, 2017), which despite their hypoglycaemic effect cause side effects on the quality of life of patients. Therefore, interest has been directed to bioactive compounds of plant origin or their source foods as adjunctive therapy for the control and prevention of diabetes (Beidokhti and Jager, 2017).

Animal models of high-fat diet (HFD)-induced obesity (Lucas *et al.*, 2011; Ojo *et al.*, 2016; Ramirez *et al.*, 2017; Sabater *et al.*, 2017), Streptozotocin (STZ)-induced diabetes (Gondi *et al.*, 2015, 2017; Rodriguez-Gonzales *et al.*, 2017), or both (Irondi *et al.*, 2016) have been used to study the antidiabetic capacity of mango. These preclinical models emulate the characteristics of human T2DM, and glycaemia reduction between 15% to 68% has been observed (Zarasvand *et al.*, 2023).

HFD-fed animals were supplemented for 8 or 10 weeks with freeze-dried mango pulp (1–10% w/w or 54 mg/kg body weight/day, respectively) (Lucas *et al.*, 2011; Ojo *et al.*, 2016; Ramirez *et al.*, 2017; Sábater *et al.*, 2017). In the STZ-induced diabetes model, animals received mango juice (0.5 g/kg body weight) prepared from peel and pulp remnants for 3 weeks (Rodriguez-Gonzalez *et al.*, 2017), ethanolic extract (100, 150, 200 mg/kg body weight, for 60 days) (Gondi *et al.*, 2015) or mango peel acetone (5% and 10%, for 16 weeks) (Gondi *et al.*, 2017). In the combined HFD + STZ effect study the animals were treated with mango seed powder (10% and 20%, for 21 days) (Irondi *et al.*, 2016). The results of these studies showed reduction of glycaemia and glycosylated haemoglobin (HbA1C), increased gut microbiota as well as production of short-chain fatty acids in faeces which reduced biomarkers of inflammation, improved lipid profile and insulin resistance; however, no reduction of body weight was observed in rodents (Zarasvand *et al.*, 2023). The hypoglycaemic effect of mango (pulp, seed, peel) was comparable with the hypoglycaemic drugs metformin (Irondi *et al.*, 2016) and rosiglitazone (Ojo *et al.*, 2016).

The results of studies in humans validate the findings of research in diabetic animals with mango pulp (fresh, frozen, purée), as well as freeze-dried fruit in obese and healthy patients with T2DM (Zarasvand *et al.*, 2023) in which the glycaemic index (GI) of mango pulp (GI = 59) has been compared with other fruit such as papaya and pineapple, whose value is lower (42.2–59) (Guevarra and Panlasigui, 2000; Fatema *et al.*, 2003), suggesting that it is a fruit that can prevent or delay the development of T2DM. Fructose has a glycaemic index (GI) of 23 compared with 61 for sucrose and 100 for glucose (Segal *et al.*, 2007). The higher the concentration of fructose in mango fruit, the lower the GI, and starch decreases digestibility and reduces the peak glucose response (Roongpisuthipong *et al.*, 1991; Vaisman *et al.*, 2006b; Edo *et al.*, 2011); however, this may vary depending on cultivar, growing conditions, ripening stage and form of fruit consumption (whole, juice or purée), as well as on type of fruit processing (fresh, freeze-dried, frozen) or shelf life, which may modify carbohydrate content.

Randomized clinical studies with obese individuals who have consumed mango pulp (400 g/day) or freeze-dried pulp (10 g/day, 100 mg/day or 300 mg/day) for short periods of time (4, 6 or 12 weeks) have reported positive effects on endothelial function and reduction of blood glucose and glycosylated haemoglobin (HbA1C), although it had no effect on body weight (Evans *et al.*, 2014; Buchwald-Werner *et al.*, 2017; Fang *et al.*, 2018).

The main hypoglycaemic mechanism of the bioactive compounds of mango peel, seed and pulp including polyphenolic compounds (tannins, quercetin, catechins), mangiferin, phenolic acids (gallic acid, ferulic acid, benzoic acid, syringic acid and vanillic acid), as well as carotenoids, vitamin C and dietary fibre, has not been identified (Maldonado-Celis *et al.*, 2019; Lebaka *et al.*, 2021). The potential mechanisms of action involved in the antidiabetic effect of mango could be the regulation of the expression of genes involved in glucose homeostasis, improvement of plasma and intracellular antioxidant and/or anti-inflammatory status, stimulation of pancreatic β-cells and increased insulin secretion, inhibition of intestinal glucose absorption, inhibition of digestive α-amylase and/or α-glucosidase enzymes. For example, tannins improve pancreatic β-cell function and enhance insulin secretion (Oh, 2015), gallic acid can induce GLUT-4 transporter expression to increase glucose uptake (Variya *et al.*, 2020), quercetin protects pancreatic cells through its antioxidant capacity, inhibition of proinflammatory cytosine expression and apoptosis (Ansari *et al.*, 2022), and mangiferin inhibits α-amylase and α-glucosidase enzyme activity (Sekar *et al.*, 2019). Carotenoids can increase insulin levels and insulin sensitivity by increasing gene expression for GLUT-4 protein and insulin receptor (Metibemu and Ogungbe, 2022) and also induce activation of Phase II enzymes and endogenous antioxidant system (Oh, 2015).

24.4.5 Antihypertensive effects

Hypertension, defined as blood pressure above 140/90 mmHg, is one of the most important chronic non-communicable diseases worldwide and the main preventable risk factor for cardiovascular disease and morbidity and mortality (Saiz *et al.*, 2020). Although generally symptomless, hypertension is strongly associated with serious conditions such as heart failure, renal disease, myocardial infarction, peripheral vascular disease and stroke. Approximately 90–95% of the cases correspond to essential or primary hypertension, whose aetiology is multifactorial, combining genetic and environmental factors (Oparil *et al.*, 2018). Despite its prevalence, it is preventable through the adoption of healthy eating habits, i.e., low salt intake, moderation in the consumption of saturated and *trans* fats, and regular intake of fruit and vegetables, along with the practice of physical activity and prevention of obesity (Zhu and Wang, 2024).

Hyperuricaemia and ageing are factors implicated in the development of hypertension, because it alters nitric oxide (NO) synthesis through the enzyme nitric oxide synthase (NOS) and causes endothelial dysfunction (Oparil *et al.*, 2018; Yang *et al.*, 2018). Gene expression of NOS enzyme decreases as an individual ages and increases expression of the enzyme arginase, which degrades L-arginine, the natural substrate of NOS (Berkowitz *et al.*, 2003). Endothelial dysfunction is the functional loss of NO and it precedes by many years, sometimes decades, structural changes in the blood vessel such as

arterial stiffness and plaque deposition, which correlates with CVD risks (Bryan, 2022). Therefore, if NO biosynthesis is insufficient, blood flow regulation is lost, and as a consequence, blood pressure increases and inflammation, oxidative stress and immune dysfunction occur (Bryan, 2022).

NO is a fat-soluble reactive species that acts as a cell signalling molecule (Bryan, 2022). Its main target is the enzyme soluble guanylyl cyclase that, once activated, converts guanosine triphosphate (GTP) to cyclic guanosine monophosphate (cGMP) to participate in biological processes such as vasodilation, angiogenesis, immune function, leucocyte–endothelium interactions, platelet aggregation, synaptic transmission, memory and reproduction (Lee *et al.*, 2016; Becerril *et al.*, 2019; Bryan, 2022).

The NOS enzyme has three isoforms: neuronal (nNOS), endothelial (eNOS) and inducible (iNOS). Under normal physiological conditions, nNOS and eNOS enzymes are constitutively expressed, whereas iNOS is activated in response to proinflammatory cytokines due to infection or inflammation. Chronic overactivity of iNOS leads to overproduction of NO and causes hypotension, oxidative stress, cellular damage and peroxynitrite (ONOO-.) accumulation (Lee *et al.*, 2015; Becerril *et al.*, 2019). Increased iNOS activity produces negative feedback from constitutive isoforms and can lead to decreased systemic NO production (Saijo *et al.*, 2010).

In vitro experiments performed on human umbilical vein endothelial cells (HUVECs) treated with mangiferin (75, 150, 300 µM) and uric acid (8 mg/dl) for 48 h reduced proteinase C reactive, intercellular adhesion molecule (ICAM-1) expression and increased eNOS expression and NO concentration with decreased ONOO- formation (Yang *et al.*, 2018). A similar result was reported with this *in vitro* cell model exposed to Careless™ immature mango fruit powder (Gerstgrasser *et al.*, 2016). After 3 h, eNOS activation of 23%, 42% and 60% was observed corresponding to the doses of 300, 1500 and 3000 mg/ml, respectively (Gerstgrasser *et al.*, 2016). The antihypertensive effect of mangiferin was also demonstrated in smooth muscle cells obtained from mesenteric resistance arteries of normotensive rats and spontaneously hypertensive rats (Beltrán *et al.*, 2004). Cells were exposed to 1 ng IL-1β/ml to increase the expression of COX-2 and iNOS enzymes, an effect that was inhaled with 0.025 mg mangiferin/ml after 24 h of treatment, without affecting the contractile function of the cells induced by noradrenaline (Beltrán *et al.*, 2004).

In a rat model with hyperuricaemia-induced hypertension, results consistent with those observed *in vitro* were obtained (Yang *et al.*, 2018). The antihypertensive effect of mangiferin (30, 60 and 120 mg/kg) was evaluated intragastrically for 12 weeks in Dawley-Sprague rats, and significant reductions in uric acid and systolic blood pressure (SBP) were observed between weeks 8 and 12. The reduction in SBP was associated with increased serum NO and decreased C-reactive protein (Yang *et al.*, 2018). In addition, mangiferin increased the expression of eNOS, ICAM-1, and decreased peroxynitrite (ONOO-) formation in aortic segments of hyperuricaemic rats (Yang *et al.*, 2018).

These findings suggest that mangiferin, a bioactive compound present in mango, might be a potential candidate for the treatment of hypertension associated with hyperuricaemia or other conditions that favour its development and improvement of endothelial function. In addition, these are encouraging results for future studies to isolate and identify other antihypertensive active principles in different parts of the mango fruit and plant, in order to evaluate whether synergies exist between the different mango phytochemicals.

24.4.6 Effects on digestive health

Gut health refers to the optimal state of the gastrointestinal system, which includes the stomach, small intestine and large intestine, as well as the gut microbiota. Good gut health implies a proper balance of beneficial bacteria, efficient digestion, adequate nutrient absorption and the absence of inflammation, irritation, or disease in the gastrointestinal tract (de Vos *et al.*, 2022).

The gut microbiota is a key element in human intestinal health. Some diseases such as obesity, T2DM, hepatic steatosis, intestinal diseases (coeliac disease, irritable bowel syndrome) and colorectal cancer are related to changes in the gut microbiota (Cani, 2018). This suggests that it affects pathways involved in the immune response, glucose and lipid metabolism.

Diet is a determining factor in the composition and diversity of the gut microbiota. Frequent consumers of foods high in saturated fat and sugary beverages have a lower diversity of gut microbiota compared with regular consumers of fruits and fish, and these changes affect the degradation capacity of dietary fibre (Partula *et al.*, 2019). The fibre present in fruits can modify and increase the amount and variety of certain phyla, genera and bacterial species in the intestine, because it provides substrates that favour their growth (Makki *et al.*, 2018)

Different parts of the mango fruit contain dietary fibre. The peel is the major source of fibre (40–72.5 g), followed by the seed (7.9 g) and the pulp (0.85–1.06 g) per 100g of fruit (Gupta *et al.*, 2022). Soluble and insoluble dietary fibre are functional components whose concentration varies among cultivars from 16% to 28% and 29% to 50%, respectively, and ripening stage, being higher in ripe mango (ICBF, 2018; Maldonado-Celis *et al.*, 2019; USDA, 2019; Lebaka *et al.*, 2021).

Therefore, dietary fibre from mango fruit may have a positive impact on the intestinal microbiota. Gutiérrez-Sarmiento *et al.* (2020) prepared a bar with the non-digestible fraction of 'Ataulfo' mango peel and pulp for *in vitro* colonic fermentation. The fibre content of mango increased the abundance of *Bifidobacterium*, *Prevotella* and *Eubacterium* bacterial species after 24 h of fermentation, which are related to the production of metabolites and the metabolism of phenolic compounds that induce positive effects on human health. Sáyago-Ayerdi *et al.* (2019) identified 80 bacterial genera following *in vitro* colonic fermentation of dietary fibre from 'Ataulfo' mango peel. After 24 h of fermentation, *Bifidobacterium* presented relative abundance of 83%, at 72 h of fermentation, the genera *Lactobacillus*, *Dorea*, *Lactococcus* and *Bifidobacterium* increased their relative abundance. These results suggest that dietary fibre from mango peel is a potential prebiotic ingredient.

The effect of mango consumption as a whole fruit (100 g/day) on intestinal microbiota, intestinal permeability proteins and bowel habits was evaluated in overweight/obese individuals for 12 weeks (Asuncion *et al.*, 2023). Obesity induces intestinal

dysbiosis that is associated with increased intestinal permeability due to impaired tight junctions (ZO-1 and occludin proteins) that can alter intestinal barrier integrity and impair immune function, and oxidative stress is favoured by increased diffusion of toxins (Lee *et al.*, 2018; Suzuki, 2020; Nagpal *et al.*, 2021). Mango consumption by overweight/obese individuals increased the abundance of *Prevotella maculosa*, *Corynebacterium pyruviciproducens* and *Mogibacterium thymidum* bacteria, which have immunomodulatory capacity, promote macrophage activity and increase antibody expression, and also regulate glucose metabolism (Tong *et al.*, 2012; Chen *et al.*, 2021). No significant differences were found in the circulating levels of intestinal permeability proteins ZO-1, occludin and claudin-2, that is attributable to the health status of the participants except overweight/obesity, no metabolic or inflammatory diseases. The number of bowel movements increased slightly, but not in terms of frequency, consistency, straining, pain and constipation (Asuncion *et al.*, 2023).

These results indicate that fresh mango consumption contributes to gut health, with positive implications for chronic diseases such as systemic inflammation, cardiovascular disease, diabetes, irritable bowel syndrome and colorectal cancer. However, while this research provides valuable insight into the benefits of fresh mango consumption, it is not without limitations.

24.5 Some Preharvest and Postharvest Factors Affecting Mango Bioactive Compounds

The nutritional and human health benefits of mango components can be affected by the many factors affecting the biochemistry and physiology of the fruit. During the ripening process, fruit undergo structural, metabolic and biochemical modifications and these changes determine the quality attributes, including the types of bioactive compounds and therefore the nutritional and health values of the fruit (Brecht and Yahia, 2009; Yahia, 2011; Yahia *et al.*, 2006, 2011).

Some of the changes occurring during fruit maturation and ripening include changes in cell wall structures, changes in starch and increases in soluble solids content, including production of soluble sugars from starch degradation by the action of enzymes such as the amylases. They also include softening of fruit due to changes in structural polysaccharides, increased biosynthesis of volatile compounds, degradation of chloroplasts and development of chromoplasts with increased carotenoid biosynthesis, among others (Brecht and Yahia, 2009; Joas *et al.*, 2012; Wongmetha *et al.*, 2015; Matheyambath *et al.*, 2016; Saleem-Dar *et al.*, 2016; Li *et al.*, 2020; see Chapter 23 this volume). All these changes occur during ripening until the fruit reaches an acceptable eating quality (Gill *et al.*, 2017).

Fruit development and ripening processes are the result of changes in the regulation of gene expression of several enzymes such as hydrolases, isomerases, ligases, lyases, oxidoreductases and transferases, etc., with transferases being the most prevalent, followed by hydrolases (Desphande *et al.*, 2017). Transcripts encoding enzymes involved in 142 biochemical pathways have been identified, including those involved in the biosynthesis of monoterpenes, diterpenes, sesquiterpenes, furanones and lactones, which are involved in flavour formation, and 79 transcripts corresponding to inhibitors of cell wall-modifying enzymes have also been identified (Desphande *et al.*, 2017).

Carotenoids biosynthesis during mango pulp development is initiated in the mesocarp closest to the seed and progresses to the outermost tissues (Tharanathan *et al.*, 2016), which increases carotenoid concentration up to 400%, serving in different functions including as index of maturity and quality (Ornelas-Paz *et al.*, 2008b).

Pectins are dietary fibre components of mango and are important for fruit texture. Their development begins 5 weeks after fruit set and continues until stone (seed) formation. De-esterification of pectin chains in mango cell walls results in the loss of calcium ions that form bridges between adjacent pectin polymers (Tharanathan *et al.*, 2016). As the fruit softens, insoluble pectin is converted to soluble pectin, and monosaccharides such as arabinose and galactose are released; this produces galacturan-rich cell wall polysaccharides (Prasanna *et al.*, 2004; Li *et al.*, 2022).

As for mango lipids, linoleic acid content decreases as the fruit ripens, while linolenic acid content increases; a similar reciprocal distribution of palmitic and palmitoleic acids is also observed, and these changes influence fruit aroma and flavour (Yahia, 2011). Palmitic acid is converted to fatty hydroxy acids, which are precursors of aromatic lactone compounds (Prasanna *et al.*, 2004). During the respiratory climacteric phase, mitochondria metabolize stearic and oleic fatty acids to produce precursors for carotenoid and volatile terpenoid biosynthesis (Yahia, 2011).

Soluble protein content in mango decreases for 44 days after fruit set, then increases until maturity is reached (Yahia, 2011). The predominant amino acids in the fruit are alanine, arginine, glycine, leucine, isoleucine and serine, and all except alanine decrease during fruit ripening (Yahia, 2011).

Vitamins also undergo important changes during fruit development and ripening. Vitamins B1, B2, B3 and B6 increase significantly during this process (Barbosa Gamez *et al.*, 2017), while vitamin C decreases during ripening, although maintaining a significant concentration (Matheyambath *et al.*, 2016). For example, 300 g of ripe 'Tommy Atkins' and 'Kent' mango pulp provide 1410 and 645 mg of vitamins, respectively; an amount higher than the dietary recommendation (75–90 mg/day) (WHO/FAO, 2003; Ibarra-Garza *et al.*, 2015; Barbosa Gamez *et al.*, 2017). The decrease of vitamin C during fruit development may be associated with its antioxidant activity in different metabolic pathways and as a coenzyme of ACC-oxidase during ethylene biosynthesis; in addition, it serves as a substrate for oxalate and tartrate (Mazid *et al.*, 2011). Vitamin E content in mango also varies during ripening; in some cultivars its content is higher in immature fruit, e.g., 'Tommy Atkins', while in 'Kent' it is lower (Barbosa Gamez *et al.*, 2017).

Phenolic compounds change little during fruit development, ripening and senescence, possibly to maintain the capacity to neutralize the reactive species produced during these processes (Palafox-Carlos *et al.*, 2012b). On the other hand, organic acids content and titratable acidity decrease during mango ripening due to changes in the activity of the Krebs cycle enzymes (Yahia, 2011). Some enzymes, such as isocitrate

dehydrogenase and succinate dehydrogenase, increase, while others, such as citrate synthase, decrease (Yahia, 2011).

Some postharvest treatments and practices used for fresh mango, i.e., sanitation, fungicide application, shelf-life extension treatments, packing, packaging, storage and transportation, etc., affect fruit nutritional and functional value (Yahia, 2011; Brecht and Yahia, 2017). Harvesting of mango fruit does not affect the total carotenoid content and antioxidant capacity (Prasad and Sharma, 2018). Treatments to control anthracnose, a fruit infection that affects the content of polyphenolic compounds, include hot water (53°C for 5 min), polyethylene wax (10%) with Imazalil fungicide (800 mg/l) and storage in the presence of an ethylene absorbent (Conserver 21), reducing the loss of phenolic compounds in infected mangoes (Pérez-Márquez *et al*., 2016). However, if these treatments are not applied correctly, they not only affect the organoleptic properties of the fruit but may also reduce the content or bioavailability of some phytochemicals (Kim *et al*., 2009). For example, treatment of 'Keitt' mango for 30 min at 50 or 75 min at 46°C maintained a stable vitamin C content and increased total carotenoid content during storage for 3 days, but when combining the same times and temperatures, vitamin C content decreased rapidly (Dijoua *et al*., 2009).

The effect of ionizing radiation (1.0–3.1 Gy) on the content of phenolic compounds, carotenoids and vitamin C was evaluated in 'Tommy Atkins' mangoes (Reyes and Cisneros-Zevallos, 2007). After 18 days of storage at 15°C, ripening was delayed in all irradiated mangoes compared with non-irradiated mangoes. The content of total phenolic compounds increased with a dose of 1.0 kGy, while treatment with 1.5 kGy lowered the concentration of vitamin C by half, but no significant changes were observed in the content of carotenoids (Reyes and Cisneros-Zevallos, 2007).

24.6 Conclusions

Mango cultivars have different morphological and compositional characteristics especially with regard to shape and external colour, but all are excellent sources of nutritional and health important components, i.e., pigments, vitamins (especially A and C), phenolic compounds, etc. *In vitro*, *in vivo* and clinical studies have demonstrated that regular consumption of mango fruit contributes to the prevention of chronic non-communicable diseases, through diverse actions such as antioxidant, anti-proliferative, ant-immunomodulatory, antidiabetic effects. Although some bioactive compounds are present in mango fruit in small quantities, they may still cause significant beneficial effects. The combination effects of the bioactive compounds, especially as a result of the consumption of whole fruit, commonly show enhanced effects compared with individual components. Therefore, the consumption of whole fruit rather than extracts of individual ingredients is important. Fruit development, maturation and ripening processes, as well as preharvest and postharvest factors and treatments, influence the production and metabolism of mango composition, especially of the bioactive phytochemicals, and therefore the nutritional and health contributions of the fruit. This chapter presents a compilation of updated information about the nutritional composition of mango fruit, particularly the important bioactive phytochemical components, and the effects on human nutrition and health.

References

Abbasi, A.M., Guo, X., Fu, X., Zhou, L., Chen, Y. *et al.* (2015) Comparative assessment of phenolic content and in vitro antioxidant capacity in the pulp and peel of mango cultivars. *International Journal of Molecular Science* 16, 13507–13527. DOI: 10.3390/ijms160613507

Abou-Baker, D.H. (2022) An ethnopharmacological review on the therapeutical properties of flavonoids and their mechanisms of actions: A comprehensive review based on up to date knowledge. *Toxicology Report* 9, 445–469. DOI: 10.1016/j.toxrep.2022.03.011

Ahmad, R., Alqathama, A., Aldholmi, M., Riaz, M., Abdalla, A.N. *et al.* (2023) Antidiabetic and anticancer potentials of *Mangifera indica* L. from different geographical origins. *Pharmaceuticals* (Basel) 16, 350. DOI: 10.3390/ph16030350

Albarracín, A.E. (2015) *Nutrición*, 1st edn. Universidad Nacional del Centro de la Provincia de Buenos Aires, Tandil, Buenos Aires.

American Association of Cereal Chemists (AACC) (2001) Dietary Fiber Technical Committee. The definition of dietary fiber. *Cereal Foods World* 46, 112.

Anilakumar, K.R., Khanum, F., Krishna, K.R.S. and Santhanam, K. (2003) Reduction of dimethylhydrazine-induced cytotoxicity by mango fruit bar: changes in antioxidant enzymes in rats. *Plant Foods and Human Nutrition* 58, 1–11. DOI: 10.1023/B:QUAL.0000040325.34853.f9

Ansari, P., Choudhury, S.T., Seidel, V., Rahman, A.B., Aziz, M.A. *et al.* (2022) Therapeutic potential of Quercetin in the management of type-2 diabetes mellitus. *Life* (Basel) 12, 1146. DOI: 10.3390/life12081146

Arbizu-Berrocal, S.H., Kin, H., Fang, C., Krenek, K.A., Talcott, S.T. and Mertens-Talcott, S.U. (2019) Polyphenols from mango (*Mangifera indica* L.) modulate PI3K/AKT/mTORassociatedmicro-RNAs and reduce inflammation in noncancer and induce cell death in breast cancer cells. *Journal of Functional Foods* 55, 9–16.

Asunción, P., Liu, C., Castro, R., Yon, V., Rosas, M. Jr., Hooshmand, S., Kern, M. and Hong, M.Y. (2023) The effects of fresh mango consumption on gut health and microbiome - Randomized controlled trial. *Food Science and Nutrition* 11, 2069–2078. DOI: 10.1002/fsn3.3243.

Badhani, B., Sharma, N. and Kakkar, R. (2015) Gallic acid: a versatile antioxidant with promising therapeutic and industrial applications. *RSC Advances* 5, 27540–27557. DOI:10.1039/C5RA01911G

Bao, L., Li, J., Zha, D., Zhang, L., Gao, P. *et al.* (2018) Chlorogenic acid prevents diabetic nephropathy by inhibiting oxidative stress and inflammation through modulation of the Nrf2/HO-1 and NF-κB pathways. *International Immunopharmacology* 54, 245–253. DOI: 10.1016/j.intimp.2017.11.021

Barbosa Gámez, I., Caballero Montoya, K.P., Ledesma, N., Sáyago Ayerdi, S.G., García Magaña, M.L. *et al.* (2017) Changes in the nutritional quality of five Mangifera species harvested at two maturity stages. *Journal of Science Food and Agriculture* 97, 4987–4994. DOI: 10.1002/jsfa.8377

Barnes, R.C., Krenek, K.A., Meibohm, B., Mertens-Talcott, S.U. and Talcott, S.T. (2016) Urinary metabolites from mango (*Mangifera indica* L. cv. Keitt) galloyl derivatives and in vitro hydrolysis of gallotannins in physiological conditions. *Molecular Nutrition and Food Research* 60, 542–550. DOI: 10.1002/mnfr.201500706

Becerril, S., Rodríguez, A., Catalán, V., Ramírez, B., Unamuno, X. *et al.* (2019) Functional relationship between leptin and nitric oxide in metabolism. *Nutrients* 11, 2129. DOI: 10.3390/nu11092129

Beidokhti, M.N. and Jäger, A.K. (2017) Review of antidiabetic fruits, vegetables, beverages, oils and spices commonly consumed in the diet. *Journal of Ethnopharmacology* 201, 26–41. DOI: 10.1016/j.jep.2017.02.031

Beltrán, A.E., Alvarez, Y., Xavier, F.E., Hernanz, R., Rodriguez, J. *et al.* (2004) Vascular effects of the *Mangifera indica* L. extract (Vimang). *European Journal of Pharmacology* 499, 297–305. DOI: 10.1016/j.ejphar.2004.07.073

Benard, O. and Chi, Y. (2015) Medicinal properties of mangiferin, structural features, derivative synthesis, pharmacokinetics and biological activities. *Mini-Reviews in Medicinal Chemistry* 15, 582–594. DOI: 10.2174/1389557515666150401111410

Berardini, M., Freezer, R., Conrad, J., Beifuss, U., Carle, R. and Schieber, A. (2005) Screening of mango (*Mangifera indica* L.) cultivars for their contents of flavonol o- and canthone c-glycosides, anthocyanins, and pectin. *Journal of Agricultural and Food Chemistry* 53, 1563–1570. DOI: 10.1021/jf0484069

Berkowitz, D.E., White, R., Li, D., Minhas, K.M., Cernetich, A. *et al.* (2003) Arginase reciprocally regulates nitric oxide synthase activity and contributes to endothelial dysfunction in aging blood vessels. *Circulation* 108, 2000–2006. DOI: 10.1161/01.CIR.0000092948.04444.C7

Boateng, J., Verghese, M., Shackelford, L., Walker, L.T., Khatiwada, J. *et al.* (2007) Selected fruits reduce azoxymethane (AOM)-induced aberrant crypt foci (ACF) in Fisher 344 male rats. *Food Chemisty and Toxicology* 45, 725–732. DOI: 10.1016/j.fct.2006.10.019

Böhm, V., Lietz, G., Olmedilla-Alonso, B., Phelan, D., Reboul, E. *et al.* (2021) From carotenoid intake to carotenoid blood and tissue concentrations – implications for dietary intake recommendations. *Nutrition Reviews* 79, 544-573. DOI: 10.1093/nutrit/nuaa008

Bohn, T. (2014) Dietary factors affecting polyphenol bioavailability. *Nutrition Reviews* 72, 429–452. DOI: 10.1111/nure.12114

Bondonno, N.P., Bondonno, C.P., Ward, N.C., Hodgson, J.M. and Croft, K.D. (2017) The cardiovascular health benefits of apples: Whole fruit vs isolated compounds. *Trends in Food Science & Technology* 69, Part B: 243-256. DOI: 10.1016/j.tifs.2017.04.012

Boots, A.W., Haenen, G.R.M.M. and Bast, A. (2008) Health effects of quercetin: from antioxidant to nutraceutical. *European Journal of Pharmacology* 585, 325–337. DOI: 10.1016/j.ejphar.2008.03.008.

Boumenna, T., Scott, T. M., Lee, J. S., Palacios, N. and Tucker, K. L. (2021) Folate, vitamin B-12, and cognitive function in the Boston Puerto Rican health study. *The American Journal of Clinical Nutrition* 113, 179–186. DOI: 10.1093/ajcn/ nqaa293

Bramley, P.M. (2013) Carotenoid biosynthesis and chlorophyll degradation. In: Seymour, G.B., Poole, M., Giovannoni, J.J. and Tucker, G.A. (eds) *The Molecular Biology and Biochemistry of Fruit Ripening*. Blackwell Publishing Ltd, Cardiff, pp. 75–116.

Brecht, J. and Yahia, E.M. (2009) Postharvest physiology. In: Litz, R. (ed.) *The Mango. Botany, production and uses*. CAB International, Wallingford, UK, pp. 484–528.

Brecht, J.K. and Yahia, E.M. (2017) Harvesting and postharvest technology of mango. In: Siddiq, M., Brecht, J.K. and Sidhu, J.S. (eds) *Handbook of Mango Fruit: Production, Postharvest Science, Processing Technology and Nutrition*. John Wiley & Sons Ltd, Ames, Iowa, pp. 105–129.

Bryan, N.S. (2022) Nitric oxide deficiency is a primary driver of hypertension. *Biochemical Pharmacology* 206, 115325. DOI: 10.1016/j.bcp.2022.115325.

Bub, A., Watzl, B., Blockhaus, M., Briviba, K., Liegibel, U., Muller, H., Pool- Zobel, B.L. and Rechkemmer, G. (2003) Fruit juice consumption modulates antioxidative status, immune status and DNA damage. *Journal of Nutritional Biochemistry* 14, 90–98. DOI: 10.1055/s-0043-103017

Buchwald-Werner, S., Schön, C., Frank, S. and Reule, C. (2017) Effects of *Mangifera indica* (Careless) on microcirculation and glucose metabolism in healthy volunteers. *Planta Medica* 83, 824–829. DOI: 10.1055/s- 0043- 103017

Burton-Freeman, B.M., Sandhu, A.K. and Edirisinghe, I. (2017) Mangos and their bioactive components: adding variety to the fruit plate for health. *Food & Function* 8, 3010–3032. DOI: 10.1039/C7FO00190H

Cabezas-Terán, K., Grootaert, C., Ortiz, J., Donoso, S., Ruales, J. *et al.* (2023) *In vitro* bioaccessibility and uptake of β-carotene from encapsulated carotenoids from mango by-products in a coupled gastrointestinal digestion/Caco-2 cell model. *Food Research International* 164, 112301. DOI: 10.1016/j.foodres.2022.112301

Cani, P.D. (2018) Human gut microbiome: hopes, threats and promises. *Gut* 67, 1716–1725. DOI: 10.1136/gutjnl-2018-316723

Carranco Jáuregui, M.E., Calvo Carrillo, M. de la C. and Pérez-Gil Romo, F. (2011) Carotenoides y su función antioxidante: Revisión. *Archivos Latinoamericanos de Nutrición* 61, 233–241.

Castro, B.J., Pedroza, K. and Hong, M.Y. (2023) The effects of mango consumption on vascular health and immune function. *Metabolism Open* 20, 100260. DOI: 10.1016/j.metop.2023.100260

Cervantes-Paz, B., Victoria-Campos, C. I. and Ornelas-Paz, J. de J. (2016) Absorption of carotenoids and mechanisms involved in their health-related properties. In: Stange, C. (ed.) *Carotenoids in Nature. Subcellular Biochemistry, Vol.* 79, Springer, Cham, pp. 415–454. DOI:10.1007/978-3-319-39126- 7_16

Cervantes-Paz, B., Ornelas-Paz, J.J., Ruiz-Cruz, S., Rios-Velasco, C., Ibarra-Junquera, V. *et al.* (2017) Effects of pectin on lipid digestion and possible implications for carotenoid bioavailability during pre-absorptive stages: A review. *Food Research International* 99, 917–927. DOI: 10.1016/j.foodres.2017.02.012

Chaudhury, A., Duvoor, C., Reddy Dendi, V.S., Kraleti, S., Chada, A., Ravilla, R, Marco, A., Shekhawat, N.S., Montales, M.T., Kuriakose, K., Sasapu, A., Beebe, A., Patil, N., Musham, C.K., Lohani, G.P. and Mirza, W. (2017) Clinical review of antidiabetic drugs: implications for type 2 diabetes mellitus management. *Frontiers Endocrinology* 8, 6. DOI: 10.3389/fendo.2017.00006

Chawla, A., Chawla, R. and Jaggi, S. (2016) Microvascular and macrovascular complications in diabetes mellitus: distinct or continuum? *Indian Journal of Endocrinology and Metabolism* 20, 546. DOI: 10.4103/2230-8210.183480

Chen, C.H., Han, R.M., Liang, R., Fu, L.M., Wang, P. *et al.* (2011) Direct observation of the β-carotene reaction with hydroxyl radical. *Journal of Physical Chemistry B* 115, 2082–2089. DOI: 10.1021/jp1100889

Chen, F., Gan, Y., Li, Y., He, W., Wu, W. *et al.* (2021) Association of gestational diabetes mellitus with changes in gut microbiota composition at the species level. *BMC Microbiology* 21, 147. DOI: 10.1186/s12866-021-02207-0

Chen, G.L., Chen, S.G., Zhao, Y.Y., Luo, C.X., Li, J. and Gao, Y.Q. (2014) Total phenolic contents of 33 fruits and their antioxidant capacities before and after in vitro digestion. *Industrial Crops and Products* 57, 150–157. DOI: 10.1016/j.indcrop.2014.03.018

Choe, E. and Min, D.B. (2009) Mechanisms of antioxidants in the oxidation of foods. *Comprehensive Reviews in Food Science and Food Safety* 8, 345–358. DOI: 10.1111/j.1541-4337.2009.00085.x

Choi, S.Y., Park, J.H., Kim, J.S., Kim, M.K., Aruoma, O.I. and Sung, M.K. (2006) Effects of quercetin and beta-carotene supplementation on azoxymethane-induced colon carcinogenesis and inflammatory responses in rats fed with high-fat diet rich in omega-6 fattyacids. *Biofactors* 27, 137–146. DOI: 10.1002/biof.5520270112

Choo, W.S. (2019) Fruit pigment changes during ripening. In: Melton, L., Shahidi, F. and Varelis, P. (eds) *Encyclopedia of Food Chemistry*. Elsevier, Amsterdam, pp. 1–7.

Chuyen, H.V, Roach, P.D., Golding, J.B., Parks, S.E. and Nguyen, H.M. (2019) Encapsulation of carotenoid-rich oil from Gac peel: optimisation of the encapsulation process using a spray drier and the storage stability of encapsulated powder. *Powder Technology* 344, 3737–379. DOI: 10.1016/j.powtec.2018.12.012

Cilla, A., Bosch, L., Barberá, R. and Alegría, A. (2018) Effect of processing on the bioaccessibility of bioactive compounds – a review focusing on carotenoids, minerals, ascorbic acid, tocopherols and polyphenols. *Journal of Food Composition and Analysis* 68, 3–15. DOI: 10.1016/j.jfca.2017.01.009

Clifford, M.N. (1999) Chlorogenic acids and other cinnamates–nature, occurrence and dietary burden. *Journal of the Science of Food and Agriculture* 79, 362–3723. DOI: 10.1002/(SICI)1097-0010(19990301)79:3<362::AID-JSFA256>3.0.CO;2-D

Corrales-Bernal, A., Amparo Urango, L., Rojano, B. and Maldonado, M.E. (2014) *In vitro* and *in vivo* effects of mango pulp (*Mangifera indica* cv. Azucar) in colon carcinogenesis. *Archivos Latinoamericanos de Nutrición* 64, 16–22.

Corrales-Bernal, A., Jaramillo, G., Rodríguez, B., Yahia, E.M. and Maldonado-Celis, M.E. (2016) Mango (*Mangifera indica* cv. Azúcar) antiinflammatory and chemopreventive role during colorectal carcinogenesis. *Emirates Journal Food Agriculture* 28, 1–9. DOI: 10.9755/ejfa.2015-08-593

Cosme, P., Rodríguez, A.B., Espino, J. and Garrido, M. (2020) Plant phenolics: Bioavailability as a key determinant of their potential health-promoting applications. *Antioxidants* (Basel) 9, 1263. DOI: 10.3390/antiox9121263

Crowe-White, K., O'Neil, C.E., Parrott, J.S., Benson-Davies, S., Droke, E. *et al.* (2016) Impact of 100% fruit juice consumption on diet and weight status of children: An evidence-based review. *Critical Reviews in Food Science Nutrition* 56, 871–884. DOI: 10.1080/10408398.2015.1061475

Crozier, A., Del Rio, D. and Clifford, M.N. (2010) Bioavailability of dietary flavonoids and phenolic compounds. *Molecular Aspects of Medicine* 31, 446–467. DOI: 10.1016/j.mam.2010.09.007.

D'Ambrosio, D.N., Clugston, R.D. and Blanner, W.S. (2011) Vitamin A metabolism: an update. *Nutrients* 3, 63–103. DOI: 10.3390/nu3010063

D'Archivio, M., Filesi, C., Varì, R., Scazzocchio, B. and Masella, R. (2010) Bioavailability of the polyphenols: status and controversies. *International Journal of Molecular Science* 11, 1321–1342. DOI: 10.3390/ijms11041321

Dar, M.S., Oak, P., Chidley, H., Deshpande, A., Giri, A. and Gupta, V. (2016) Nutrient and flavor content of mango (*Mangifera indica* L.) cultivars: An appurtenance to the list of staple foods. In: Simmonds, M.S.J. and Preedy, V.R. (eds) *Nutritional Composition of Fruit Cultivars*. Elsevier, Amsterdam, pp. 445–467. DOI: 10.1016/B978-0-12-408117-8.00019-2

de Vos, W.M., Tilg, H., Van Hul, M. and Cani, P.D. (2022) Gut microbiome and health: mechanistic insights. *Gut* 71, 1020–1032. DOI: 10.1136/gutjnl-2021-326789

Deshpande, A.B., Anamika, K., Jha, V., Chidley, H.G., Oak, P.S. *et al.* (2017) Transcriptional transitions in Alphonso mango (Mangifera indica L.) during fruit development and ripening explain its distinct aroma and shelf life characteristics. *Science Reports* 7, 8711. DOI: 10.1038/s41598-017-08499-5

Djioua, T., Charles, F., Lopez-Lauri, F., Filgueiras, H., Coudret, A. *et al.* (2009) Improving the storage of minimally processed mangoes (*Mangifera indica* L.) by hot water treatments. *Postharvest Biology and Technology* 52, 221–226. DOI: 10.1016/ j.postharvbio.2008.10.006

Djuricic, I. and Calder, P.C. (2021) Beneficial outcomes of omega-6 and omega-3 polyunsaturated fatty acids on human health: An update for 2021. *Nutrients* 13, 2421. DOI: 10.3390/nu13072421

Doseděl, M., Jirkovský, E., Macáková, K., Krčmová,L-K., Javorská, L. *et al.* (2021) Vitamin C – Sources, physiological role, kinetics, deficiency, use, toxicity, and determination. *Nutrients* 13, 615. DOI: 10.3390/nu13020615

Ediriweera, M.K., Tennekoon, K.H. and Samarakoon, S.R. (2017) A Review on ethnopharmacological applications, pharmacological activities and bioactive compounds of mango (*Mangifera indica* L.). *Evidence-Based Complementary Alternative Medicine* 24, 6949835. DOI: 10.1155/2017/6949835

Edo, A.E., Eregie, A., Adediran, O.S. and Ohwovoriole, A.E. (2011) Glycaemic response to some commonly eaten fruits in type 2 diabetes mellitus. *West African Journal of Medicine* 30, 94–98. PMID: 21984455.

Epriliati, I. and Ginjom, I.R. (2012) Bioavailability of phytochemicals. In: Rao, V. (ed.) *Phytochemicals – A Global Perspective of Their Role in Nutrition and Health*. IntechOpen, London, pp. 401–428.

Eun, J.-B., Maruf, A., Das, P.R. and Nam, S.-H. (2020) A review of encapsulation of carotenoids using spray drying and freeze drying. *Critical Reviews in Food Science and Nutrition* 60, 3547–3572. DOI: 10.1080/10408398.2019.1698511

Evans, S.F., Meister, M., Mahmood, M., Eldoumi, H., Peterson, S. *et al.* (2014) Mango supplementation improves blood glucose in obese individuals. *Nutrition and Metabolic Insights* 7, 77–84. DOI: 10.4137/NMI.S17028.

Evans, S.F., Beebe, M., Mahmood, M., Janthachotikun, S., Eldoumi, H. *et al.* (2017) Mango supplementation has no effects on inflammatory mediators in obese adults. *Nutrition Metabolism Insights* 10, 1178638817731770. DOI: 10.1177/1178638817731770.

Fang, C., Kim, H., Barnes, R.C., Talcott, S.T. and Mertens-Talcott, S.U. (2018) Obesity-associated diseases biomarkers are differently modulated in lean and obese individuals and inversely correlated to plasma polyphenolic metabolites after 6 weeks of mango (*Mangifera indica* L.) consumption. *Molecular Nutrition and Food Research* 62, 1800129. DOI: 10.1002/mnfr.201800129

FAOSTAT (2022) Agricultural production statistics 2000–2021. Available at: https://www.fao.org/food-agriculture-statistics/data-release/data-release detail/es/c/1627788/ (accessed 8 March 2024).

Fatema, K., Ali, L., Rahman, M.H., Parvin, S. and Hassan, M.Z. (2003) Serum glucose and insulin response to mango and papaya in type 2 diabetic subjects. *Nutrition Research* 23, 9–14. DOI: 10.1016/S0271- 5317(02)00492- X

Galati, S., Boni, C., Gerra, M.C., Lazzaretti, M. and Buschini, A. (2019) Autophagy: A player in response to oxidative stress and DNA damage. *Oxidative Medicine and Cellular Longevity* 1–12. DOI: 10.1155/2019/5692958

Gerstgrasser, A., Röchter, S., Dressler, D., Schön, C., Reule, C. and Buchwald-Werner, S. (2016) *In vitro* activation of eNOS by *Mangifera indica* (Careless™) and determination of an effective dosage in a randomized, double-blind, human pilot study on microcirculation. *Planta Medicine* 82, 298–304. DOI: 10.1055/s-0035-1558219

Ghosh, S., Avinashe, H. and Dubey, N. (2023) Nutritional and phytochemical changes during ripening in mango: a review. *Current Nutrition and Food Science* 19, 519–528. DOI: 10.2174/1573401319666221014141807

Gill, P.P.S., Jawandha, S.K., Kaur, N. and Singh, N. (2017) Physico-chemical changes during progressive ripening of mango (*Mangifera indica* L.) cv. Dashehari under different temperature regimes. *Journal of Food Science and Technology* 54, 1964–1970. DOI: 10.1007/s13197-017-2632-6.

Godswill, A.G., Somtochukwu, I.V., Ikechukwu, A.O. and Kate, E.C. (2020) Health benefits of micronutrients (vitamins and minerals) and their associated deficiency diseases: A systematic review. *International Journal of Food Sciences* 3, 1–32. DOI: 10.47604/ijf.102

Gomes Natal, D.I., Castro Moreira, M.E., Miliao Graduate, M.S., Benjamin, L.A., de Souza Dantas, I. *et al.* (2016) Ubá mango juices intake decreases adiposity and inflammation in high-fat diet-induced obese Wistar rats. *Nutrition* 32, 1011–1108. DOI: 10.1016/j.nut.2016.02.008

Gomes Natal, D.I., da Cruz Rodrigues, C., Castro Moreira, M.E., Queiroz, J.H., dos Anjos Benjamin, L. *et al.* (2017) Bioactive compounds of the Ubá mango juices decrease inflammation and hepatic steatosis in obese Wistar rats. *Journal of Functional of Foods* 32, 409–418. DOI: 10.1016/j.jff.2017.03.023

Gondi, M., Basha, S.A., Bhaskar, J.J., Salimath, P.V. and Prasada Rao, U.J (2015) Anti-diabetic effect of dietary mango (*Mangifera indica* L.) peel in streptozotocin-induced diabetic rats. *Journal of Science Food Agriculture* 95, 991–999. DOI: 10.1002/jsfa.6778

Gondi, M., Basha, S.A., Salimath, P.V. and Rao, U.J.S.P. (2017) Supplementation of mango (*Mangifera Indica* L.) peel in diet ameliorates cataract in streptozotocin-induced diabetic rats. *Journal of Food Biochemistry* 41, e12300. DOI: 10.1111/jfbc.12300.

Guevarra, M.T.B. and Panlasigui, L.N. (2000) Blood glucose responses of diabetes mellitus type II patients to some local fruits. *Asia Pacific Journal of Clinical Nutrition* 9, 303–308. DOI: 10.1046/j.1440-6047.2000.00159.x

Gupta, A.K., Gurjar, P.S, Beer, K., Pongener, A., Ravi, S.C. *et al.* (2022) A review on valorization of different byproducts of mango (*Mangifera indica* L.) for functional food and human health. *Food Biosciences* 48, 101783. DOI: 10.1016/j.fbio.2022.101783

Gutiérrez-Sarmiento, W., Sáyago-Ayerdi, S.G., Goñi, I., Gutiérrez-Miceli, F.A., Abud-Archila, M. *et al.* (2020) Changes in intestinal microbiota and predicted metabolic pathways during colonic fermentation of mango (*Mangifera indica* L.)-based bar indigestible fraction. *Nutrients* 12, 683. DOI: 10.3390/nu12030683

Han, D.H., Lee, M.J. and Kim, J.H. (2006) Antioxidant and apoptosis-inducing activities of ellagic acid. *Anticancer Research* 26, 3601–3606.

Hanna, M., Jaqua, E., Nguyen, V. and Clay J. B. (2022) Vitamins: Functions and Uses in Medicine. *The Permanente Journal* 26, 89–97. DOI: 10.7812/TPP/21.204

Haytowitz, D.B., Wu, X. and Bhagwat, S. (2018) USDA database for the flavonoid content of selected foods release 3.3. US Department of Agriculture, Washington, DC.

Hernández-Maldonado, L.M., Blancas-Benítez, F.J., Zamora-Gasga, V.M., Cárdenas-Castro, A.P., Tovar, J. and Sáyago-Ayerdi, S.G. (2019) *In vitro* gastrointestinal digestion and colonic fermentation of high dietary fiber and antioxidant-rich mango (*Mangifera indica* L.) 'Ataulfo'-based fruit bars. *Nutrients* 11, 1564. DOI: 10.3390/nu11071564

Hewitt, R.E., Mcmarlin, A., Kleiner, D., Wersto, R., Martin, P. *et al.* (2000) Validation of a model of colon cancer progression. *Journal of Pathology* 192, 446–454. DOI: 10.1002/1096-9896(2000)9999: 9999<:: AID-PATH775>3.0.CO;2-K

Hou, S., Wang, F., Li, Y., Li, Y., Wang, M. *et al.* (2012) Pharmacokinetic study of mangiferin in human plasma after oral administration. *Food Chemistry* 132, 289–294. DOI: 10.1016/j.foodchem.2011.10.079

Hu, K., Dars, A.G., Liu, Q., Xie, B. and Sun, Z. (2018) Phytochemical profiling of the ripening of Chinese mango (Mangifera indica L.) cultivars by real-time monitoring using UPLC-ESI-QTOF-MS and its potential benefits as prebiotic ingredients. *Food Chemistry* 256, 171–180. DOI: 10.1016/j.foodchem.2018.02.014

Ibarra-Garza, I.P., Ramos-Parra, P.A., Hernández-Brenes, C. and Jacobo-Velazquez, D.A. (2015) Effects of postharvest ripening on the nutraceutical and physicochemical properties of mango (*Mangifera indica* L. cv Keitt). *Postharvest Biology and Technology* 103, 45–54. DOI: 10.1016/j.postharvbio.2015.02.014

Imran, M., Arshad, M.S., Butt, M.S., Kwon, J.H., Arshad, M.U. and Sultan, M.T. (2017). Mangiferin: a natural miracle bioactive compound against lifestyle related disorders. *Lipids in Health and Disease* 16, 84. DOI: 10.1186/s12944-017-0449-y

Instituto Colombiano de Bienestar Familiar (ICBF) (2018) Tabla de composición de alimentos colombianos. Available at: https://www.icbf.gov.co/bienestar/nutricion/tabla-alimentos (accessed 14 March 2024)

Irondi, E.A., Oboh, G. and Akindahunsi, A.A. (2016) Antidiabetic effects of Mangifera indica kernel flour-supplemented diet in streptozotocin-induced type 2 diabetes in rats. *Food Science & Nutrition* 4, 828–839. DOI: 10.1002/fsn3.348

Jahurul, M.H.A., Zaidul, I.S., Ghafoor, K., Al-Juhaimi, F., Nyam, K-L., Norulaini, N.A.N., Sahena, F. and Mohd Omar, A.K. (2015) Mango (*Mangifera indica* L.) by-products and their valuable componentes: A review. *Food Chemistry* 183, 173–180. DOI: 10.1016/j.foodchem.2015.03.046.

Jang, S.H., Lim, J.W. and Kim, H. (2009) β-Carotene inhibits *Helicobacter pylori*–induced expression of inducible nitric oxide synthase and cyclooxygenase-2 in human gastric epithelial AGS cells. *Journal of Physiology and Pharmacology* 60, 131–137. PMID: 20388956.

Joas, J., Vulcain, E. and Desvignes, C. (2012) Physiological age at harvest regulates the variability in postharvest ripening, sensory and nutritional characteristics of mango (*Mangifera indica* L.) cv. Coghshall due to growing conditions. *Journal of Science Food and Agriculture* 92, 1282–1290. DOI: 10.1002/jsfa.4696

Kang, H. and Kim, B. (2023) Bioactive compounds as inhibitors of inflammation, oxidative stress and metabolic dysfunctions via regulation of cellular redox balance and histone acetylation state. *Foods* 12, 925. DOI: 10.3390/foods12050925

Kennedy, D.O. (2014) *Plants and the Human Brain.* Oxford University Press, New York.

Khadim, R.M. and Al-Fartusie, F.S. (2021) Antioxidant vitamins and their effect on immune system. *Journal of Physics: Conference Series* 1853, Article 012065.

Kim, H., Moon, J.Y., Kim, H., Lee, D.S., Cho, M. *et al.* (2010) Antioxidant and antiproliferative activities of mango (*Mangifera indica* L.) flesh and peel. *Food Chemistry* 121, 429–436. DOI: 10.1016/j.foodchem.2009.12.060

Kim, H., Banerjee, N., Barnes, R.C., Pfent, C.M., Talcott, S.T., Dashwood, R.H. *et al.* (2016) Mango polyphenolics reduce inflammation in intestinal colitis-involvement of the miR-126/PI3K/AKT/mTOR axis in vitro and in vivo. *Molecular Carcinogenesis* 56, 197–207. DOI: 10.1002/mc.22484

Kim, H., Venancio, V.P., Fang, C., Dupont, A.W., Talcott, S.T. and Mertens-Talcott, S.U. (2020) Mango (*Mangifera indica* L.) polyphenols reduce IL-8, GRO, and GM-SCF plasma levels and increase Lactobacillus species in a pilot study in patients with inflammatory bowel disease. *Nutrition Research* 75, 85–94. DOI: 10.1016/j.nutres.2020.01.002

Kim, H., Castellon-Chicas, M.J., Arbizu, S., Talcott, S.T., Drury, N. L. *et al.* (2021) Mango (*Mangifera indica* L.) polyphenols: Anti-inflammatory intestinal microbial health benefits, and associated mechanisms of actions. *Molecules* 26, 2732. DOI: 10.3390/molecules26092732

Kim, Y., Lounds-Singleton, A.J. and Talcott, S.T. (2009) Antioxidant phytochemical and quality changes associated with hot water immersion treatment of mangoes (*Mangifera indica* L.). *Food Chemistry* 115, 989–993. DOI: 10.1016/j.foodchem.2009.01.019

Koga, M., Nakagawa, S., Kato, A. and Kusumi, I. (2019) Caffeic acid reduces oxidative stress and microglial activation in the mouse hippocampus. *Tissue Cell* 60, 14-20. DOI: 10.1016/j.tice.2019.07.006

Kominsky, D.J., Campbell, E.L. and Colgan, S.P. (2010) Metabolic shifts in immunity and inflammation. *Journal Immunology* 184, 4062–4068. DOI: 10.4049/jimmunol.0903002

Kordiak, J., Bielec, F., Jabłoński, S. and Pastuszak-Lewandoska, D. (2022) Role of beta-carotene in lung cancer primary chemoprevention: a systematic review with meta-analysis and meta-regression. *Nutrients* 24(14), 1361. DOI: 10.3390/nu14071361.

Kumar, V., Dwivedi, V. and Kashyap, A.S. (2021) Comparative studies of malic acid and citric acid contents in three varieties of mango (*Mangifera indica*) pulp. *Remarking an Analysation* 6, E24–E30.

Lebaka, V.R., Wee, Y., Ye, W., and Korivi, M. (2021) Nutritional composition and bioactive compounds in three different parts of mango fruit. *International Journal of Environmental Research in Public Health* 18, 741. DOI: 10.3390/ijerph18020741

Lee, B., Moon, K.M. and Kim, C.Y. (2018) Tight junction in the intestinal epithelium: Its association with diseases and regulation by phytochemicals. *Journal of Immunology Research* 16, 2018. DOI: 10.1155/2018/2645465

Lee, D.I., Zhu, G., Sasaki, T., Cho, G.S., Hamdani, N. *et al.* (2015) Phosphodiesterase 9A controls nitric-oxide-independent cGMP and hypertrophic heart disease. *Nature* 519, 472–476. DOI: 10.1038/nature14332

Lee, J. and Schwartz, S. (2006) *Pigments in Plant Foods: Handbook of Food Science, Technology and Engineering*. CRC Taylor, New York.

Lee, J., Bae, E.H., Ma, S.K. and Kim, S.W. (2016) Altered nitric oxide system in cardiovascular and renal diseases. *Chonnam Medicine Journal* 52, 81–90. DOI: 10.4068/cmj.2016.52.2.81

Leite Neta, M.T.S., de Santana, K.L., dos Santos, R.A.R., Galvão, M.S., Fontes, A.S. and Narain, N. (2018) Fatty acids profile of pulp and peel of mango (Mangifera indica Linn.) cultivar 'Espada' from Brazilian northeast region. *Acta Horticulturae* 1198, 197–198. DOI: 10.17660/actahortic.2018.119

Lenucci, M.S., Tornese, R., Mita, G. and Durante, M. (2022) Bioactive compounds and antioxidant activities in different fractions of mango fruits (*Mangifera indica* L., cultivars Tommy Atkins and Keitt). *Antioxidants* 11, 484. DOI: 10.3390/antiox11030484

Li, D., Deng, L., Dai, T., Chen, M., Liang, R. *et al.* (2022) Ripening induced degradation of pectin and cellulose affects the far infrared drying kinetics of mangoes. *Carbohydrate Polymers* 291, 119582. DOI: 10.1016/j.- carbpol.2022.119582 119582

Li, L., Wu, H.X., Ma, X.W., Xu, W.T., Liang, Q.Z. *et al.* (2020) Transcriptional mechanism of differential sugar accumulation in pulp of two contrasting mango (*Mangifera indica* L.) cultivars. *Genomics* 112, 4505–4515. DOI: 10.1016/j.ygeno.2020.07.038

Li, M., Ma, H., Yang, L. and Li, P. (2016) Mangiferin inhibition of proliferation and induction of apoptosis in human prostate cancer cells is correlated with downregulation of B-cell lymphoma-2 and upregulation of microRNA. *Oncology Letters* 182, 817–822. DOI: 10.3892/ol.2015.3924

Li, X., Zhang, W., Niu, D. and Liu, X. (2024) Effects of abiotic stress on chlorophyll metabolism. *Plant Science* 342, 112030. DOI: 10.1016/j.plantsci.2024.112030

Liu, R.H. (2013) Health-promoting components of fruits and vegetables in the diet. *Advanced Nutrition* 4, 384s–392s. DOI: 10.3945/an.112.003517

Liu, X., Bi, J., Xiao, H. and McClements, D.J. (2016) Enhancement of nutraceutical bioavailability using excipient nanoemulsions: role of lipid digestion products on bioaccessibility of carotenoids and phenolics from mangoes. *Journal of Food Sciences* 81, N754–N761. DOI: 10.1111/1750-3841.13227

Low, D.Y., D'Arcy, B. and Gidley, M.J. (2015) Mastication effects on carotenoid bioaccessibility from mango fruit tissue. *Food Research International* 67, 238–246. DOI: 10.1016/j.foodres.2014.11.013

Lozano-Casabianca, G.A., Arango-Varela, S.S., Aguillón-Osma, J., Llano-Ramírez, M.A. and Maldonado-Celis, M.E. (2022) Inhibition of cell proliferation and induction of cell cycle arrest in colon cancer cells by lyophilized mango (*Mangifera indica* L.) pulp extract. *Preventive Nutrition and Food Science* 27, 436–447. DOI: 10.3746/pnf.2022.27.4.436

Lozano-Casabianca, G.A., Arango-Varela, S.S. and Maldonado-Celis, M.E. (2023) Induction of apoptosis and decrease of autophagy in colon cancer cells by an extract of lyophilized mango pulp. *International Journal of Environmental Research and Public Health* 20, 4165. DOI: 10.3390/ijerph20054165

Lucas, E.A., Li, W., Peterson, S.K., Brown, A., Kuvibidila, S., Perkins-Veazie, P. *et al.* (2011) Mango modulates body fat and plasma glucose and lipids in mice fed a high-fat diet. *British Journal of Nutrition* 106, 1495–1505. DOI: 10.1017/S0007114511002066.

Madalageri, D., Bharati, P.C., Orsat, V., Raghavan, V. and Kage, U. (2015) Antioxidant activity in pulp and peel of three mango varieties. *Journal of Horticultural Sciences* 10, 199–209. DOI: 10.24154/jhs.v10i2.130

Makki, K., Deehan, E.C., Walter, J. and Bäckhed, F. (2018) The impact of dietary fiber on gut microbiota in host health and disease. *Cell Host & Microbe* 23, 705–715. DOI: 10.1016/j.chom.2018.05.012

Maldonado, M.E. and Urango, L.A. (2017) Dietary fiber and colon cancer. In: Hossenian, F., Ooomah, D. and Campos Vega, R. (eds) *Dietary Fiber Functionality in Food and Nutraceuticals: From Plant to Gut*. John Wiley & Sons, Hoboken, New Jersey, pp. 179–203.

Maldonado-Celis, M.E., Bousserouel, S., Gossé, F., Minker, C., Lobstein, A. and Raul, F. (2009) Differential induction of apoptosis by apple procyanidins in TRAIL-sensitive human colon tumor cells and derived TRAIL-resistant metastatic cells. *Journal of Cancer Molecules* 5, 21–30. Available at: https://hdl.handle.net/10495/21982

Maldonado-Celis, M.E., Yahia, E.M., Bedoya, R., Landázuri, P., Loango, N. *et al.* (2019) Chemical composition of mango (*Mangifera indica* L.) fruit: Nutritional and phytochemical compounds. *Frontiers in Plant Science* 10, 1073. DOI: 10.3389/fpls.2019.01073

Malherbe, C.J., Willenburg, E., De Beer, D., Bonnet, S.L., van der Westhuizen, J.H. and Joubert, E. (2014) Iriflophenone-3-C-glucoside from *Cyclopia genistoides*: Isolation and quantitative comparison of antioxidant capacity with mangiferin and isomangiferin using on-line HPLC antioxidant assays. *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences* 30, 951–952, 164–171. DOI: 10.1016/j.jchromb.2014.01.038

Manach, C., Scalbert, A., Morand, M., Rémésy, C. and Jiménez L. (2004) Polyphenols: food sources and bioavailability. *American Journal of Clinical Nutrition* 79, 727–747. DOI: 10.1093/ajcn/79.5.727.

Manach, C., Williamson, G., Morand C., Scalbert, A. and Remesy, C. (2005) Bioavailability and bioefficacy of polyphenols in humans: I. Review of 97 bioavailability studies. *American Journal of Clinical Nutrition* 81, 230S–2 42S. DOI: 10.1093/ajcn/81.1.230S

Manivasagan, P., Bharathiraja, S., Moorthy, M.S., Mondal, S., Seo, H. *et al.* (2018) Marine natural pigments as potential sources for therapeutic applications. *Critical Reviews in Biotechnology* 38, 745–761. DOI: 10.1080/07388551.2017.1398713

Manson, M. (2003) Cancer prevention- the potential for diet to modulate molecular signaling. *Trends Molecular Medicine* 9, 11–18. DOI: 10.1016/s1471-4914(02)00002-3

Manthey, J.A. and Perkins-Veazie, P. (2009) Influences of harvest date and location on the levels of β-carotene, ascorbic acid, total phenols, the in vitro antioxidant capacity, and phenolic profiles of five commercial varieties of mango (*Mangifera indica* L.). *Journal of Agricultural and Food Chemistry* 57, 10825–10830. DOI: 10.1021/jf902606h

Márquez, L., García-Bueno, B., Madrigal, J.L.M. and Leza, J.C. (2012) Mangiferin decreases inflammation and oxidative damage in rat brain after stress. *European Journal of Nutrition* 51, 729–739. DOI: 10.1007/s00394-011-0252-x

Masibo, M. and He, Q. (2008) Major mango polyphenols and their potential significance to human health. *Comprehensive Reviews in Food Science and Food Safety* 7, 309–319. DOI: 10.1111/j.1541-4337.2008.00047.x

Matheyambath, A.C., Subramanian, J. and Paliyath, G. (2016) Mangoes. In: Caballero, B., Finglas, P. and Toldrá, F. (eds) *Encyclopedia of Food and Health*. Elsevier, Amsterdam, pp. 641–645.

Matsumura, Y., Kitabatake, M., Kayano, S.I. and Ito, T. (2023) Dietary phenolic compounds: their health benefits and association with the gut microbiota. *Antioxidants* (Basel) 12, 880. DOI: 10.3390/antiox12040880

Mattila, P. and Kumpulainen, J. (2002) Determination of free and total phenolic acids in plant-derived foods by HPLC with diode-array detection. *Journal of Agricultural and Food Chemistry* 50, 3660–3667. DOI: 10.1021/jf020028p

Mazid, M., Khan, T.A., Khan, Z.H., Quddusi, S. and Mohammad, F. (2011) Occurrence, biosynthesis and potentialities of ascorbic acid in plants. *International Journal of Plant, Animal and Environmental Science* 1, 167–184.

Metibemu, D.S. and Ogungbe, I.V. (2022) Carotenoids in drug discovery and medicine: pathways and molecular targets implicated in human diseases. *Molecules* 27, 6005. DOI: 10.3390/molecules27186005

Milani, A., Basirnejad, M., Shahbazi, S. and Bolhassani, A. (2017) Carotenoids: biochemistry, pharmacology and treatment. *British Journal of Pharmacology* 174, 1290–1324. DOI: 10.1111/bph.13625

Minniti, G., Laurindo, L.F., Machado, N.M., Duarte, L.G., Guiguer, E.L. *et al.* (2023) *Mangifera indica* L., by-products, and mangiferin on cardio-metabolic and other health conditions: A systematic review. *Life* (Basel) 13, 2270. DOI: 10.3390/life13122270

Muoki, P.N., Makokha, A.O., Onyango, C.A. and Ojijo, N.K. (2009) Potential contribution of mangoes to reduction of vitamin A deficiency in Kenya. *Ecology of Food and Nutrition* 48, 482–498. DOI: 10.1080/03670240903308604

Nagpal, R., Indugu, N. and Singh, P. (2021) Distinct gut microbiota signatures in mice treated with commonly used food preservatives. *Microorganisms* 9, 2311. DOI: 10.3390/microorganisms9112311

National Institutes of Health, Office of Dietary Supplements (2021) Vitamin C. Available at: https://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/ (accessed 01 April 2024).

Negi, J.S., Bisht, V.K., Singh, P., Rawat, M.S.M. and Joshi, G.P. (2013) Naturally occurring xanthones: chemistry and biology. *Journal of Applied Chemistry* 2013, 621459, 1–9. DOI: 10.1155/2013/621459.

Njiru, M.K., Nawiri, P.M., Wanjau, R. and Odundo, J.O. (2014) Residues of *Mangifera indica* L. as alternative animal feed in Embu county, Kenya. *Green Chemistry* 16, 1–10.

Noratto, G.D., Bertoldi, M.C., Krenek, K., Talcott, S.T., Stringheta, P.C. and Mertens-Talcott, S.U. (2010) Anticarcinogenic effects of polyphenolics from mango (*Mangifera indica*) varieties. *Journal of Agricultural and Food Chemistry* 58, 4104–4112. DOI: 10.1021/jf903161g

Ockermann, P., Headley, L., Lizio, R. and Hansmann, J. (2021) A review of the properties of anthocyanins and their influence on factors affecting cardiometabolic and cognitive health. *Nutrients* 13, 2831. DOI: 10.3390/nu13082831

Oh, Y.S. (2015) Plant-derived compounds targeting pancreatic beta cells for the treatment of diabetes. *Evidence Based Complementary and Alternative Medicine* 629863. DOI: 10.1155/2015/629863

Ojo, B., El-Rassi, G.D., Payton, M.E., Perkins-Veazie, P., Clarke, S. *et al.* (2016) Mango supplementation modulates gut microbial dysbiosis and short-chain fatty acid production independent of body weight reduction in C57BL/6 mice fed a high-fat diet. *Journal of Nutrition* 146, 1483–191. DOI: 10.3945/jn.115.226688

Oparil, S., Acelajado, M.C., Bakris, G.L., Berlowitz, D.R., Cífková, R. *et al.* (2018) *Hypertension. Nature Reviews Disease Primers* 4, 18014. DOI: 10.1038/nrdp.2018.14

Ordoñez-Díaz, J.L., Moreno-Ortega, A., Roldán-Guerra, F.J., Ortíz-Somovilla, V., Moreno-Rojas, J.M. and Pereira-Caro G. (2020) *In vitro* gastrointestinal digestion and colonic catabolism of mango (*Mangifera indica* L.) pulp polyphenols. *Foods* 9, 1836. DOI: 10.3390/foods9121836

Ornelas-Paz, J.J., Yahia, E.M., Failla, M. and Gardea, A. (2008a) Impact of stage of ripening and dietary fat on in vitro bioaccessibility of b-carotene in 'Ataulfo' mango. *Journal of Agricultural and Food Chemistry* 56, 1511–1516. DOI: 10.1021/jf072751r

Ornelas-Paz, J.J., Yahia, E.M. and Gardea-Bejar, A. (2008b) Changes in external and internal color and during postharvest ripening of 'Manila' and 'Ataulfo' mango fruit and relationship with carotenoid content determined by liquid chromatography-APcI+- time of flight mass spectrometry. *Postharvest Biology and Technology* 50, 145–152.

Palafox-Carlos, H., Yahia, E.M. and González-Aguilar, G.A. (2012a) Identification and quantification of major phenolic compounds from mango (*Mangifera indica*, cv. Ataulfo) fruit by HPLC–DAD–MS/MS-ESI and their individual contribution to the antioxidant activity during ripening. *Food Chemistry* 135, 105–111. DOI: 10.1016/j.foodchem.2012.04.103

Palafox-Carlos, H., Yahia, E., Islas-Osuna, M.A., Gutierrez-Martínez, P. and Robles-Sánchez, M. (2012b) Effect of ripeness stage of mango fruit (Mangifera indica L., cv. Ataulfo) on physiological parameters and antioxidant activity. *Science Horticulturae* 135, 7–13. DOI: 10.1016/j.scienta.2011.11.027

Palozza, P., Serini, S., Torsello, A., Di Nicuolo, F., Piccioni, E. *et al* (2003) Beta-carotene regulates NF-kappaB DNA-binding activity by a redox mechanism in human leukemia and colon adenocarcinoma cells. *Journal of Nutrition* 133, 381–388. DOI: 10.1093/jn/133.2.381

Palozza, P., Parrone, N., Catalano, A. and Simone, R. (2010) Tomato lycopene and inflammatory cascade: basic interactions and clinical implications. *Current Medicinal Chemistry* 17, 2547–2563. DOI: 10.2174/092986710791556041

Pan, L.L., Wang, A.Y., Huang, Y.Q., Luo, Y. and Ling, M. (2014) Mangiferin induces apoptosis by regulating Bcl-2 and bax expression in the CNE2 nasopharyngeal carcinoma cell line. *Asian Pacific Journal of Cancer Prevention* 15, 7065–7068. DOI: 10.7314/apjcp.2014.15.17.7065

Paolini, M., Antelli, A., Pozzetti, L., Spetlova, D., Perocco, P. *et al.* (2001) Induction of cytochrome P450 enzymes and over-generation of oxygen radicals in betacarotene supplemented rats. *Carcinogenesis* 22, 1483–1495. DOI: 10.1093/carcin/22.9.1483

Pardo-Andreu, G.L., Philip, S.J., Riaño, A., Sánchez, C., Viada, C. *et al.* (2006) *Mangifera indica* L. (Vimang) protection against serum oxidative stress in elderly humans. *Archives of Medical Research* 37, 158–164. DOI: 10.1016/j.arcmed.2005.04.017

Pardo-Andreu, G.L., Barrios, M.F., Curti, C., Hernández, I., Merino, N. *et al.* (2008) Protective effects of *Mangifera indica* L extract (Vimang), and its major component mangiferin, on iron-induced oxidative damage to rat serum and liver. *Pharmacology Research* 57, 79–86. DOI: 10.1016/j.phrs.2007.12.004

Pareek, S., Alok Sagar, N., Sharma, S., Kumar, V., Agarwal, T. *et al.* (2018) Chlorophylls: Chemistry and biological actions. In: Yahia, E.M. (ed.) *Fruit and Vegetable Phytochemicals: Chemistry and Human Health*. Wiley-Blackwell, Oxford, pp. 269–284.

Partula, V., Mondot, S., Torres, M.J., Kesse-Guyot, E., Deschasaux, M. *et al.* (2019) Associations between usual diet and gut microbiota composition: Results from the Milieu Intérieur cross-sectional study. *American Journal of Clinical Nutrition* 109, 1472–1483. DOI: 10.1093/ajcn/nqz029

Percival, S.S., Talcott, S.T., Chin, S.T., Mallak, A.C., Lounds-Singleton, A. and Pettit-Moore, J. (2006) Neoplastic transformation of BALB/3T3 cells and cell cycle of HL-60 cells are inhibited by mango (*Mangifera indica* L.) juice and mango juice extracts. *Journal of Nutrition* 136, 1300–1304. DOI: 10.1093/jn/136.5.1300

Pérez-Márquez, A., Vidal-Aguiar, Y. and Mulkay-Vitón, T. (2016) Contenido de fenoles totales en frutos de mango super Haden dañados por antracnosis y tratados en poscosecha. *Cultivos Tropicales* 37, 71–77.

Pezzuto, J.M. and Vang, O. (2020) Perspective: A positive cocktail effect of the bioactive components in the diet. In: Pezzuto, J.M. and Vang, O. (eds) *Natural Products for Cancer Chemoprevention*. Springer, Cham, Switzerland, pp. 613–629.

Prasad, K. and Sharma, R.R. (2018) Impact of harvesting method on cosmetic appeal, physiological and biochemical attributes of mango fruits (*Mangifera indica* L.). *Journal of Pharmacognosy and Phytochemistry* 7, 1468–1473.

Prasanna, V., Prabha, T.N. and Tharanathan, R.N. (2004) Pectic polysaccharides of mango (Mangifera indica L): structural studies. *Journal of Science Food and Agriculture* 84, 1731–1735. DOI: 10.1002/ jsfa.1874

Quirós-Sauceda, A.E., Sañudo-Barajas, J.A., Vélez-de la Rocha, R., Domínguez-Avila, J.A., Ayala-Zavala, J.F. *et al.* Villegas-Ochoa, M.A. and González-Aguilar, G.A. (2019) Effects of ripening on the *in vitro* antioxidant capacity and bioaccessibility of mango cv. 'Ataulfo' phenolics. *Journal of Food Science and Technology* 56, 2073–2082. DOI: 10.1007/s13197-019-03685-x

Ramirez, J.E., Zambrano, R., Sepúlveda, B. and Simirgiotis, M.J. (2014) Antioxidant properties and hyphenated HPLC-PDA-MS profiling of Chilean Pica mango fruits (*Mangifera indica* L. cv. Piqueño). *Molecules* 19, 438–458. DOI: 10.3390/molecules19010438

Ramirez, N.M., Toledo, R.C.L., Moreira, M.E.C., Martino, H.S.D., Benjamin, L.D.A. *et al.* (2017) Anti-obesity effects of tea from *Mangifera indica* L. leaves of the Uba variety in high-fat diet-induced obese rats. *Biomedical Pharmacotherapy* 91, 938–945. DOI: 10.1016/j.biopha.2017.05.015

Ramos, S. (2007) Effects of dietary flavonoids on apoptotic pathways related to cancer chemoprevention. *Journal of Nutritional Biochemistry* 18, 427–442. DOI: 10.1016/j.jnutbio.2006.11.004

Ranganath, K.G., Shivashankara, K.S., Roy, T.K., Dinesh, M.R., Geetha, G.A. *et al.* (2018) Profiling of anthocyanins and carotenoids in fruit peel of different colored mango cultivars. *Journal of Food Science & Technology* 55, 4566–4577. DOI: 10.1007/s13197-018-3392-7

Rasoanaivo, P., Wright, C.W., Willcox, M.L. and Gilbert, B. (2011) Whole plant extracts versus single compounds for the treatment of malaria: synergy and positive interactions. *Malaria Journal* 10, Suppl. 1, S4. DOI: 10.1186/1475-2875-10-S1-S4.

Reyes, L.F. and Cisneros-Zevallos, L. (2007) Electron-beam ionizing radiation stress effects on mango fruit (*Mangifera indica* L.) antioxidant constituents before and during postharvest storage. *Journal of Agriculture and Food Chemistry* 55, 6132–6139. DOI: 10.1021/jf0635661

Richter, D.B., Oh, N.H., Fimmen, R. and Jackson, J. (2007) The rhizosphere and soil formation. In: Cardon, Z.G. and Whitbeck, J.L. (eds.) *The Rhizosphere: an Ecological Perspective*. Elsevier, Cham, Switzerland, pp. 179–200. DOI: 10.1016/ B978-012088775-0/50010-0

Robles-Sánchez, M., Astiazaran-Garcıa, H., Martın-Belloso, O., Gorinstein, S., Alvarez-Parrilla, E. *et al.* (2011) Influence of whole and fresh-cut mango intake on plasma lipids and antioxidant capacity of healthy adults. *Food Research International* 44, 1386–1391. DOI: 10.1016/j.foodres.2011.01.052

Rodriguez-Gonzalez, S.M., Gutierrez-Ruiz, I., Perez-Ramirez, I.F., Mora, O., Ramos-Gomez, M. and Reynoso-Camacho, R. (2017) Mechanisms related to the anti-diabetic properties of mango (*Mangifera indica* L.) juice by-product. *Journal of Functional Foods* 37, 190–199. DOI: 10.1016/j.jff.2017.07.058

Roongpisuthipong, C., Banphotkasem, S., Komindr, S. and Tanphaichitr, V. (1991) Postprandial glucose and insulin responses to various tropical fruits of equivalent carbohydrate content in non-insulin-dependent diabetes mellitus. *Diabetes Research and Clinical Practice* 14, 123–131. DOI: 10.1016/ 0168- 8227(91)90118- w

Rosas Jr, M., Pinneo, S., O'Mealy, C., Tsang, M., Liu, C. *et al.* Kern, M., Hooshmand, S. and Hong M.Y. (2021) Effects of fresh mango consumption on cardiometabolic risk factors in overweight and obese adults. *Nutrition, Metabolism & Cardiovascular Diseases* 32, 494–503. DOI: 10.1016/j.numecd.2021.11.001

Sabater, A.G., Ribot, J., Priego, T., Vazquez, I., Frank, S. *et al.* (2017) Consumption of a mango fruit powder protects mice from high-fat induced insulin resistance and hepatic fat accumulation. *Cell Physiology and Biochemistry* 42, 564–478. DOI: 10.1159/000477606

Saijo, F., Milsom, A.B., Bryan, N.S., Bauer, S.M., Vowinkel, T. *et al.* (2010) On the dynamics of nitrite, nitrate and other biomarkers of nitric oxide production in inflammatory bowel disease. *Nitric Oxide* 22, 155–167. DOI: 10.1016/j.niox.2009.11.009

Saiz, L.C., Gorricho, J., Garjón, J., Celaya, M.C., Erviti, J. and Leache, L. (2020) Blood pressure targets for the treatment of people with hypertension and cardiovascular disease. *Cochrane Database Systematic Review* 9, CD010315. DOI: 10.1002/14651858.CD010315.pub4

Saeedi, P., Petersohn, I., Salpea, P., Malanda, B., Karuranga, S. *et al.* (2019) Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas. *Diabetes Research and Clinical Practice* 157, 107843. DOI: 10.1016/j.diabres.2019.107843

Sakaki, J.R., Rodriguez, N.R., Fernandez, M.L., Puglisi, M.J., Chen, M.H. and Chun, O.K. (2023) Fruit juice and childhood obesity: a review of epidemiologic studies. *Critical Reviews of Food Science and Nutrition* 63, 6723–6737. DOI: 10.1080/10408398.2022.2044284

Saleem-Dar, M.O.P., Chidley, H., Deshpande, A., Giri, A. and Gupta, V. (2016) Nutrient and flavor content of mango (*Mangifera indica* L.) cultivars: An appurtenance to the list of staple foods. In: Simmonds, M.S.J. and Preedy, V. (eds) *Nutritional Composition of Fruit Cultivars*. Academic Press, Cambridge, pp. 445–468. DOI: 10.1016/B978-0-12- 408117-8.00019-2

Samtiya, M., Aluko, R.E., Dhewa, T. and Moreno-Rojas, J.M. (2021) Potential health benefits of plant food-derived bioactive components: An overview. *Foods* 10, 839. DOI: 10.3390/foods10040839

Samuel, V.T. (2011) Fructose induced lipogenesis: from sugar to fat to insulin resistance. *Trends in Endocrinology & Metabolism* 22, 60–65.

Sáyago-Ayerdi, S.G., Zamora-Gasga, V.M. and Venema, K. (2019 Prebiotic effect of predigested mango peel on gut microbiota assessed in a dynamic in vitro model of the human colon (TIM-2). *Food Research International* 118, 89–95. DOI: 10.1016/j.foodres.2017.12.024

Segal, M.S., Gollub, E. and Johnson, R.J. (2007) Is the fructose index more relevant with regards to cardiovascular disease than the glycemic index? *European Journal of Nutrition* 46, 406–417. DOI: 10.1007/s00394- 007- 0680- 9 .

Sekar, V., Chakraboty, S., Mani, S., Sali, V.K. and Vasanthi, H.R. (2019) Mangiferin from *Mangidera indica* fruits reduces post-prandial glucose level by inhibiting α-glucosidase and α-amylase activity. *South African Journal of Botany* 120, 129–134. DOI: 10.1016/j.sajb.2018.02.001.

Selvaraj, Y., Kumar, R. and Pal, D.K. (1989) Changes in sugars, organic acids, amino acids, lipid constituents and aroma characteristics of ripening mango (*Mangifera indica* L.) fruit. *Journal of Food Science and Technology* 26, 308–313.

Sensoy, I. (2021) A review on the food digestion in the digestive tract and the used *in vitro* models. *Current Research Food Science* 4, 308–319. DOI: 10.1016/j.crfs.2021.04.004

Shi, N., Chen, X. and Chen, T. (2021a) Anthocyanins in colorectal cancer prevention review. *Antioxidants* (Basel) 10, 1600. DOI: 10.3390/antiox10101600

Shi, T., van Soest, D.M.K., Polderman, P.E., Burgering, B.M.T. and Dansen, T.B. (2021b) DNA damage and oxidant stress activate p53 through differential upstream signaling pathways. *Free Radical Biology and Medicine* 172, 298–311. DOI: 10.1016/j.freeradbiomed.2021.06.013

Siddhartha, R. and Garg, M. (2021) Molecular and clinical insights of matrix metalloproteinases into cancer spread and potential therapeutic interventions. *Toxicology and Applied Pharmacology* 426, 115593. DOI: 10.1016/j.taap.2021.115593

Singh, R.K., Ali, S.A., Nath, P. and Sane, V.A. (2011) Activation of ethylene-responsive phydroxyphenylpyruvate dioxygenase leads to increased tocopherol levels during ripening in mango. *Journal of Experimental Botany* 44, 1254–1263. DOI: 10.1093/jxb/err006

Smith, A.G., Croft, M.T., Moulin, M. and Webb, M.E. (2007) Plants need their vitamins too. *Current Opinion of Plant Biology* 10, 266–275. DOI: 10.1016/j.pbi.2007.04.009

Srivastava, R.P. (1998) *Mango Cultivation*. International Book Distributing Company, Lucknow.

Surh, Y.J. (2003) Cancer chemoprevention with dietary phytochemicals. *Nature Reviews* 3, 768–780. DOI: 10.18632/oncotarget.9593

Suwimol, S., Pimpanit, L., Aporn, M., Pichita, S., Ratiyaporn, S. and Wiroj, J. (2012) Impact of fruit and vegetables on oxidative status and lipid profiles in healthy individuals. *Food Public Health* 2, 113–118. DOI: 10.5923/j.fph.20120204.06

Suzuki, T. (2020) Regulation of the intestinal barrier by nutrients: The role of tight junctions. *Animal Science Journal* 91, e13357. DOI: 10.1111/asj.13357

Tajik, N., Tajik, M., Mack, I. and Enck, P. (2017) The potential effects of chlorogenic acid, the main phenolic components in coffee, on health: a comprehensive review of the literature. *European Journal of Nutrition* 56, 2215–2244. DOI: 10.1007/s00394-017-1379-1

Tanaka, T., Shnimizu, M. and Moriwaki, H. (2012) Cancer chemoprevention by carotenoids. *Molecules* 17, 3202–3242. DOI: 10.3390/molecules17033202

Tang, S.Y., Whiteman, M., Peng, Z.F., Jenner, A., Yong, E. and Halliwell, B. (2004) Characterization of antioxidant and antiglycation properties and isolation of active ingredients from traditional Chinese medicines. *Free Radical Biology and Medicine* 36, 1575–1587. DOI: 10.1016/j.freeradbiomed.2004.03.017

Tharanathan, R.N., Yashoda, H.M. and Prabha, T.N. (2016) Mango (*Mangifera indica* L.), The king of fruits – An overview. *Food Reviews International* 22, 95–123. DOI:10.1080/87559120600574493

Tong, J., Han, Q., Wang, S., Su, Z., Zheng, D., Shen, P., Xia, S., Huang, X., Shao, Q. and Xu, H. (2012) *Corynebacterium pyruviciproducens*, as an immune modulator, can promote the activity of macrophages and up-regulate antibody response to particulate antigen. *Experimental Biology and Medicine* 237, 1322–1330. 10.1258/ebm.2012.012181.

Trekli, M.C., Riss, G., Goralczyk, R. and Tyrrell, R.M. (2003). Betacarotene suppresses UVA-induced HO-1 gene expression in cultured FEK4. *Free Radical Biology and Medicine* 34, 456–464. DOI: 10.1016/s0891-5849(02)01303-5

Uauy, R. and Valenzuela, A. (2000) Marine oils: the health benefits of n-3 fatty acids. *Nutrition* 16 (7–8), 680–684. DOI: 10.1016/S0899-9007(00)00326-9

United States Department of Agriculture, Agricultural Research Service (USDA) (2019) National nutrient database for standard reference, Release 1 April, Food Data Central. Available at: https://fdc.nal.usda.gov/fdc-app.html#/food-details/169910/nutrients (accessed 14 March 2024)

Vaisman, N., Haenen, G.R., Zaruk, Y., Verduyn, C., Bindels, J.G. *et al.* (2006a) Enteral feeding enriched with carotenoids normalizes the carotenoid status and reduces oxidative stress in long-term enterally fed patients. *Clinical Nutrition* 25, 897–905. DOI 10.1016/j.clnu.2006.06.002.

Vaisman, N., Niv, E. and Izkhakov, Y. (2006b) Catalytic amounts of fructose may improve glucose tolerance in subjects with uncontrolled non-insulin-dependent diabetes. *Clinical Nutrition* 25, 617–621. DOI: 10.1016/j.clnu.2005.11.013.

Vallarino, J.G. and Osorio, S. (2019) Organic acids. In: Yahia, E.M. and Carrillo-López, A., (eds) *Postharvest Physiology and Biochemistry of Fruits and Vegetables*. Elsevier, Cambridge, pp. 207–224.

van Breda, S.G.J. and de Kok, T.M.C.M. (2018) Smart combinations of bioactive compounds in fruits and vegetables may guide new strategies for personalized prevention of chronic diseases. *Molecular Nutrition and Food Research* 62, 1700597. DOI: 10.1002/mnfr.201700597

Varakumar, S., Kumar, Y.S. and Sarathi Reddy, O.V. (2011) Carotenoid composition of mango (Mangifera indica L.) wine and its antioxidant activity. *Journal of Food Chemistry* 35, 1538–1547. DOI: 10.1111/j.1745-4514.2010.00476.x

Variya, B.C., Bakrania, A.K. and Patel, S.S. (2020) Antidiabetic potential of gallic acid from Emblica officinalis: improved glucose transporters and insulin sensitivity through PPAR- γ and Akt signaling. *Phytomedicine* 73, 152906. DOI: 10.1016/j.phymed.2019.152906

Veda, S., Platel, K. and Srinivasan, K. (2007) Varietal differences in the bioaccessibility of b-carotene from mango (*Mangifera indica*) and papaya (*Carica papaya*) fruits. *Journal of Agricultural and Food Chemistry* 55, 7931– 7935. DOI: 10.1021/jf0712604

Wang, D. and Dubois, R.N. (2006) Prostaglandins and cancer. *Gut* 55, 115–122. DOI: 10.1136/gut.2004.047100

Watzl, B., Kulling, S.E., Möseneder, J., Barth, S.W. and Bub, A. (2005) A 4-wk intervention with high intake of carotenoid-rich vegetables and fruit reduces plasma C-reactive protein in healthy, nonsmoking men. *American Journal of Clinical Nutrition* 82, 1052–1058. DOI: 10.1093/ajcn/82.5.1052

WHO/FAO (2003) *Diet, nutrition and prevention of chronic diseases*. Report of a joint WHO/FAO expert consultation. WHO technical report series 916. World Health Organization, Geneva. Available at: http://apps.who.int/iris/bitstream/10665/42665/1/WHO_TRS_916.pdf?ua=1 (accessed 13 June 2024)

Wollowski, G.R. and Pool-Zobel, B.L. (2001) Protective role of probiotics and prebiotics in colon cancer. *American Journal of Clinical Nutrition* 73, 451–455. DOI: 10.1093/ajcn/73.2.451s

Wongmetha, O., Ke, L. and Liang, Y. (2015) The changes in physical, biochemical, physiological characteristics and enzyme activities of mango cv. Jinhwang during fruit growth and development. *Journal of Life Sciences* 72–73, 1–6. DOI: 10.1016/j.njas.2014.10.001

Yahia, E.M. (2011) Mango (*Mangifera indica* L.). In: Yahia, E. (ed.) *Postharvest Biology and Technology of Tropical and Subtropical Fruits. Cocona to Mango*. Elsevier, Cambridge, UK, pp. 492–567.

Yahia, E.M. and Ornelas-Paz, J.J. (2010) Chemistry, stability and biological actions of carotenoids. In: Gonzalez Aguilar, G.A., de la Rosa, L.A. and Alvarez Parrilla, E. (eds) *Fruit and Vegetable Phytochemicals: Chemistry, Nutritional Value and Stability*. Blackwell Publishing, Oxford, UK, pp. 177–222.

Yahia, E.M., Ornelas Paz, J.J. and Ariza Flores, R. (2006) *The Mango* [in Spanish]. Editorial Trillas, México City, Mexico.

Yahia, E.M., De Jesús Ornelas-Paz, J., and Gonzalez-Aguilar, G.A. (2011) Nutritional and health-promoting properties of tropical and subtropical fruits. In: Yahia, E.M. (ed.) *Postharvest biology and technology of tropical and subtropical fruits. Volume* 1. *Fundamental Issues*. Woodhead Publishing, Cambridge, UK, pp. 21–78.

Yahia, E.M., Maldonado Celis, M.E. and Svendsen, M. (2018a) The contribution of fruit and vegetable consumption to human health. In: Yahia, E.M. (ed.) *Fruit and Vegetable Phytochemicals: Chemistry and Human Health*. John Wiley & Sons, Oxford, UK, pp. 3–51.

Yahia, E.M., Ornelas-Paz, J.J., Emanuelli, T., Jacob-Lopes, E., Queiroz-Zepka, L. and Cervantes-Paz, B. (2018b) Chemistry, stability and biological actions of carotenoids. In: Yahia, E.M. (ed.) *Fruit and Vegetable Phytochemicals*. Blackwell Publishing, Oxford, UK, pp. 285–345. DOI: 10.1002/9780813809397.ch7

Yahia, E.M., Garcia-Solis, P., and Maldonado Celis, M.E. (2019a) Contribution of fruits and vegetables to human nutrition and health. In: Yahia, E.M. (ed.) *Postharvest Physiology and Biochemistry of Fruits and Vegetables*. Woodhead Publishing, Cambridge, UK, pp. 19–45.

Yahia, E.M., Carrillo-López, A., and Bello-Pérez, L.A., (2019b) Carbohydrates. In: Yahia, E.M. and Carrillo-Lopez, A. (eds) *Postharvest Physiology and Biochemistry of Fruits and Vegetables*. Woodhead Publishing Co., Cambridge, UK, pp. 175–206.

Yahia, E.M., Carrillo-López, A., Malda-Barrera, G., Suzan-Aspiri, H. and Queijeiro Bolaños, M., (2019c) Photosynthesis. In: Yahia, E.M. and Carrillo-Lopez, A. (eds) *Postharvest Physiology and Biochemistry of Fruits and Vegetables*. Woodhead Publishing Co., Cambridge, UK, pp. 47–72.

Yahia, E.M., Ornelas-Paz, J.J, Brecht, J.K., García-Solis, P. and Maldonado-Celis, M.E. (2023) The contribution of mango fruit (*Mangifera indica* L.) to human nutrition and health. *Arabian Journal of Chemistry* 16, 104860. DOI: 10.1016/j.arabjc.2023.104860

Yang, C.S., Landau, J.M., Huang, M.-T. and Newmark, H.L. (2001) Inhibition of carcinogenesis by dietary. *Annual Reviews of Nutrition* 21, 381–406. DOI: 10.1146/annurev.nutr.21.1.381

Yang, H., Bai, W., Gao, L., Jiang, J., Tang, Y., Niu, Y., Lin, H. and Li, L. (2018) Mangiferin alleviates hypertension induced by hyperuricemia via increasing nitric oxide releases. *Journal of Pharmacological Sciences* 137, 154–161. DOI: 10.1016/j.jphs.2018.05.008

Yap, K.M., Sekar, M., Seow, L.J., Gan, S.H., Bonam, S.R., Mat Rani, N.N.I., Lum, P.T., Subramaniyan, V., Wu, Y.S., Fuloria, N.K. and Fuloria, S. (2021) *Mangifera indica* (Mango): A promising medicinal plant for breast cancer therapy and understanding its potential mechanisms of action. *Breast Cancer* 13, 471–503. DOI: 10.2147/BCTT.S316667.

Zapata-Londoño, M.B., Ramos, A., Alzate-Arbeláez, A.F., Rojano, B.A. and Maldonado-Celis, M.E. (2019) Behaviour of bioactive compounds and antioxidant activity of mango (Azucar cultivar) juice during storage at 4°C. *Revista Facultad Nacional de Agronomía* 72, 8743–8750. DOI: 10.15446/rfnam.v72n1.72628.

Zapata-Londoño, M.B., Ramos-Polo, A., Alzate-Arbeláez, A.F., Restrepo-Betancur, L.F., Rojano, B.A. and Maldonado-Celis, M.E. (2020) Effect of mango (Mangifera indica) cv. Azúcar juice consumption on plasma antioxidant capacity and oxidative stress biomarkers. *Vitae* 27, 1–10. DOI: 10.17533/udea.vitae.v27n1a03

Zapata-Londoño, M.B., Uribe Yunda, D.F, Aguillón Osma, J. and Maldonado-Celis, M.E. (2022) Coffee, ginger and cinnamon. In: Campos-Vega, R. and Oomah, B.D. (eds) *Molecular Mechanisms of Functional Food*. John Wiley & Sons, Hoboken, New Jersey, pp. 404–430.

Zarasvand, S.A., Mullins, A.P., Arjmandi, B. and Haley-Zitlin, V. (2023) Antidiabetic properties of mango in animal models and humans: A systematic review. *Nutrition Research* 111, 73–89. DOI: 10.1016/j.nutres.2023.01.003.

Zhang, M., Hongyu, J., Bin, W., Chao, M., Fatao, H. *et al.* (2023) A prospective review on the research progress of citric acid modified starch. *Foods* 12, 458. DOI: 10.3390/foods1203045

Zhu, Y. and Wang Z. (2024) Association between joint physical activity and healthy dietary patterns and hypertension in US adults: cross-sectional NHANES study. *BMC Public Health* 24, 855. DOI: 10.1186/s12889-024-18346-8

Zou, B., Hailian, W., Liu, Y., Qi, P., Lei, T. *et al.* (2017) Mangiferin induces apoptosis in human ovarian adenocarcinoma OVCAR3 cells via the regulation of Notch3. *Oncology Reports* 38, 1431–1441. DOI: 10.3892/or.2017.5814