Chapter 1
Introducing Chapter: Phytochemicals, Antioxidant Therapy, Opportunities and Challenges

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Abstract The use of phytochemicals for health promotion and disease prevention and treatment has gained increased interest worldwide particularly because of their availability, low cost and minimal side effects. Phytochemicals have a wide range of biological properties such as antioxidative, anti-proliferative, anti-inflammatory and antiobesogenic. They are believed to reduce oxidative stress in the body and the risk of noncommunicable diseases (NCDs). The interest in phytotherapy lies in the use of whole or parts of plants, or plant-derived extracts, containing different antioxidants, which function synergistically and in combination with each other to reduce oxidative stress. There is also an increasing tendency to recommend regular intake of plant-based diets to forestall oxidative stress-induced human diseases. Although the primary strategy of disease prevention should focus on health promotion, there are people in many regions all over the world still dying of preventable and curable diet-related and/or lifestyle-related NCDs, which are often associated with undernutrition, malnutrition, unhealthy lifestyle behaviours and exposure to human-made pollutants. Although multiple strategies are needed to ensure and improve a healthy life, such as changes in dietary habits, food production and consumption, and lifestyle behaviours, physicians and many people are unaware of the benefits of good nutrition based on plant antioxidants that could be used in NCD prevention. This is a challenging area of interest that presents important promise for the near future. Last but not least, feeding a growing world population; fighting hunger, undernourishment and malnutrition; preserving the environment and biodiversity; and producing healthy foods that promote health and prevent diseases are the major global challenges we face today.

Keywords Plants • Phytochemicals • Plant-based diet • Antioxidant therapy • Oxidative stress • Noncommunicable diseases

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1.1 Plants and History of Traditional Medicine

The knowledge of medicinal plants is as old as human early civilization. Plant and animal domestication and the emergence of agriculture in the Fertile Crescent (Upper Mesopotamia), which took place under favourable environmental conditions (Araus et al. 2014), inspired and propelled communities to promote the use of phytotherapy. Indeed, archaeological and textual evidence have revealed that the usage of plants and their derivatives to treat human pathology has contributed to our understanding of the science of medicine and healing that was born in the cradle of flourishing ancient civilizations, Mesopotamia (Borchardt 2002; Kelly 2009), the land (current Iraq) between the Tigris and Euphrates rivers. In more recent time, people around the world have searched and used plants to cure many diseases even before the discovery of a broad range of bioactive phytochemical compounds including antioxidants (Bernhoft 2010; Chikezie et al. 2015).

The number of described flowering plants in the world varies from 223,300 to 315,903 (Chapman 2009), and many of them are valuable sources of therapeutic molecules "medicinal plants" that represent an important reserve for the identification of novel drug leads (Atanasov et al. 2015). Traditional medicine refers to health practices, approaches, knowledge and beliefs incorporating plant-, animal- and mineral-based medicines, spiritual therapies, manual techniques and exercises, applied singularly or in combination to prevent and treat illnesses or maintain well-being (WHO 2008). The key facts reported by World Health Organization (WHO 2008) regarding the use, practices and expenditure of traditional medicine and complementary/alternative medicine in many developed, developing and underdeveloping countries are listed below:

- In China, traditional herbal preparations account for 30–50% of the total medicinal consumption.
- In Ghana, Mali, Nigeria and Zambia, the first line of treatment for 60% of children with high fever resulting from malaria is the use of herbal medicines at home.
- WHO estimates that in several African countries, traditional birth attendants assist in the majority of births.
- In Europe, North America and other industrialized regions, over 50% of the population have used complementary or alternative medicine at least once.
- In San Francisco, London and South Africa, 75% of people living with HIV/AIDS use traditional medicine and complementary/alternative medicine.
- Seventy percent of the population in Canada have used complementary medicine at least once.
- In Germany, 90% of the population have used a natural remedy at some point in their life.
- Between 1995 and 2000, the number of doctors who had undergone special training in natural remedy medicine had almost doubled to 10,800.
- In the United States, 158 million of the adult population use complementary medicines, and according to the US Commission for Alternative and

Complementary Medicines, US$ 17 billion was spent on traditional remedies in 2000.
- In the United Kingdom, annual expenditure on alternative medicine is US$ 230 million.
- The global market for herbal medicines currently stands at over US$ 60 billion annually and is growing steadily.

Currently, there is a renewed and growing interest in plant traditional medicine, mainly in the African continent and Indian subcontinent. An example of traditional medicine, which dates back to about 5000 years ago, is the Ayurveda (science of life) in use today for individuals and communities in the Indian subcontinent. Ayurveda is an easily accessible and natural medical system, which possesses an established body of written knowledge. Ayurveda was recognized by the government of India as a complete health system comparable to allopathic medicine, as well as by the National Institutes of Health (NIH) as a complementary and alternative medicine (Mishra 2004). Ayurveda has a considerable scientific base and therapeutic potential that can be used alone or in addition to conventional healthcare (Mishra 2004). The basic concepts reported in Mishra's book (Mishra 2004) regarding the use of Ayurvedic medicine in developed, developing and underdeveloping countries are listed below:

- Whereas conventional medicine is primarily oriented towards the treatment of disease, Ayurvedic medicine is oriented towards prevention, health maintenance and treatment.
- In conventional medicine, drugs are developed based on the concept that the elimination of specific causes of a disease, such as microorganisms, will cure a disease.
- The belief in Ayurvedic medicine is that a disease is the product of an imbalance in the body and mental elements that reduce the body's resistance to diseases.
- If the imbalance is corrected and the body's defence mechanisms are strengthened by herbal formulas, lifestyle changes and diet, then the body will resist a disease with a goal of eliminating it.
- Herbal and herb mineral products regularly used in Ayurveda are believed to strengthen the body's defences.
- Scientific evidence is gradually developing in support of the Ayurvedic concept.

The antioxidant, anti-inflammatory, anti-atherosclerotic, anti-proliferative, anti-carcinogenic, anti-diabetic or neuroprotective properties of Ayurveda have been extensively studied in humans and animal models, both in vitro and in vivo (Thabrew et al. 2001; Auddy et al. 2003; Chainani-Wu 2003; Kaur et al. 2004; Govindarajan et al. 2005; Reddy et al. 2005; Dhanasekaran et al. 2007; Jurenka 2009; Baliga 2010; Choedon et al. 2010; Krishnaveni and Mirunalini 2010; Mishra et al. 2011; Chahar et al. 2012; Bag et al. 2013; Cock 2015; Riya et al. 2015; Durg et al. 2015; Baliga et al. 2016; Patwardhan and Bhatt 2016; Keshari et al. 2016; Qadir et al. 2016;

Meghwani et al. 2017). A recent report indicates that traditional medicine based on the use of plants can be applied in health promotion, as well as adjuvant therapy to modern medicine in India (Oyebode et al. 2016).

The United Nations (UN) reported that the current world population has exceeded seven billion, and the continent of Africa is the second most populous (UN 2016). Over the past 36 years, Africa's population increased by almost 722 million, from an estimated 478 million in 1980 to 1.2 billion in 2016, and is projected to reach nearly 2.92 billion in 2063 (UN 2016). Such a demographic situation threatens food and health security. In addition, poverty forces people to undernourishment and/or unhealthy diets, which are major risk factors for non-communicable diseases (NCDs). The galloping demography, poverty, undernutrition and lack of basic healthcare are among the reasons why plants and phytotherapy are used and needed by the majority of the population in Africa for healthcare. Traditional medicine using plants became an important medical system for health promotion and disease treatment in Africa (Abdullahi 2011; Moyo et al. 2015; Innocent 2016). Like the Ayurvedic medicine, the African traditional healthcare system also offers a wide variety of phytochemicals proven as antioxidants with anti-inflammatory, anti-proliferative, anti-mutagenic, anti-carcinogenic, anti-hyperglycaemic or anti-diabetic properties (Gyamfi et al. 1999; Ohtani et al. 2000; Okoli and Akah 2000; Gyamfi and Aniya 2002; Osadebe and Okoye 2003; Ojewole 2006, 2007, 2008; Verschaeve and Van Staden 2008; Fawole et al. 2010; Suleiman et al. 2010; Adeyemi et al. 2011; Tamiru et al. 2012; Bothon et al. 2013; Ishola et al. 2014; Mohammed et al. 2014; Ochwang'i et al. 2014; Birru et al. 2015; Sulyman et al. 2016; Zingue et al. 2016; Amuri et al. 2017). In Africa, more than 5400 plant species are used in traditional medicine for the prevention and treatment of various pathologies (Van Wyk 2015).

1.2 Plant Antioxidants

The kingdom Plantae comprises eukaryotic and multicellular organisms, mostly autotrophic. Thanks to sunlight, plants can make their own food via photosynthesis in the chloroplast. Plant cells function to convert the atmospheric carbon dioxide into carbohydrates, fats, proteins and various molecules, which are indispensable for survival of all living organisms. Plants also provide the oxygen required for all aerobic organisms. Plant mitochondria and chloroplasts, functionally linked to cellular respiration and photosynthesis, respectively, are originally derived from endosymbiotic bacteria (Raven 1970; Andersson et al. 1998). In photosynthesis, the light energy brought to the plant cells is used by the chloroplasts to produce glucose ($C_6H_{12}O_6$) and oxygen (O_2) from carbon dioxide (CO_2). Aerobic respiration requires O_2 in order to produce ATP from $C_6H_{12}O_6$ as follow:

- $6CO_2 + 6H_2O \rightarrow C_6H_{12}O_6 + 6O_2$
- $C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + ATP$

Plant cells produce reactive oxygen species (ROS) in chloroplasts and mitochondria as by-products of photosynthesis and respiration (Pitzschke et al. 2006). Under field stress conditions, plants also produced ROS in response to more than one environmental factor at a time. Overproduction of ROS leads to a degradation of key photosynthetic regulatory proteins and can trigger programmed cell death (Demmig-Adams and Adams 2002). Therefore, plants do not survive under extreme environmental stress without producing their own antioxidant defence systems (Foyer and Shigeoka 2011). Plants respond to ROS-generating abiotic (UV radiation, temperature, drought, soil moisture and salinity) and biotic (herbivore, pathogens) environmental stress factors by increasing the synthesis of a wide variety of phytochemicals, also known as secondary metabolites (Suzuki et al. 2014). Phytochemicals are low molecular weight non-enzymatic antioxidants including ascorbate (vitamin C), tocopherols (vitamin E), beta-carotenoids, glutathione and polyphenolic compounds (Bartley and Scolnik 1995; Decker 1997; Noctor and Foyer 1998; Wheeler et al. 1998; Demmig-Adams and Adams 2002; Munné-Bosch and Alegre 2002) that play important roles in the protection of plants against environmental threats and oxidative stress (Ahmad et al. 2010; Gill and Tuteja 2010; Choudhury et al. 2013; Kasote et al. 2015). Plants, plant-based whole foods and plant-derived products contain multitude phytonutrient antioxidants (Asensi-Fabado and Munné-Bosch 2010; Bolling et al. 2010; Chon 2013; Benzie and Choi 2014; Kasote et al. 2015; Škrovánková et al. 2015; Pisoschi et al. 2016; Van Hung 2016). Climatic and seasonal variations, regions of growth, degree of maturity, agriculture practices and postharvest treatment and processing influence the quality of plants and their antioxidant contents (Bolling et al. 2011; Škrovánková et al. 2012; Hur et al. 2014; Wang et al. 2014; McSweeney and Seetharaman 2015; Villa-Rodriguez et al. 2015; Kamiloglu et al. 2016).

1.3 Antioxidants and Phytotherapy

The healthcare systems in developed, developing, underdeveloping low-income countries have primarily focused on discovering and/or using medical drugs to treat and cure diseases. The production of drugs is a time-consuming process and extremely costly. Plants are easily accessible and a low-cost source of therapeutic molecules to a vast majority of world populations. Traditional medicine is now applied in different regions of the world depending on plant resources, human interaction with the natural environment, intercultural exchange and diffusion of traditional knowledge and population's socioeconomic status.

During the last decade, several studies emphasize the central role for ROS, oxidative stress and inflammation in the initiation and promotion of NCDs, including reproductive, gastrointestinal, hepatic, renal, pulmonary, cardiovascular, certain cancer and neurological diseases (Cachofeiro et al. 2008; Reuter et al. 2010; Perše 2013; Piechota-Polanczyk and Fichna 2014; Hawa et al. 2015; Tucker et al. 2015;

Verdile et al. 2015; Wiegman et al. 2015; Xu et al. 2015; Li et al. 2016). Phytochemicals have a wide range of biological activities such as antioxidative, anti-proliferative, anti-inflammatory and antiobesogenic and the concept of using plant antioxidants as effective agents to lower disease risk stemming from excessive production of ROS in the body (Upadhyay and Dixit 2015). Different antioxidants present in plant parts used in phytotherapy include roots, bark, leaves, flowers, fruit, seeds, berries as well as the whole plants, function synergistically and in combination with each other and are therefore much more effective in disease prevention and treatment.

The use of phytochemicals for health promotion, primary healthcare and disease prevention and treatment has gained increased interest worldwide particularly because of their availability, low cost and minimal side effects (WHO 2008; Cordell 2011; Rodriguez-Casado 2016; Shakya 2016). Whole plants are used by various ethnic cultures for their health benefits, as well as sources of medical drugs to prevent and treat NCDs (Howes and Houghton 2003; Abubakar et al. 2007; Ky et al. 2009; Ibarra-Alvarado et al. 2010; Alachkar et al. 2011; Kasabri et al. 2011, 2017; Hajdu and Hohmann 2012; Sawadogo et al. 2012; Semenya et al. 2012; Assaf et al. 2013; Al-Asmari et al. 2014; Kadir et al. 2014; Rokaya et al. 2014; Shil et al. 2014; Subramoniam 2014; Chege et al. 2015; Goyal 2015; Shweta and Boaz 2015; Stanifer et al. 2015; Apaya et al. 2016; Giovannini et al. 2016; Hitziger et al. 2016; Jacobo-Herrera et al. 2016; Ju et al. 2016; Kaufmann et al. 2016; Rastogi et al. 2016; Suroowan and Mahomoodally 2016; Zarshenas et al. 2016a, b; Tandon and Yadav 2017).

1.4 Healthy Plant-Based Diet

A healthy diet must promote health and reduce the incidence and development of nutrition-related disorders and chronic diseases. A healthy plant-based diet comprises essentially of a variety of fruit and vegetables, including legumes, beans, seeds, whole grains and nuts, on one hand, and limited animal products, added saturated and trans fats and refined carbohydrates, on the other hand. This type of diet is believed to lower the risk of coronary artery disease in the Mediterranean and Asian countries (Willett 1994). Finally, a healthy plant-based diet must contain fresh and minimally processed fruit and vegetables, mainly those without pesticides and genetically modified organisms. Following World War II, the use of a wide range of pesticides, including insecticides, fungicides, herbicides, rodenticides, molluscicides, nematicides and plant growth regulators aiming at protecting crops from pests in conventional agricultural systems and enhancing crop yields, has increased dramatically worldwide. The presence of a non-negligible amount of chemicals especially pesticide residues in fruit, vegetables and plant-derived products from the conventional agricultural systems is of a major health concern. Consumers are increasingly aware of health risk associated with the consumption of pesticide-contaminated fruit, vegetables and plant-based foods.

Conventional agriculture cannot meet the nutritional needs of the current and ever-increasing human population without compromising the integrity of the environment. Pesticide residues are now found in soil, air and ground water. Environmental contamination by pesticide residues can adversely affect the life of many beneficial soil microorganisms, insects, plants, fish and birds (Aktar et al. 2009). Compared to conventional farming, organic agriculture is a sustainable production system that essentially maintains soil fertility by crop rotation, intercropping, polyculture, cover crops and mulching, and at the same time, it preserves biodiversity and environment and promotes human health. Although crop yields are 20% lower in the organic agricultural system than in the conventional agricultural system, input of fertilizer and energy was reduced by 34–53% and pesticide input by 97% (Mäder et al. 2002). A meta-analysis of studies provides evidence that organic agriculture enhances richness and abundance of plants, birds and predatory insects (Bengtsson et al. 2005). Over the past two decades, there has been a growing interest in organic products (Willer and Kilcher 2011). According to the International Federation of Organic Agriculture Movements (IFOAM), organic agriculture should be guided by four principles (Gomiero et al. 2011). The four principles of organic agriculture, established by the IFOAM (Luttikholt 2007), are:

- The Principle of Health—Organic agriculture should sustain and enhance the health of soil, plant, animal and human as one and indivisible.
- The Principle of Ecology—Organic agriculture should be based on living ecological systems and cycles, work with them, emulate them and help sustain them.
- The Principle of Fairness—Organic agriculture should build on relationships that ensure fairness with regard to the common environment and life opportunities.
- The Principle of Care—Organic agriculture should be managed in a precautionary and responsible manner to protect the health and well-being of current and future generations and the environment.

Besides providing healthy vegetables, the organic agriculture system is more sustainable than conventional agriculture system because they allow higher soil fertility and biodiversity (Gabriel et al. 2013), as well as being less dependent on external inputs. Many areas in different regions of the world such as Oceania, Europe and South and North America become organic farmland again.

1.5 Antioxidants and Prevention of Noncommunicable Chronic Diseases

Of the 57 million global deaths in 2008, 36 million were due to NCDs, and nearly 80% of NCD deaths occurred in low- and middle-income countries, of which 29% were among people under the age of 60 years (WHO 2011). The key facts regarding NCDs reported by WHO (WHO 2014) are:

- NCDs currently cause more deaths than all other causes combined, and NCD deaths are projected to increase from 38 million in 2012 to 52 million by 2030.
- Four major NCDs (cardiovascular diseases, cancer, chronic respiratory diseases and diabetes) are responsible for 82% of NCD deaths.
- Approximately 42% of all NCD deaths globally occurred before the age of 70 years; 48% of NCD deaths in low- and middle-income countries and 28% in high-income countries were in individuals aged under 70 years.

Unhealthy diets, alcohol consumption, tobacco smoking, second-hand smoke exposure and insufficient physical activity are the major risk factors for health disorders and NCDs, including obesity, hyperglycaemia, diabetes, hyperlipidaemia, raised blood pressure, cardiovascular diseases, respiratory diseases and cancers. Unhealthy nutritional patterns collectively termed the "Western dietary pattern", including intake of high-fat and high-cholesterol diets, fatty domestic red meats, refined vegetable oils, highly refined sugars and salt and consumption of processed, fast foods and alcohol, promote many of the chronic disorders and diseases, such as obesity, cardiovascular disease and cancer (Cordain et al. 2005). Contrary to the Western diet, the Mediterranean diet is low in saturated and trans fatty acids but contains plentiful plant foods, including fruit, vegetables, breads, nuts, seeds and olive oil. There is nowadays an increasing tendency to recommend regular intake of plant-based diets to forestall medical conditions, such as obesity, prenatal and postnatal disorders and complications, diabetes, cardiovascular disease, cancer, Alzheimer's disease (AD) and ageing (Tuso et al. 2013). Nutritional strategies for prevention of health disorders and NCDs are summarized below.

1.5.1 Early Life Origin of Obesity

The programming of adult obesity by intrauterine food restriction was identified 40 years ago in a historical cohort study of 300,000 men born from mothers exposed to the Dutch famine of 1944–1945 (Ravelli et al. 1976). Currently, obesity is a global public health threat that affects people of all ages, sexes and racial/ethnic groups (Chan and Woo 2010) that contributes to a global burden of NCDs and mortality (Savini et al. 2013). Widespread overweight and obesity were estimated to affect nearly 1.5 billion adults in 2008 (Popkin et al. 2012) and more than 1.9 billion adults in 2014 (WHO 2015). The key facts regarding obesity and overweight reported by WHO (WHO 2015) are:

- Worldwide obesity has more than doubled since 1980.
- In 2014, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 600 million were obese.
- 39% of adults aged 18 years and over were overweight in 2014, and 13% were obese.

- Most of the world's population live in countries where overweight and obesity kill more people than underweight.
- Forty-one million children under the age of 5 were overweight or obese in 2014.
- Obesity is preventable.

Obesity is characterized by mitochondrial dysfunction, low antioxidant defences, increased ROS production, systemic oxidative stress, organ dysfunction and health disorders (Fernández-Sánchez et al. 2011), including hyperlipidaemias, atherosclerosis, hypertension, insulin resistance, hyperglycaemia and inflammation, which in combination play a significant role in the development and progression of NCDs, such as infertility, type 2 diabetes, non-alcoholic fatty liver disease, obstructive sleep apnea, coronary artery disease, stroke, peripheral arterial disease, cardiomyopathy, congestive heart failure and cancer (Savini et al. 2013). Maternal obesity also increases the risk of a number of pregnancy complications, including gestational diabetes, gestational hypertension, foetal macrosomia, large for gestational age, postpartum retention and perinatal morbidity and mortality (Moussa et al. 2016). Maternal obesity and excessive gestational weight gain influence foetal development and contribute to long-term metabolic consequences of children born to obese pregnant mothers (Stang and Huffman 2016). Faced by the rising prevalence of obesity and its related prenatal and postnatal disorders and complications that potentially predispose the infant to adult disease through foetal programming (Moussa et al. 2016), there is an urgent need for lifestyle and nutritional strategies to promote general health and prevent obesity, including weight loss, physical activity and a shift towards plant-based antioxidant-rich diets.

Periconceptional nutrition and dietary antioxidants are important for early developmental processes, mainly embryogenesis, placentation and foetal health and organ development (Cetin et al., 2010; Mistry and Williams 2011; Twigt et al. 2012; Al-Gubory 2013). Nutritional strategies before and during pregnancy that combat environmental factor-induced maternal and foetal oxidative stress can promote prenatal development, improve foetal health and reduce the onset and development of pathologies in adulthood. An interesting strategy is the adherence to the Mediterranean-type dietary pattern that enhances fertility (Toledo et al. 2011). Therefore specific nutritional formulas that are designed to reduce oxidative stress need to be developed and promoted for obese patients. Further research is needed to establish whether intake of a plant-based antioxidant-rich diet can prevent obesity before and during pregnancy and its associated prenatal and postnatal health complications and disorders.

1.5.2 Diabetes

Over the last three decades, the epidemic of diabetes has become a major worldwide public health concern. Diabesity, an association of obesity and diabetes, is the leading cause of NCDs. Type 2 diabetes and associated conditions known as "metabolic

syndrome" increased dramatically worldwide particularly due to changes in lifestyle behaviours, including a significant decline in physical activity and frequent sedentary behaviour (Zimmet et al. 2001). Obesity is associated with an increased risk of developing insulin resistance, dysfunction of pancreatic islet beta cells and failure to control blood glucose levels and type 2 diabetes (Kahn et al. 2006). The key facts regarding diabetes reported by WHO (WHO 2016a) are:

- The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014.
- The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014.
- Diabetes prevalence has been rising more rapidly in middle- and low-income countries.
- Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.
- In 2012, an estimated 1.5 million deaths were directly caused by diabetes, and another 2.2 million deaths were attributable to high blood glucose.
- Almost half of all deaths attributable to high blood glucose occur before the age of 70 years. WHO projects that diabetes will be the seventh leading cause of death in 2030.
- Healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use are ways to prevent or delay the onset of type 2 diabetes.
- Diabetes can be treated and its consequences avoided or delayed with diet, physical activity, medication, regular screening and treatment for complications.

The cost of diabetes in the United States of America (USA) is estimated to be more than US$ 174 billion per year in 2007, and the US diabetes prevalence rate is likely to increase dramatically over the next 30 years (Boyle et al. 2010). The world cost of diabetes is more than US$ 827 billion (WHO 2016a). In addition to high cost of treating diabetes, synthetic antihyperglycaemic agents have adverse side effects, such as hypoglycaemia, weight gain and hepato-renal toxicity. Therefore, many efforts are ongoing to discover low-cost, plant-derived natural products with hypoglycaemic property. The antihyperglycaemic property together with antioxidant activity of fruit, fruit peels, leaves and bark of many plants selected on the basis of their availability is established in experimental animals (Nain et al. 2012; Shivanna et al. 2013; Colomeu et al. 2014; Ali et al. 2015; Gondi et al. 2015; Joshi et al. 2016; Keshari et al. 2016). Clinical trials and animal studies suggest that fruit flavonoids have a favourable effect in management of diabetes without compromising cellular homeostasis and importantly with minimal side effects on the body (Tanveer et al. 2017).

1.5.3 Cardiovascular Diseases

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels, including coronary heart disease (heart attacks), cerebrovascular disease (stroke), raised blood pressure (hypertension), peripheral artery disease, rheumatic

heart disease, congenital heart disease and heart failure. The major causes of CVDs are unhealthy dietary habits and unhealthy lifestyle behaviours, such as tobacco smoking, alcohol consumption, insufficient physical activity and/or physical inactivity. The key facts reported by World Health Organization (WHO 2016b) regarding CVDs are:

- CVDs are the number one cause of death globally: more people die annually from CVDs than from any other cause.
- An estimated 17.5 million people died from CVDs in 2012, representing 31% of all global deaths. Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke.
- Over three quarters of CVD deaths take place in low- and middle-income countries.
- Out of the 16 million deaths under the age of 70 due to NCDs, 82% are in low- and middle-income countries, and 37% are caused by CVDs.
- Most cardiovascular diseases can be prevented by addressing behavioural risk factors such as tobacco use, unhealthy diet and obesity, physical inactivity and harmful use of alcohol using population-wide strategies.
- People with cardiovascular disease or who are at high cardiovascular risk (due to the presence of one or more risk factors such as hypertension, diabetes, hyperlipidaemia or already established disease) need early detection and management using counselling and medicines, as appropriate.

A well-balanced and healthy diet is of utmost importance for prevention of CVDs (Verlangieri et al. 1985; Law and Morris 1998; Kromhout 2001). Plants and plant-derived products are rich sources of polyphenols that promote cardiovascular health. Inflammation underlies the molecular basis of atherosclerosis. Flavanols have a range of cardiovascular-protective properties by modulating pro-inflammatory cytokine production, eicosanoids synthesis and platelet activation (Selmi et al. 2008). The anti-inflammatory and antioxidant effects of cocoa flavanols and other phenolic compounds explain, at least in part, the beneficial effects of cocoa on blood pressure, activity of platelets and leukocytes, flow-mediated vasodilatation and/or vascular function that collectively improve cardiovascular health and/or reduce CVD risk in healthy adults (Fisher et al. 2003; Engler et al. 2004; Heptinstall et al. 2006; Schroeter et al. 2006; Shiina et al. 2009), healthy smokers (Hermann et al. 2006), hypertensives (Grassi et al. 2005, 2008), hypercholesterolaemic postmenopausal women (Wang-Polagruto et al. 2006) and overweight men and women (Esser et al. 2014; West et al. 2014). A prospective study using data from the European Prospective Investigation into Cancer (EPIC)-Norfolk cohort suggests that higher chocolate intake is associated with a lower risk of future cardiovascular events among healthy men and women (Kwok et al. 2015). A Japanese cohort studies support a significant inverse association between chocolate consumption and risk of developing stroke in women (Dong et al. 2017).

Adoption of the Mediterranean diet reduces the risk of developing coronary heart disease in the elderly (Dontas et al. 2007). Adherence to a Mediterranean diet increases plasma levels of carotenoids, vitamin A and vitamin E (Azzini et al. 2011). The antioxidant (Mancini et al. 1995; Ghiselli et al. 1997) and anti-inflammatory

(Mena et al. 2009) effects of the Mediterranean dietary pattern can explain the low incidence of coronary heart in Mediterranean (Estruch et al. 2006, 2013; Turati et al. 2015) and non-Mediterranean populations (Tektonidis et al. 2015; Tong et al. 2016; Stefler et al. 2017).

1.5.4 Cancer

Globally, the number of people with cancer is projected to double by the year 2030, with most of this increase likely to occur in middle- and low-income countries of Africa and Asia (WCRF 2007). Almost 90–95% of cancers have their roots in exposure to environmental pollutants including heavy metals, particulate matter, ozone, sulphur oxides, carbon monoxide and nitrogen oxides (Sørensen et al. 2003; Huang et al. 2004; Møller et al. 2008; Wise et al. 2008; Yang and Omaye 2009) and also due to unhealthy lifestyle behaviours (Anand et al. 2008), including intake of diet high in fats, free sugars, salt, processed foods and red meat, as well as cigarette smoking, alcohol consumption and physical inactivity (Irigaray et al. 2007; Anand et al. 2008). Therefore, cancer is a preventable disease that requires major changes in lifestyle behaviours. The key facts regarding cancer reported by WHO (WHO 2017) are:

- Cancer is one of the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases in 2012.
- The number of new cases is expected to rise by about 70% over the next two decades.
- Cancer is the second leading cause of death globally and was responsible for 8.8 million deaths in 2015. Globally, nearly one in six deaths is due to cancer.
- Approximately 70% of deaths from cancer occur in low- and middle-income countries.
- Around one third of deaths from cancer are due to the five leading behavioural and dietary risks: high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use and alcohol use.
- Tobacco use is the most important risk factor for cancer and is responsible for approximately 22% of cancer deaths.
- Cancer-causing infections, such as hepatitis and human papilloma virus (HPV), are responsible for up to 25% of cancer cases in low- and middle-income countries.
- Late-stage presentation and inaccessible diagnosis and treatment are common. In 2015, only 35% of low-income countries reported having pathology services generally available in the public sector. More than 90% of high-income countries reported treatment services are available compared to <30% of low-income countries.
- The economic impact of cancer is significant and is increasing. The total annual economic cost of cancer in 2010 was estimated at approximately US$ 1.16 trillion.

- Only one in five low- and middle-income countries have the necessary data to drive cancer policy.

The suggested cancer-protective effect of fruit and vegetable antioxidants is attributed to their ability to scavenge ROS and prevent DNA damage and subsequent mutation (Collins 1999). A balanced plant-based diet with a variety of fruit and vegetables can lower the risk for many types of cancer (La Vecchia et al. 2001; Donaldson 2004; Vainio and Weiderpass 2006; Liu et al. 2013; Maasland et al. 2015; Wang et al. 2015; Mut-Salud et al. 2016; Vieira et al. 2016). Polyphenols and carotenoids are of particular interest because they can reduce the risk of prostate (Giovannucci et al. 1995; Davalli et al. 2012), lung (Mayne et al. 1994; Shareck et al. 2017), breast (Freudenheim et al. 1996; Eliassen et al. 2012; Braakhuis et al. 2016; Yan et al. 2016), colon (Slattery et al. 2000), ovary (Zhang et al. 2007), liver (Darvesh et al. 2012), cervical (Di Domenico et al. 2012), oesophagus (Ge et al. 2013) and pancreas (Huang et al. 2016) cancer. Antioxidant compounds in plant extracts can play a preventative role against oxidative stress-induced mutation of DNA and development of cancer (Makhafola et al. 2016). In Europe, the Mediterranean diet is an important nutritional pattern of choice for cancer prevention (Giacosa et al. 2013; Grosso et al. 2013). The Mediterranean diet is naturally rich in chemopreventive agents, including polyphenols and carotenoids (Pelucchi et al. 2009; Scoditti et al. 2012), and may play a role in preventing skin (Fortes et al. 2008), breast (Trichopoulou et al. 2010; Hoffmann and Schwingshackl 2016), uterus (Filomeno et al. 2015), lung (Hodge et al. 2016) and colorectal (Rosato et al. 2016) cancer.

1.5.5 Ageing and Alzheimer's Disease

The free radical theory of ageing postulates that accumulated insults of biological systems during the ageing process induce damage of vital cellular macromolecules, which contribute to the decline in organ functional efficiency and onset of age-related complications and diseases (Harman 1956). Ageing is characterized by a decline in the efficiency of antioxidative defences and a progressive inability of organs to defend against environmental stressors. The accumulation of cellular ROS and the consequent oxidative modification of biological molecules have been proposed as responsible for the ageing process (Finkel and Holbrook 2000). Mitochondrial DNA (mtDNA) mutations and deletions play a role in the ageing process (Sastre et al. 2003; Lee and Wei 2012).

Life expectancy has markedly increased (~27 years) during the last three decades, mainly in developed and developing countries (Hayflick 2000). Therefore, health maintenance of the ageing population has become an economic and social concern. In addition, progressive loss of the ability to walk is associated with a decline in physical and social activities and a loss of independence. Longer lifespan will lead to a considerable increase in medical spending. Alzheimer's disease (AD) is the most common neurodegenerative disease in the

elderly. The lack of an effective treatment of AD is a real challenge due to its rising prevalence, and therefore preventive strategies of this chronic disease become a priority in many countries. AD patients have lower plasma levels of phytochemical antioxidants including folate vitamin A, vitamin B12, vitamin C and vitamin E (Jeandel et al. 1989; Lopes da Silva et al. 2014). Therefore, multiple antioxidant intervention strategies might be beneficial for the maintenance of a good cognitive function. In addition to the preventive effects of physical exercise against cognitive decline and the risk of dementia with age advancement (Paillard 2015), there is evidence suggesting that adopting healthy lifestyle behaviours and early intervention strategies, including intake of a balanced plant-based diet rich in antioxidants, can promote healthy ageing and may reduce risk for chronic age-associated diseases, mainly AD (Polidori et al. 2009; Arab and Sabbagh 2010; Shah 2013; Vassallo and Scerri 2013; Barnard et al. 2014).

1.6 Conclusions

Prevention of diseases requires a change in mindset from "live to eat" to "eat to live in a good health". This could prevent us from suffering the heavy physical and psychological consequences of many preventable and curable diet-related and/or lifestyle-related NCDs for which conventional medicinal and surgical care costs will be more and more expensive. Multiple strategies are needed to ensure and improve a healthy life, such as changes in dietary habits, food production and consumption and lifestyle behaviours. Physicians and many people are unaware of the potential benefits of healthy nutrition based on plants rich in antioxidant molecules. This is a challenging area of interest that holds important promise for the near future. Currently, the use of natural antioxidants in the prevention of oxidative stress-related NCDs is in its infancy and requires intensive investigations.

National and international policies should be directed towards sustainable agriculture to meet the need for healthy foods and diets. Feeding a growing world population; fighting hunger, undernourishment and malnutrition; preserving the environment and biodiversity; and producing healthy foods that promote health and prevent diseases are the major global challenges we face today. Another palpable challenge is climate change, which will reduce the availability of viable agricultural land. Under these conditions, the demand for water, agricultural land and food will increase considerably in the world. Last but not least, another major challenge for food security is the rapid growth of the world's population.

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