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Review

Are South African Wild Foods the Answer to Rising Rates of Cardiovascular Disease?

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Abstract: The rising burden of cardiovascular disease in South Africa gives impetus to managerial changes, particularly to the available foods in the market. Since there are many economically disadvantaged groups in urban societies who are at the forefront of the CVD burden, initiatives to make healthier foods available should focus on affordability in conjunction with improved phytochemical diversity to incentivize change. The modern obesogenic diet is deficient in phytochemicals that are protective against the metabolic products of sugar metabolism, i.e., inflammation, reactive oxygen species and mitochondrial fatigue, whereas traditional southern African food species have high phytochemical diversity and are also higher in soluble dietary fibres that modulate the release of sugars from starches, nurture the microbiome and produce digestive artefacts that are prophylactic against cardiovascular disease. The examples of indigenous southern African food species with high horticultural potential that can be harvested sustainably to feed a large market of consumers include: *Aloe marlothii*, *Acanthosicyos horridus*, *Adansonia digitata*, *Aloe ferox*, *Amaranthus hybridus*, *Annesorhiza nuda*, *Aponogeton distachyos*, *Bulbine frutescens*, *Carpobrotus edulis*, *Citrullus lanatus*, *Dioscorea bulbifera*, *Dovyalis caffra*, *Eleusine coracana*, *Lagenaria siceraria*, *Mentha longifolia*, *Momordica balsamina*, *Pelargonium crispum*, *Pelargonium sidoides*, *Pennisetum glaucum*, *Plectranthus esculentus*, *Schinziophyton rautanenii*, *Sclerocarya birrea*, *Solenostemon rotundifolius*, *Talinum caffrum*, *Tylosema esculentum*, *Vigna unguiculata* and *Vigna subterranea*. The current review explains the importance of phytochemical diversity in the human diet, it gives a lucid explanation of phytochemical groups and links the phytochemical profiles of these indigenous southern African foods to their protective effects against cardiovascular disease.

Keywords: antioxidant; phytochemical; microbiome; anti-inflammatory; nutrition; diabetes; nutraceutical; functional food; flavonoids; polyphenols

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1. Introduction

Cardiovascular disease (CVD) accounts for 31% of deaths globally, making it one of the biggest challenges to human health in the modern era [1]. At a global scale, the average percentage of people diagnosed with CVD has been steadily rising during the 20th century, so it is necessary for interventions to be enacted with a vision of halting or reversing this trend. While CVD was initially considered a disease of the 'western world', in the last 50–70 years there has been a significant rise in other countries, such as China [2], Iran [3] and sub-Saharan Africa [4,5].

The highest percentage of people living with CVD is still in the 'the west', but mortality from CVD has reached a plateau and is decreasing [6]. The increase to the global average rate of mortality, therefore, is due to the rising rate in developing nations, such as South Africa [7]. It is noteworthy that the problem of rising diagnosis rates of CVD in non-Western countries started several generations after countries such as the UK, USA and Australia. A popular theory to explain this phenomenon is that the 'western diet' and lifestyle were assimilated into those societies more recently in history, delaying the trans-generational consequences of the atherogenic lifestyle [8].

The South African people now face a similar CVD burden as in the developed world, but statistics and reporting are not yet able to corroborate the full extent of the problem [9]. Nevertheless, prioritizing for intervention has been put forward as a matter of urgency [7]. Understandably, hitherto antiretroviral therapies have been the priority in South Africa's health research, which has taken the focus away from the increasing burden of CVD.

While it is firmly established that CVD is related to the atherogenic 'western' diet [10,11], atherogenic eating does not always create immediate negative consequences in first and second generations that transition into the Western diet. It does, however, create epigenetic modifications (histone acetylation) that are passed down in progeny and accumulated in successive generations [12]. This increases genetic susceptibility to CVD in family lineages over time [13]. The South African people have transitioned into the Western lifestyle and atherogenic eating in waves, with geographically specific trends related to urbanization [14]. Adoption of an atherogenic lifestyle is a consequence of socioeconomic obstacles [15] and detachment from traditional lands [14].

The Western diet is characterized by sweeter foods, i.e., foods that have been selected specifically for propagation in agriculture due to higher satiation and lower bitterness. However, the excluded bitter principle derives from the phytochemicals that affect taste but confer protective cardiovascular effects that 'health-compensate' for the fat, sugar or carbohydrate content of the foods [11]. Evidently, removal of the bitter component of foods reduces the quality of the nutritional package by excluding the principle that modulates the release of energy from starch and sugar and protects against the reactive oxygen species generated in mitochondrial respiration (utilization of the energy) [11,16,17], among others, such as probiotic effects [18].

Western foods are also processed to remove the less aesthetic components, such as the bran from wheat or molasses from sugar cane. Consumers prefer the foods that are refined for maximum satiety, because of a desire to feel full at a faster rate while enjoying the sweetness of the food item. Unfortunately, the processing of foods for maximum satiety creates a meal that is low in minerals, vitamins, fibres and plant phytochemicals (bitters), thereby converting the sugar/starch and fat fraction from a potential nutritional package to a serving of mere calories [19].

Modern lifestyles that are dominated by the Western diet are characterized by regular caloric loading, low phytochemical content and less regular exercise. The lack of space between meals (no intermittent fasting) causes a rate of caloric loading that limits time for a redox balance to be reached in organs and tissues between meals. The consequences include the accumulation of reactive oxygen species (ROS) as by-products of starch/sugar metabolism [17,20]. High caloric loading also triggers a change to the metabolism of glucose, favoring the polyol pathway that generates lipids [17], increasing the risk for the formation of advanced glycation end products (AGEs) [21]. ROS and AGEs promote fatty liver disease and confer inflammatory effects to the body's tissues. Inflammation in tissues nullifies the effect of insulin, creating acute insulin resistance, and from there further problems develop, such as CVD [20,21], among others.

In other parts of the world, scientists have started the process of putting phytochemicals back onto society's food plate. This is carried out either in the form of a nutraceutical, a supplement, a breed of vegetable with high anthocyanin content (purple cauliflowers) or a 'superfood' that is a wild crop relative, introduced into agriculture. Foods can also be fortified with nutrients, but industries often practice fortification merely for advertisement purposes, with a phytochemical content that is less than the requirement for true benefit [22,23]. Unfortunately, this has made the fortification and supplementation initiative controversial, and researchers are encouraging a return to nutritional foods [24]. This is corroborated by the many examples of plant extracts used as food supplements that fail to deliver the entire nutritional package of the raw material [22,23].

Hence, by far it is better to invest in wild foods that are protective against CVD. South Africa has many examples of nutritional foods [25,26] that have phytochemical profiles that are theoretically prophylactic against CVD. The nutritional advantage can be interpolated

from the chemical groups present, either known from other studies for their benefit or prospective due to mechanistic/structural overlap with known beneficial metabolites. The current review gives some pharmacological interpretations of a selection of the potential vegetable and fruit crops that South Africans could be trialing on a larger scale.

2. Cardiovascular Disease, Comorbidities and Pre- or Probiotics

The epidemiology of CVD can be thought of in terms of the numbers of people living with CVD as a proportion of those who progress to mortality. Analysis of the cross-section of diagnosis versus mortality reveals a difference between developed and developing nations. Those living with CVD in developed nations are having longer lives, i.e., in the UK and USA mortality from CVD peaked in the 1960's and then started to decline, continuing to the present day [27]. This improvement in survival is due to the availability of treatments that are keeping people with CVD alive. In contrast, those living with CVD in developing nations, such as South Africa, are vulnerable to a higher rate of mortality [28], particularly those in lower socioeconomic areas.

Early diagnosis, surgical intervention and the availability of modern pharmaceuticals have played a significant role in increasing the lifespan of those living with CVD in developed nations. However, in the same countries, the improvement to health education has seen a rise in the numbers of people who are making better dietary and lifestyle choices, not only to prevent the disease but also to improve prognosis of those living with the disease.

Lifestyle and dietary changes are the preferred method of improving the status of CVD in any human population, either through prevention or improvement to quality-of-life following diagnosis. However, the development and utilization of pharmaceuticals to treat CVD is more active than the initiatives to bring about changes that prevent the formation of the disease. Pharmaceutical approaches to CVD may utilize lipid-lowering drugs, antihypertensives, antiplatelet and anticoagulation therapies [1]. Research that corroborates the efficacy of these pharmaceuticals uses measures of blood or urine biomarkers. These same biomarkers are also used to assess the viability of plant-based foods or phytochemicals in improving risk factors for CVD or symptoms.

Thus, research of phytochemicals or nutraceuticals that are protective against CVD commonly describe antioxidant activity, antiplatelet activity [29], vasorelaxant, anti-hyperlipidaemic, anti-uraemic, antithrombotic and diuretic effects [30]. Newer methods include inhibition of a variety of processes and enzymes, which include angiotensin converting enzyme (ACE) [31,32], ferroptosis [33], 'A Disintegrin and Metalloproteinases' (ADAM) [34] (such as ADAM17) [35] and matrix metalloproteinases (MMP) (such as MMP-9) [36,37].

2.1. Characteristics of Cardiovascular Diseases

The three main traits of cardiovascular degeneration, that form the basis of several diseases under the umbrella of CVD, include either hardening of arteries (through atherosclerotic plaque) or the opposite, softening of the artery walls (aneurysms), and thirdly, increased risk of blood clotting (thrombosis).

When hardening of the arteries is advanced enough to create health complications it is diagnosed as atherosclerotic cardiovascular disease. This process occurs through accumulation of plaque inside arteries. The plaque layer is a conglomerate of fat, cholesterol and calcium, which hardens and becomes insoluble. As the plaque grows over time the arteries become narrower, and circulation of oxygen-rich blood to organs is limited, creating numbness in the extremities and heart problems. The diseases that are associated with atherosclerosis include coronary heart disease (angina, heart attacks, heart failure; i.e., myocardial infarction) and peripheral arterial disease (numbness, ulcers, cramping) [38].

Atherogenic eating has been clearly linked to the progression of the plaque accumulation process [39]. Atherosclerotic plaque is potentially reversible in early stages of development [40,41], but there is limited evidence of reversibility when the plaque matures [41,42],

requiring surgical intervention to break it to facilitate its removal. Cholesterol-lowering pharmaceuticals (i.e., statins) are put forward as the conventional line of treatment to reverse early-stage atherosclerosis and to slow or halt the progression in late stages [41]. There are many botanical ingredients that can also lower cholesterol, such as stanols, sterols [43] and soluble non-starch polysaccharides [44,45], making it feasible that dietary changes toward suitable plant-based interventions can reverse early atherosclerosis and stabilize advanced cases.

When softening or weakening of the arteries progresses to a point of health-risk, aneurysms may form, which are bulges in the artery walls that risk rupturing. Ruptures can be small or big, leading to strokes, internal bleeding and other life-threatening complications. The diseases that represent considerable risk include strokes in general, transient ischaemic attack (mini stroke) and aortic disease (aortic aneurysm).

Although counterintuitive, softening and hardening of artery walls commonly occur together in individuals with CVD, meaning candidates with atherosclerotic plaque may also experience aneurysm. Theories deliberate over whether one causes the other, if they are the same disease or if they are associated merely by the same lifestyle factors as comorbidities [38]. Modern pharmaceuticals used to reduce risk of aneurysm are angiotensin-converting enzyme inhibitors (or angiotensin 2 receptor blockers), which reduce blood pressure [46]. There are many natural products that are known to inhibit angiotensin-converting enzyme [47], reiterating the importance of phytochemical diversity in the diet as prophylactic of CVD.

Atherosclerotic plaque and aneurysm also commonly occur with blood clotting, known as 'thrombosis' or 'deep vein thrombosis' [48]. The disease symptoms of thrombosis are similar to that of a ruptured aneurysm or the atherosclerotic condition, which makes prima facie diagnosis difficult without the use of imaging techniques. Common symptoms are pain, warmth, redness and swelling of the lower extremities [49]. Nevertheless, due to the co-occurrence of thrombosis with plaque and aneurysm, thrombosis also may be associated with heart attack, strokes in general, transient ischemic attack (mini stroke) and peripheral arterial disease (painful, discolored and cold limbs).

Clinical anticoagulants are used as part of pharmaceutical intervention against thrombosis, including heparin [50], but symptom treatment is the major focus of thrombosis complications in medicine. Natural products should not be considered as anything other than prophylactic, and a possible area of therapeutic intervention is in resolving chronic systemic inflammation, particularly because of the link between inflammatory leukocytes and thrombosis etiology [51].

The three major characteristics of CVD, plaque, aneurysm and thrombosis can create similar symptoms, but the treatment strategies after diagnosis will differ significantly. To confound further, there are differences between ethnic groups according to the type of CVD diagnosed [52]. Racial disparities between CVD pathogenesis may be partly related to the different lifestyles and risk factors that are reflective of culture [53], in combination with the atherogenic lifestyle brought about by the globalization process, creating epigenetic changes that are passed on through the generations [12]. However, it may be argued that in CVD prophylaxis the benefits of dietary intervention are non-discriminatory of race or culture.

Many diseases that are not classified under the umbrella of CVD are regarded as a comorbidity or risk factor for CVD. Such diseases include subclinical magnesium deficiency [54], kidney disease or uremia [55], insulin resistance, metabolic syndrome [56], diabetes [57], hypertension and dyslipidemia [58], inflammatory bowel disease [59], osteoporosis or loss of bone mineral density [60] and chronic obstructive pulmonary disease [61]. A common denominator of all such complications is chronic systemic inflammation, and it is possible that resolving systemic inflammation removes the risk of CVD progression. A similar concept was put forward by one group of authors who recognized that the comorbidities of CVD generate systemic inflammation and go on to argue that analysis of cohort studies supports the notion that general inflammation can lead to heart disease [59].

In this regard, anti-inflammatory dietary components, such as various flavonoids [62], higher terpenoids such as carotenoids [63], volatile sesquiterpenes [64] and phenols generally [65], may be useful in CVD prophylaxis, and the diversity of anti-inflammatory compounds highlights that efficacy is not limited to a mere few specific compounds.

2.2. The Links between Gut and CVD

Gastrointestinal bacterial dysbiosis is strongly linked with CVD [66]. Dysbiosis occurs with an imbalance of gut bacteria, which triggers symptoms of digestive disturbance. This may include 'small intestinal bacterial overgrowth' (SIBO), inflammatory bowel disease and chronic inflammation in more serious cases, but milder symptoms may involve bloating, cramping, indigestion, diarrhea or constipation.

An interaction known as the gut–kidney–heart triangle is dependent upon a trio of health between the associated organs. In this scenario, the gastrointestinal system can impact the cardiovascular and renal system. Gut microbiota are strong participants in this crosstalk, and disruption will impact cardiovascular function. On the converse, negative changes to the renal or cardiovascular system will impact the gut. Since each of these organs impact the other, enough of a disruption to the function of any one many initiate a positive feedback loop, sometimes referred to as a 'vicious cycle' [67].

The way in which the gut microbiome can impact CVD is initiated by local inflammation, as it can eventuate in leakage of bacterial lipopolysaccharides into the intestinal mucosal or epithelial barrier and transverse to become systemic [67]. In more severe cases, live bacteria can escape the gut lumen and translocate into circulation and partake in the etiology of atherosclerosis and myocardial infarction [68]. Thus, the use of pre- or probiotics can be justifiably linked to prophylaxis of CVD by strengthening the intestinal epithelial barrier through the generation of digestive artefacts and also through the modulation of the bacterial species index [69]. A greater diversity of species is protective against systemic inflammation [70], as demonstrated in Chinese centenarians [71].

The concept of the gut–kidney–heart triangle is often referred to as an 'axis', which highlights that there are interdependent triggers between the organs. There are many axis identified, such as the gut–brain axis [72], the neuro-immune axis [73] and the gut–renal axis [74]. Disruption to the latter gut–renal axis is considered to be a significant participant in CVD, because it often leads to hypertension [74]. Nevertheless, there are several axes that have been given due consideration in the context of the pathogenesis of CVD [67].

2.3. Plants as Prebiotics

Both pro- and prebiotics are being explored as measures to improve gastrointestinal health and improve CVD prognosis. However, probiotics are generally not derived from plants but are rather given as bacterial cultures. Hence, this discussion is aligned to the prebiotic polymers and tannins that are derived from plants. Prebiotics can be defined as a food source for favorable species of bacteria, to increase the population density and create a healthy gut microbiome [75].

The prebiotics from plants are diverse, ranging from tannins to polymers, minerals and vitamins. Most research has focused on the polymers, which are present in the diet as either non-digestible soluble fibre that is digested by microbes, and polyphenol polymers, such as tannins [76]. In this regard, diets that include ellagitannins and procyanidins confer prebiotic effects, coming from nuts, such as almonds [77], as well as berries and grapes [78].

Non-digestible soluble fibre is evidently not digested with human enzymes, so they become food for able colonic bacteria. They are generally carbohydrates that are sometimes also referred to as 'dietary fiber' or water-soluble oligosaccharide polymers and hydrogels. Examples of these in plants include β-glucan recovered from wheat germ [79], fructooligosaccharide from yacon [80], glucomannan from konjac [81], galactomannan from fenugreek [82] and acemannan from *Aloe vera* [44,83].

Probiotics are digested into derivatives during microbial digestion, conferring further therapeutic effects to the epithelial barrier of the intestines before entering into systemic cir-

culation where other health-conferring effects can occur. When procyanidins are digested, phenyl-γ-valerolactones are the main artefacts [84], whereas digestion of ellagitannins and catabolism of ellagic acid produces urolithins [85]. From dietary fibres, the artefacts of microbial digestion include various short-chain fatty acids (propionic and butyric acids) [77].

There are various phenyl-γ-valerolactone derivatives that have been linked with anti-inflammatory effects, as well as improved cognitive function [84] and platelet modulation [86], with the latter potentially attenuating occasions of thrombosis. There are also various urolithin derivatives that also confer anti-inflammatory effects [85], in addition to normalization of lipid profiles [87]. The short-chain fatty acids, such as butanoic acid, propanoic acid and others, have been recognized in various positive contexts, particularly improving gut barrier function, but after absorption into circulation they suppress appetite (increase satiation), attenuate insulin resistance, lower cholesterol and reduce body mass [88].

3. General Phytochemical Classes That Protect against Cardiovascular Disease

While the cultivated foods of the world have changed under selective pressures in agriculture, led by the demand for sweeter more satiating foods in the market, there are many foods in the Western world that have retained nutritional attributes. A recent systematic review identified three plant foods that may be associated with CVD prevention (prophylaxis). These are the tomato, cranberry and pomegranate [89]. Therapeutic and prophylactic effects are due to the higher expression of phytochemicals that confer favorable cardiovascular effects, such as lycopene [90], anthocyanins [91] and the phloroglucinol class [92], respectively.

Nevertheless, South Africa is home to a substantial 'wild foods market' that has not been the subject of selective pressures in agriculture. While the modern paradigm in the West considers fruits, vegetables and nuts [93] as most important in CVD prophylaxis, species of South African origin have been hardly considered, due to the limited availability to the global market. This challenge is not faced by South African people [26], who enjoy the benefit of exclusive access to the wild natives for the purpose of cultivation and propagation.

While vitamins, minerals and metal chelates are an important aspect of CVD prevention and treatment, evidence for the efficacy of isolated or synthesized versions is very limited [94]. While it is true that they benefit in cases of deficiency [95], either clinical or sub-clinical [54], the same vitamins and minerals in the whole plant package may be of greater benefit [96,97], for reasons such as antagonisms or synergisms [96].

Alternatively, modern fruits and vegetables in the market may not contain the vitamin and mineral content that is currently believed, because of chemical and mineral differences in biota according to geography [98], light and water availability [99] or cultivar and chemotype [100–102]. Reduced chemical diversity in food crops is recognized as a 'quality' issue [103]. The quality of modern food crops may also be affected by weather patterns [103] that would not normally impact wild crops [104]. While there is limited nutritional advantage to a reduced harvest from the conventional foods of today, many wild food crops express an increase to their chemical diversity under abiotic stress [105], even when the crop yields are negatively affected [106].

Phytochemicals that are significant in the context of CVD prophylaxis include the flavonoids, phenols, organosulfur compounds, lignans, sterols, phloroglucinols and the dietary fibres.

3.1. Flavonoids: Diversity and Pharmacokinetics

Modern fruits and vegetables have low levels of flavonoids, yet flavonoids are the most rigorously researched in the context of health augmentation [107]. Multiple types of flavonoid confer anti-inflammatory [108], antioxidant [109] and antithrombotic effects [110]. For example, a meta-analysis demonstrated a 14% reduction to the rate of stroke in men who took orally 20 mg a day of a flavonol [111].

The flavonoids group is diverse, and the diversity is increased through glycosylation. The diversity of the flavonoid aglycones can be categorized in the following way: flavones, flavanones, flavonols, isoflavones, isoflavanones, flavanols (catechins), chalcones, anthocyanins and procyanidins [112]. Through glycosylation, the diversity of these aglycones increases significantly, ranging from monosaccharides (e.g., glucose, rhamnose, ribose, fructose, galactose, etc.) to disaccharides or polysaccharides.

Flavonoids as glycosides are pharmacokinetically different by comparison with the aglycones [23]. For example, aglycones tend to be easily absorbed across the intestinal barrier, enter circulation and are quickly metabolized in the liver to the form of a glucuronide (a glucuronic acid is attached as an ester to a hydroxyl group). The glucuronide is circulated in blood plasma and slowly eliminated via the kidneys or returned to the colon for further metabolic elimination. However, during the sojourn through the body's tissues, the glucuronide may come into contact with an enzyme called β-glucuronidase, which returns the flavonoid to its aglycone form, at which point it can enact biological effects locally. The expression of β-glucuronidase is increased in inflamed tissues, and while this mechanism reduces androgen glucuronides to free androgens for anti-inflammatory effects, the same mechanism is enacted against the flavonoid glucuronides [113–117].

Glycosides are generally not as efficiently absorbed as the aglycones, but the sugars are cleaved off in the digestive process. An exception to this is the monosaccharide flavonoid (one sugar), which is easily absorbed in the small intestine following the hexose transport pathway; however, some flavonoid monosaccharides will not be absorbed and subsequently reduced to an aglycone before absorption. The disaccharides (two sugars) are poorly absorbed and will be reduced before entering portal circulation. Flavonoids with multiple sugars will also follow the same process [23].

3.2. Flavonoids: Fortification of Diets

Dietary fortification with flavonoids is becoming common practice in most societies, marketed as nutraceuticals. A common flavonoid is biochanin A [118], which is extracted from red clover (*Trifolium pratense*) but is common in vegetables from the legume and *Brassica* families. Biochanin A is marketed as a phytochemical that confers protective effects against the comorbidities of CVD. Some of the biochanin A is also absorbed without modification. As a phytoestrogen, it is a selective agonist of the estrogen receptor [118]. This may explain the alleged positive outcome in candidates with age-related cardiovascular disorders. However, biochanin A may be thought of as a prodrug, since microbial digestion converts it into genistein or daidzein; then, daidzein may be further converted into equol in people who drink high amounts of green tea [119]. Equol is a flavanol that is held in high regard as protective against CVD [120].

There are several other flavonoids that are used in food fortification strategies, such as the isoflavones genistein and daidzein, which are extracted from soy and celery (also produced from digestion of biochanin A), quercetin, which is extracted from onion, red grapes, citrus fruits, broccoli, cherries and apples and kaempferol, which is extracted from broccoli and radishes [118].

3.3. Flavonoids: Anthocyanins and Fortification of Foods

Society's fortification strategies have also involved the reintroduction of anthocyanin pigment to vegetables. Anthocyanins are a visibly colored form of a flavonoid that is normally present as the color of flower petals, autumn leaves and blueberries. They are typically found in a mixture of different types of aglycones and glycosides [121].

An example of an initiative to put anthocyanins back into the human diet is the breeding efforts to put the purple color into the flower head of cauliflowers. These cauliflowers express *p*-coumaroyl and feruloyl esters of cyanidin-3-sophoroside-5-glucoside in the flower head [122] due to encoding of the gene BoMYB2 [123]. The purple-headed cauliflowers existed previously as a smaller vegetable known as the Sicilian purple variety; however, the common white-headed cauliflower that is known as a curd was created by selective

breeding, which removed the anthocyanin pigment in exchange for a bigger flower head. This was achieved by breeding the Sicilian purple variety with a cabbage [124]. The return of color to the flower head was not achieved with genetic modification, but rather genetic analysis was used to guide breeding to bring about expression of recessive genes [125].

3.4. Phenols or Polyphenols

Technically, a flavonoid is a subgroup of the phenols; however, convention tends to regard phenols as the non-flavonoid phenols. Not all chemists are in agreement on a distinction between flavonoids and phenols, because flavonoids, such as phenols, are structures with aromatic rings, with one or more hydroxyl groups attached to an aromatic ring or rings, creating a slightly acidic molecule. Nevertheless, for the sake of clarity, phenols are treated as non-flavonoid phenols in the current review.

The stilbene resveratrol is a phenol that acts as a phytoalexin in grapes subjected to attack by a parasite from the genus *Botrytis* [126]. Resveratrol was put forward as the most promising bioactive metabolite behind the 'French Paradox' [127]. This paradox was identified and publicized in 1992 when it was observed that the French people were less susceptible to CVD yet had a diet that was high in fat. It was postulated that the regular drinking of red wine in the French population could be linked to this apparent contradiction [128]. Red wine is rich in phenols, including tannins and resveratrol, but because resveratrol is less common, research focused on the biological effects of this latter stilbene, which demonstrated in vitro and in vivo corroboration of the anticipated outcome [129], and clinical evidence was produced to support a role in prophylaxis of CVD [130].

Several other phenols are implicated in prophylaxis of CVD, including epigallocatechin gallate from green tea (a flavanol-phenol ester), caffeic acid from olives or propolis, rosmarinic acid from rosemary, chlorogenic acid from coffee, curcumin from turmeric and gallic acid from gallnuts. The biological effects of these phenols or their metabolic derivatives are similar albeit milder than resveratrol, by attenuation of chronic low-grade inflammation of the body's tissues and organs, by quenching reactive oxygen species, opposing platelet aggregation and reducing the production of advanced glycation end products [131].

3.5. Organosulfur Compounds

There are many small organosulfur compounds expressed in onions, garlic and cruciferous vegetables that are regarded as prophylactic for CVD [132]. Two common classes of organosulfur compound are isothiocyanates and sulfoxides. Two prominent sulfoxides from onion and garlic are derivatives of the amino acid cysteine, which are alliin and its product allicin. Both of the latter two sulfoxides have empirical corroboration of efficacy against cardiovascular disorders. Because of the combination of the sulfoxides with the dietary fibres in onion, they attenuate gut dysbiosis, which has positive implications against chronic kidney disease [133], via the gut–kidney–heart triangle.

The isothiocyanates are produced by the action of the enzyme myrosinase, which produces them from a glucosinolate precursor. Myrosinase separates the glucose from the glucosinolate by enzymatic hydrolysis at the thioglucoside link, producing the isothiocyanate product and a sugar [134]. In onions and cruciferous vegetables, slicing, crushing or mastication (if eating) breaks open cells, and the barrier between myrosinase and the glucosinolate precursor is removed. If the vegetable is eaten raw (by an animal or human), the enzyme and precursor will be mixed during chewing, at which point one may experience a sudden boost of flavor. A list of the isothiocyanates that are significant in health are sulforaphane, allyl isothiocyanate, benzyl isothiocyanate, phenethylisothiocyanate and goitrin [135].

3.6. Alkaloids

The alkaloids are the chemical group most associated with dramatic physiological effects, some of which are poisonous, while others can be therapeutic or benign. Abuse of alkaloids can also be associated with adverse cardiovascular and cerebrovascular events, for example, a performance enhancement alkaloid ephedrine is now banned in the US due to adverse events, as people abused the drug to experience stamina and weight loss [136].

Thus, alkaloids with recognized therapeutic attributes are best used intermittently or at reasonable doses. A group known as the berberine alkaloids are relatively safe and well-known for both lipid- and glucose-lowering effects [137]. Another alkaloid, known as colchicine, that is normally used to treat gout and osteoarticular pain (familiar Mediterranean fever) has recently demonstrated promise in reducing the severity of CVD [138]. Colchicine has a long history of human use in the form of a bulb-like corm from *Colchicum autumnale*. The corm is described as a medicine in the Egyptian Ebers Papyrus (1500 BCE) [139]. Another alkaloid with a long history of use is present in the husk fibre of the coconut (*Cocus nucifera*), which was used in traditional Nigerian medicine. A recent pharmacological study demonstrated that it lowers HDL cholesterol in mice [140].

3.7. Lignans

Lignans are widely distributed in the plant kingdom, particularly in legumes, seeds and grains. They are produced by a condensation of two cinnamic acid derivatives, i.e., two phenols. Some well-known lignans include matairesinol, secoisolariciresinol, pinoresinol and lariciresinol. Lignans sometimes occur as glycosides, for example, secoisolariciresinol diglucoside from flax seed [141]. Dietary lignans tend to be metabolized into 'enterolignans' by gut microbiota. It is the enterolignans that are believed to be protective against CVD by attenuating or improving hypertension and hypercholesterolemia [142].

3.8. Sterols

As previously mentioned, foods are fortified with sterols to tackle the problem of cholesterol. This is often carried out using sitosterol, stigmasterol or campesterol. If consumed, all three of these will lower low-density lipoprotein cholesterol (LDL-C, also known as non-HDL-C). The mechanism behind this is via reduction to the amount of cholesterol absorbed from the intestines [143]. While a recent meta-analysis on phytosterols in CVD improvement was inconclusive on the evidence [144], the in vivo animal studies have persuaded the European Atherosclerosis Society to publish its recommendation to use phytosterols in challenging the problem of LDL-C.

3.9. Tannins

Tannins are constructed of phenols, commonly around a core sugar molecule but not as a rule. Tannins are very common in the plant kingdom, particularly in geophytes, tree bark and fruits such as pomegranate and grapes. Tannins can be divided as hydrolysable and condensed. Hydrolysable tannins that are common include ellagitannins, which are constructed of ellagic acid and sometimes gallic acid, and then there are gallotannins, which are constructed of gallic acid, and lastly phlorotannins, which are constructed of phloroglucinols.

Hydrolysable tannins are quickly degraded in stomach acid, reducing them to their simpler phenols, such as ellagic acid, gallic acid or phloroglucinol, respectively. Ellagic and gallic acid are partially absorbed from the intestine, but a large amount is catabolized by gut microbes into smaller molecules. Ellagic acid is reduced to either urolithin A or B, and gallic acid is catabolized to pyrogallol [145]. Alternatively, phloroglucinol enters portal circulation without catabolism. Phloroglucinol is also an artefact of the catabolism of quercetin [146]. After entering portal circulation, phloroglucinol has a short half-life as it is quickly conjugated in phase two liver processes [147].

The prophylactic effects of phenols in CVD were defined in the subsection on phenols. However, phloroglucinol, one of the simplest phenols, demonstrates anti-platelet

activity in vitro. The activity is related to inhibiting the production of thromboxane A_2 [92]. Similarly, extracts of pomegranate that are rich in tannins and phenols have demonstrated platelet aggregation inhibition at physiologically relevant concentrations [148].

3.10. Dietary Fibre

As mentioned earlier, dietary fibre is a good prebiotic; however, dietary fibre also modulates the glycaemic index of starchy foods, which helps to stabilize blood sugar levels [149]. This occurs by slowing gastric emptying and delaying the action of digestive enzymes, so that the glucose released in starch digestion is at a moderate pace, giving the pancreatic insulin release time to respond [82,150]. Thus, foods that are either fortified with or contain fructooligosaccharide [80], galactomannan [82], glucomannan [81], acemannan [83] or β-glucan [79] are better for health by reducing chances of diabetic complaints, which is a comorbidity and potential risk factor of CVD.

4. South Africa's Healthy Wild Foods with Horticultural Potential

While the most comprehensive review of South African indigenous food plants listed 1740 items [151], a narrower review of the food and beverage items that are on a natural trajectory toward entering cultivation gave a list of 126 items, either as condiments, teas or nutritious foods [26]. Among those listed, fruits, grains, nuts and tubers represent nutritional items that could serve as substitutes for lesser nutritious items of the modern staple diet. It is estimated that 95% of wheat consumed in the world is from *T. aestivum*, and this corresponds to the species eaten as a staple in South Africa. Over several hundred years, this grass has saved an innumerable number of people from famine, but now that it is available in excess, processed to increase satiety and sown in mineral-deficient soils [54], it is regarded as a suspect in the modern health crisis [152]. However, South Africa is home to many grass species that provide grains that can be used as healthier alternatives [25]. A few of these will be elaborated on in the following text.

Teas and condiments, on the other hand, increase the phytochemical diversity of one's palate. For example, the addition of *Mentha longifolia* (L.) Huds. to a meal, or taken as a tea, will add to the diet several compounds such as monoterpenes (i.e., menthol) and a variety of phenols, such as rosmarinic acid, and flavonoids, such as apigenin, luteolin and rutin [153]. Another food condiment not mentioned in the above review is *Pelargonium crispum* (P.J.Bergius) L'Hér., which is rich in citral (geranial and neral) and pinocembrin, a flavanone with known health benefits [154].

The nutritional attributes of indigenous food plants, teas and condiments are evident by reading through the published literature, but it is of essence that they are available to the lower socioeconomic communities, so that these alternatives are incentivized in the communities at risk of CVD development. Inspiration can be taken from neighbouring countries where nutritious indigenous fruits are sold on roadsides and have become dietary staples in remote communities, as well as economically important items. For example, in the Kalahari a fruit known in the local vernacular as *tsama* (*Citrullus lanatus* (Thunb.) Matsum. and Nakai) is central to the survival of local communities. In Namibia, the *nara* (*Acanthosicyos horridus* Welw. ex Benth. and Hook.f.) occupies a similar nutritional niche, as does *mongongo* (*Schinziophyton rautanenii* (Schinz) Radcl.-Sm.) in Botswana.

Incidentally, *C. lanatus* is the common watermelon that is available in home gardens and the marketplace worldwide, and it is also native to South Africa [26]. The flesh of the watermelon is comprised of a high sugar content, but it also has a rich phytochemical profile, particularly of terpenoid origin. The most common variety of *C. lanatus* that is eaten in the Kalahari has a yellow flesh, unlike the variety that is popularized over the world, which has a reddish pink flesh [25].

The red color of the flesh is due to >0.4% lycopene, the same component that puts the red color in tomato, and a similar albeit slightly lower amount of β-carotene [155]. These terpenes are known for CVD prophylaxis, particularly by reversing oxidative stress. However, there is limited information on the phytochemical character of the yellow-flesh variety

eaten by the people of the Kalahari. It is noteworthy that a study in the 1960s reported an unusually high number of Kalahari bushmen at all ages with healthy blood pressure levels [156], and this group of people have not hitherto been mentioned in the rising burden of CVD in the southern African peoples. Thus, *C. lanatus* might be considered an example of a food item that combines sugar with a phytochemical package that enables the body to tolerate the oxidative challenges derived in sugar metabolism. Further phytochemical work is necessary to characterize the chemical diversity of the flesh of this species.

World foods that derive from Africa, such as the watermelon, represent worldwide successes, but the current narrative seeks to elaborate on the lesser-known foods of South Africa (naturalized of native) that could achieve agricultural status, particularly within the country as a benefit to the health of the people. A small selection of promising candidates (Table 1) is given here under the subcategories of South African dietary fibres, greens for cooking, grains, fruits, roots, nuts and beans. The nutritional advantages of these are discussed in the following sections as a snapshot of the wider potential of wild foods in southern Africa.

Table 1. A summary of the wild foods that are reviewed, and the mechanism of health benefit interpreted from the groups of phytochemicals present in the food item.

Species	Category	Details	Health Benefit
Aloe marlothii A.Berger	Fibre	Anthraquinones drained out, fibre I.D., possibly galactomannan	Prebiotic
Acanthosicyos horridus Welw. ex Benth. and Hook.f.	Fruit	Sterols (dihydroxycucurbitacin)	Cholesterol lowering
Adansonia digitata L.	Fruit	Rich source of calcium, fibre, polyphenols	Probiotic and protective to the liver
Aloe ferox Mill.	Fibre	Anthraquinones drained out, fibre I.D., possibly galactomannan	Prebiotic
Amaranthus hybridus L. *	Leafy vegetable	Magnesium, β-carotene, protein (17%)	Protects thyroid function, aids in metabolism, source of amino acids after digestion
Annesorhiza nuda (Aiton) B.L.Burtt	Tuber (starch)	Phenylpropanoid rich starch	Anti-inflammatory
Aponogeton distachyos L.f.	Vegetable (flower, young fruit)	flavonoids and dietary fibre	Protects mitochondria, prophylactic for insulin resistance
Bulbine frutescens (L.) Willd.	Fibre	Source of dietary fibre	Prebiotic
Carpobrotus edulis (L.) N.E.Br.	Fibre	Source of dietary fibre	Prebiotic
Citrullus lanatus (Thunb.) Matsum. and Nakai	Fruit	Specific variety not studied, staple food for Kalahari bushmen	n.d.
Dioscorea bulbifera L., *	Tuber (starch)	Low GI starch: polyphenols	Protects mitochondria, prophylactic for insulin resistance
Dovyalis caffra (Hook.f. and Harv.) Hook.f.	Fruit	High phytochemical diversity, including polyphenols	Anti-inflammatory
Eleusine coracana (L.) Gaertn.	Grain	Low GI grain: polyphenols	Protects mitochondria, prophylactic for insulin resistance
Lagenaria siceraria (Molina) Standl.	Vegetable (fruit)	Phenolic glycosides	Antioxidants and anti-inflammatory
Mentha longifolia (L.) Huds.	Condiment	Rich in flavonoids	Antioxidants and anti-inflammatory
Momordica balsamina L.	Vegetable (fruit)	Phytochemically diverse	Protects mitochondria, prophylactic for insulin resistance

Table 1. *Cont.*

Species	Category	Details	Health Benefit
Pelargonium crispum (P.J.Bergius) L'Hér.	Condiment	Flavonoids and citral	Anti-inflammatory
Pelargonium sidoides DC.	Tuber (starch)	Sitosterol and tannins	Lowers cholesterol absorption. Catabolism of ellagic acid produces urolithins
Pennisetum glaucum (L.) R.Br.	Grain	Low GI grain: polyphenols	Protects mitochondria, prophylactic for insulin resistance
Plectranthus esculentus N.E.Br.	Tuber (starch)	Low GI starch: polyphenols	Protects mitochondria, prophylactic for insulin resistance
Schinziophyton rautanenii (Schinz) Radcl.-Sm.	Kernel	Protein	Novel amino acids profile
Sclerocarya birrea (A.Rich.) Hochst.	Fruit	High phytochemical diversity, including polyphenols	Anti-inflammatory
Coleus rotundifolius (Poir.) A.Chev. and Perrot (syn. *Solenostemon rotundifolius* (Poir.) J.K.Morton) *	Tuber (starch)	Low GI starch: polyphenols	Protects mitochondria, prophylactic for insulin resistance
Talinum caffrum (Thunb.) Eckl. and Zeyh.	Leafy vegetable	Vitamin C, calcium, iron	Nutrition: protective against deficiencies
Tylosema esculentum (Burch.) A.Schreib	Bean, fibre, starch	Tuber: source of dietary fibre. Bean: source of protein rich in basic (high pH) amino acids	Tuber: prebiotic. Bean: digestion produces bioactive peptides
Vigna unguiculata (L.) Walp	Bean	Protein-rich in basic amino acids	Lysine-rich peptides stimulate tissue rejuvenation
Vigna subterranea (L.) Verdc.	Bean	Protein-rich in basic amino acids	Lysine-rich peptides stimulate tissue rejuvenation

* Naturalized exotic.

4.1. South African Dietary Fibres

South Africa is home to many species that produce high yields of dietary fibres that are valued by the Xhosa, Sotho and Zulu people. The Cape aloe (*Aloe ferox* Mill., Asphodelaceae) and the very similar mountain aloe (*A. marlothii* A.Berger) are two of the world's richest sources of galactomannan [157], which is similar to acemannan, the dietary fibre that constitutes the gel from *Aloe vera*. Both the Cape and mountain aloes boast succulent leaves that reach an average length of 50–70 cm. In contrast with *A. vera*, these species are a much richer source of anthraquinone 'bitters' that require removal by draining from the leaf [25] prior to processing the leaf flesh as a topical gel or drink. The 'bitters' are dominated by an anthraquinone that is not present in *A. vera*, together with aloe emodin and related derivatives [158]. The bitters are concentrated by boiling and used in therapeutic applications [159], whereas the residual compounds that remain in the flesh of the leaf add a mild digestive benefit when taken orally. The leaves are 'filleted' to remove the skin, and the flesh is blended with fruits or made into a juice to augment the health benefit.

In light of the prophylactic effects from dietary fibres, such as acemannan, glucomannan or galactomannan from species of *Aloe*, it may be of benefit to fortify common foods that contain wheat flour, such as breads and cakes. Such an initiative would reduce the glycemic index of the food item and add the digestive benefit of short-chain fatty acids produced via microbial digestion of the fibre [11].

A much smaller species that expresses a soluble fibre is *ibhuca* (*Bulbine frutescens* (L.) Willd.) (Asphodelaceae). This species is used similarly to *A. vera* for topical applications to promote skin healing and moisturizing. There is little chemical information on the species

and sparing records of its use in food [26]; however, it is similarly dominated by a hydrogel that contains anthraquinones, though the types of anthraquinones [160] are very different to those in aloe. Because plantations have been successfully established in Limpopo [25], this species may represent a renewable commodity and should be investigated in the context of disease prophylaxis through dietary fortification.

Another indigenous succulent is known in vernacular as common sour fig (*Carpobrotus edulis* (L.) N.E.Br.) (Aizoaceae). This species is the only one with a yellow flower, distinguishing it from several other southern African species such as *C. acinaciformis* (L.) L.Bolus, which all have pink, purple or rarely white flowers and are all also used as sources of edible fruits to some extent [25], but the yield is not sustainable to industry. However, similar to the patented method used to extract galactomannan from the Cape aloe [157], *C. edulis* (or other species) could become a useful source of dietary fibre. Fibres can be extracted into a hot aqueous matrix that is filtered to remove solids and then, with the addition of ethanol, the fibres precipitate. If the process is repeated, the fibres can be obtained in relatively high purity and then used accordingly.

Marama bean (*Tylosema esculentum* (Burch.) A.Schreib.) (Fabaceae) is known for its bean as a food source [161]; however, it grows from a large tuber, ranging in size from 50 g in young specimens to 200 kg in mature specimens [25], and in one case the size was recorded at 277 kg [162], with a water content of 81%. The root has a soluble fibre content of 4% (in dried specimens), making it comparable to the earlier cultivars of sweet potato [163]. For this reason, this potential food crop might be thought of as a source of dietary fibre that is combined with digestible starches for energy and nutrition. Fortification of breads or wheat flour with flour from the tuber of *T. esculentum* may improve the nutritional quality of these grains, attaining similar physical attributes to those achieved with other members of Fabaceae [164].

4.2. South African Greens for Cooking

The advantage associated with cultivating edible greens for commercialization is that they are fast-growing, making them a viable agricultural commodity. Several of the South African edible greens can be grown more easily than common spinach, making them a versatile and nutritious alternative to spinach with more horticultural potential, as they require less maintenance and drought tolerance in many circumstances. Edible greens are generally low in sugar and contain moderate amounts of starch and dietary fibre.

A good example is the exotic but naturalized species marog, *Amaranthus hybridus* L. (Amaranthaceae), because it represents an economically viable crop, which should make the product available to the lower socioeconomic peoples. While half of the dry mass of marog is carbohydrate for energy and 8.6% fibre, it has a protein content of 17.9%, making it comparable to some legumes, and for every 100 g of leaf it contains >230 mg of magnesium, which is comparable to an over-the-counter supplement. The β-carotene content is 3.3 mg per 100 g [165], which is comparable to the levels in other foods that are considered good candidates in prophylaxis of CVD, aside from carrot (at 8.3 mg). Thus, marog should be promoted as a nutritious and economically viable food for lower socioeconomic South Africans and as a health option for economically able people.

The tuberous species known in the vernacular as osbossie, *Talinum caffrum* (Thunb.) Eckl. and Zeyh., (Talinaceae ex. Portulacaceae), produces a herbaceous fleshy stem and leaves that have been utilized as edible greens by people of east and southern Africa since before contact by the European peoples [25,26]. A few records were found that reported use of the tuber as a snack food or source of water [151,166], describing it as having an onion-type aroma but comparing its nutritional attributes to that of the sweet potato. However, the fleshy leaves may underscore a sustainable agricultural initiative that is the preferred option, as there are many tuberous species in southern Africa that have more economic value, from the perspective of propagation and nutritional advantage to the consumer. Nevertheless, all plant parts were a major source of food for the Nama people of the upper Karoo [166]. While the aerial parts of osbossie are poorer in energy, they are quite high in

vitamin C, calcium and iron [167]. It has been suggested that they are eaten as a condiment to more energy dense food items, adding variety, taste and nutrition to staple meals.

A food item with a niche market is waterblommetjies, *Aponogeton distachyos* L.f. (Aponogetonaceae). This is an aquatic species that is available in the Cape, not only as a historically significant species used in stews by the pioneers but as an attractive local cuisine to the tourists. It is available on the market in canned form, i.e., as part of the range from the 'All Gold' brand [25]. The part eaten is the flower head and young fruit [26]. Because this food item is dependent upon aquacultural farming, it is not feasible for it to reach a grand scale in commerce; however, those who can attain it will appreciate the nutraceutical value described by Pieterse and Millan [168].

Some greens that are comparable to vegetable fruits include balsam pear, *Momordica balsamina* L. (Cucurbitaceae) and bottle gourd *Lagenaria siceraria* (Molina) Standl. (Cucurbitaceae). These two items are compared to the cucumber and pumpkin/squash, respectively; however, both the fruit and leaves are more often cooked rather than eaten raw [25]. To the former, *M. balsamina* expresses leaves that are rich in minerals, and a phytochemically dense fruit containing triterpenes [169], flavonoids, saponins and cardiac glycosides, among others [170]. The dense phytochemical profile of groups that are known to be protective against systemic inflammation and hyperglycemia makes it a good candidate for CVD prophylaxis. To the latter, *L. siceraria*, a dense profile of phenolic glycosides has been characterized from the fruits/vegetables that are known for anti-oxidant activity [171] but are nonetheless in a class of metabolites that are protective against a range of health challenges via multiple mechanisms [11]. While these greens are utilized in a traditional context in southern Africa, the propagation for agriculture in other parts of the world exemplifies the potential these two vegetables have in the societies of South Africa.

4.3. Southern African Grains (Poaceae)

Suitable alternatives to wheat, particularly refined wheat, have found a niche in the health foods market. However, motivating the lower socioeconomic community to choose these healthier options is a challenge, i.e., choosing one type of bread or cake over another presents a challenge if the healthier choice is more expensive. At present, the most affordable starches on the market are maize meal (mealie meal) and white breads [172]. For this reason, the healthier grain alternatives can only be made available to the lower socioeconomic communities as part of a government initiative or through community-level work that ensures availability of alternatives in bakeries at affordable or competitive prices.

The two best examples of grain alternatives in South Africa are African finger millet, *Eleusine coracana* (L.) Gaertn. (Poaceae), and pearl millet *Pennisetum glaucum* (L.) R.Br. (Poaceae). The former, finger millet, originates from East Africa, and the latter, pearl millet, was originally from central Sub-Saharan Africa. Both are currently farmed in South Africa and available in the market at a higher price, compared to maize or wheat flours [172]. Two nutritional advantages of these crops are that they are gluten free and have a high dietary fibre content ranging from 8–9% [173] or 13.0–13.8% [174]; however, because most of the dietary fibre in the millets is insoluble, it is better to think of the millets as a source of polyphenols (up to 3%) that are prophylactic for CVD. These specialized metabolites compensate for the lack of soluble dietary fibre by slowing down the digestion of the starch, which is another way that the glycemic index of the meal is improved [175]. Furthermore, millet polyphenols are potent antioxidants and are anti-inflammatory [175]. In other parts of the world, millet is accessed by lower socioeconomic groups, meaning it is feasible that such access can be granted to the urban lower socioeconomic groups of South Africa, but this is yet to be realized [172].

4.4. South African Fruits

Some of South Africa's food items may be marketed as healthy to international visitors or used for export to boost the local economy. For example, the fruit of the baobab tree, *Adansonia digitata* L. (Malvaceae), requires several hundreds of years of forward planning

before large-scale plantations can reach a yield mass capable of creating a sustainable large-scale market. For this reason, in the foreseeable future, it makes sense for wild harvested fruits to be marketed to the foreign market to achieve a sales price that meets the supply–demand curve. Traditionally, baobab seeds and fruits were a nutritional staple to the local people in Limpopo province where the tree grows naturally [25]. The addition of the fruit pulp to fruit juices and nut bars is motivated by a lemony taste, but the nutritional fortification serves as the primary motivation. Baobab fruit pulp tends to be a rich source of calcium and dietary fibre, and while values vary for specimens across the African continent, these two characteristics tend to be the most consistent [176]. It is also noteworthy that the fruit pulp is rich in procyanidins, flavonol glycosides and phenols that are both antioxidants and inhibitors of α-glucosidase [177], making it a logical addition to fruit juices, as it exerts protective effects against the sugar content of such beverages.

Two fruits that have reached market status in South Africa and are destined to grow into a bigger industry are marula, *Sclerocarya birrea* (A.Rich.) Hochst. (Anacardiaceae) (Figure 1), and Kei-apple, *Dovyalis caffra* (Hook.f. and Harv.) Hook.f., (Salicaceae) (Figure 2).

Figure 1. *Sclerocarya birrea* (A.Rich.) Hochst. (Anacardiaceae). Image provided by Ben-Erik van Wyk.

Experimental plantations of marula have been a success, which demonstrates the ability to expand the empire to well beyond its current status. At present, the fruit is available commercially as a jam, but it can be eaten fresh or used in the brewing of various alcohols [25]. The nutritional quality of the fruit, with high dietary fibre and protein content, as well as vitamins (A, B3, C, E and carotene), amino acids and minerals, confers a nutritional advantage with its consumption. However, the phytochemical diversity is also strongly relevant, as there are numerous polyphenols, flavonoids, condensed tannins and polysaccharides in the pulp [178]. For these reasons, marula is regarded as a 'functional food'.

Figure 2. *Dovyalis caffra* (Hook.f. and Harv.) Hook.f., (Salicaceae). Image provided by Ben-Erik van Wyk.

The Kei-apple has a similar appearance to marula, as it is a yellow rounded fruit. While it has also been made into jams and jellies, it is not commonly used in the brewing of alcohol, like marula. While it is not yet determined if Kei-apple is as cultivatable as marula, the nutritional attributes are nevertheless similar. It is regarded as a good source of amino acids, vitamin C and polyphenols, of which the most common is pyrogallol [179]. Pyrogallol is commonly produced as a microbial metabolite in the digestion of epigallocatechin gallate (EGCG). It is allegedly the intermediate that is responsible for the health benefits of EGCG by regulation of genes associated with Nrf2 activation [180], a process that is known to protect against inflammation and mitochondrial dysfunction [181], making it a good candidate in prophylaxis of CVD.

4.5. South African Roots (Geophytes)

South African geophytes represent a realistic alternative staple food item, due not only to a starch content that provides energy, but to a phytochemical diversity. Importantly, as a healthy alternative to the common potato, the phytochemical diversity is protective against the glucose load released when the starches are digested [11].

An example of a species that has high horticultural potential is the mountain anise root, *Annesorhiza nuda* (Aiton) B.L.Burtt (Apiaceae). This species grows in the Cape region of South Africa and has been eaten by all peoples throughout history, including the wave of pioneers [182]. Not much has been conducted to understand the starch chemistry, but phytochemical analysis of the volatiles in our group identified the phenylpropanoids that confer the anise-type flavour to the rhizome and a new α,β-unsaturated methylsulfanyl ester, called (−)-nudaic ester [183]. The major phenylpropanoid estragole is a known anti-inflammatory compound [184], which is important in prophylaxis of inflammatory diseases [64]. Because nudaic ester is a new compound, the biological effects remain to be determined.

The marama bean plant (*Tylosema esculentum* (Burch.) A.Schreib., (Fabaceae)) was mentioned earlier. It is worth reiterating that it produces the largest known rhizome in

southern Africa and possibly the world. If, however, the bean of the plant is to be utilized sustainably, commercial plantations that specifically propagate the rhizomes will be at the cost of a potentially valuable bean. Nevertheless, as previously mentioned, the main value of the starchy rhizome is in the content of soluble dietary fibre [163], but specifically as a food item, it is better for it to be compounded with a nutraceutical to augment the health benefit to the consumer. It has been suggested that the bean and the starch from the rhizome are compounded together to produce a quality nutritious food item. The nutritional properties of the bean are explained in the next section.

Another item worth mentioning is unlikely to be considered as a potential food. While *Pelargonium sidoides* DC. (Geraniaceae) is popularly known for its medicinal properties [185], there are records of it being eaten by the European settlers [166]. Because the root is extremely rich in hydrolysable tannins, it is difficult to imagine it being used as a meal. Purportedly, the root was boiled in water until it was softened, and the tannin content was extracted into the water, leaving behind a mildly red fibrous starch item for consumption. While it is almost inconceivable that such an item would be embraced as a nutraceutical, due to bitterness and minimal sensory reward, it can be used to fortify other more satiating foods. There are several farms and markets for *P. sidoides* as a medicine, meaning that a significant mass of post-extracted root material is disposed of every year.

Chemical analysis has demonstrated that the rhizome of *P. sidoides*, and other related geophytes, is rich in sitosterol (unpublished results), a sterol that is commonly added to foods to help reduce the amount of cholesterol absorbed from the gastrointestinal tract [143]. The ethanolic extraction process to produce the liquid medicine would remove much of the tannin, but most of the sitosterol would remain in the biota. If the waste material of the *P. sidoides* industry is put to use in fortification strategies, cholesterol-lowing food items may be produced.

Southern Africa is home to a vast selection of nutritious geophytes, such as the exotic but naturalized yam, *D. bulbifera* L., and various potatoes, including the wild potato *Plectranthus esculentus* N.E.Br. (Lamiaceae) and another exotic but naturalized species, the Zulu round potato, *Coleus rotundifolius* (Poir.) A.Chev. and Perrot (syn. *Solenostemon rotundifolius* (Poir.) J.K.Morton (Lamiaceae)).

The majority of research on the yam species grown in southern Africa derives from analysis of the west African germoplasm, particularly the Nigeria cultivars and those from neighbouring countries. For this reason, it is expected that some chemical differences might be relevant between southern African cultivars and the information in the published literature. Nevertheless, steroidal saponins appear to be ubiquitously expressed across the genus Dioscorea, and they have been confirmed in high yields from the edible southern African species [186], albeit sourced from other locations in Africa. Whether or not the saponins remain in the yams after processing is dependent upon the method of cooking. Furthermore, because some of the yams require leaching in water to improve palatability and reduce potential anti-nutrient effects, it is possible that the majority of saponins would be removed. As a rule, however, species that express saponins will also have the aglycone forms of the triterpene, or the sterol, present in the same material, and this family of specialized metabolite is not removed with aqueous leaching. For this reason, processed yams may be rich in triterpenes and sterols. In digestion, this invariably reduces cholesterol absorption, particularly when consumed with meat dishes [143]. For this reason, among others, the yams can be considered as healthier sources of starch, by comparison with the staple potato of south American origin (*Solanum tuberosum* L.).

The southern African potatoes can be eaten raw or cooked. They demonstrate stronger nutrient profiles compared to conventional potatoes in the market. The wild potato is high in protein (13.5%) and high in amino acids, exceeding the quantities in the Irish potato, sweet potato, taro and cassava [187]. It has been suggested that phytochemicals present in the wild potato are inhibitory to α-amylase and α-glucosidase, which delays the release of sugar in starch digestion, thereby lowering the glycemic index of the food item and

reducing the risk of glucose spikes [188]. Since diabetic complaints are a risk factor for CVD, this improves the projected health benefits of this particular food item.

Similarly, the Zulu round potato is potentially beneficial in the context of diabetes prophylaxis, which in turn protects against CVD. This food item contains a yield of 0.24% flavonoid, which was shown in a rat model to be protective against high-fat diets by stimulating the expression of antioxidant genes and increasing natural antioxidants, such as superoxide dismutase [189]. Thus, a starch item with a moderate flavonoid profile is protective against dietary items that promote free radical generation.

4.6. South African Nuts and Beans (Fabaceae)

Nutritional items from Fabaceae are sources of plant proteins that are digested to release bioactive peptides that may promote cellular and tissue rejuvenation [190]. The previously mentioned marama bean (Figure 3) *Tylosema esculentum* (Burch.) A.Schreib., (Fabaceae) [161], is a good source of protein that is unique compared to soya by having more basic proteins with limited disulphide links and a higher amount of tyrosine [191]. This is an interesting finding because basic proteins (proteins with amino acids that act as bases) are rich in the high pH amino acids lysine, arginine and histidine. When digested, the proteins from marama bean will produce absorbable peptides that are rich in these basic amino acid subunits. These types of peptides were recognized in a recent review as interesting candidates in the context of rejuvenating effects in human tissues, particularly by stimulating tissue regeneration [190]. Thus, the marama bean constitutes a rich protein source that is quite rare and should be examined in the context of not just food but also in the development of cosmetics.

Figure 3. Marama bean (*Tylosema esculentum* (Burch.) A.Schreib., (Fabaceae). Image provided by Ben-Erik van Wyk.

Two other legume foods in southern Africa are the jugo bean, *Vigna subterranea* (L.) Verdc., (Fabaceae), and the cowpea, *V. unguiculata* (L.) Walp. Similar to the marama bean, the jugo bean was found to be rich in basic amino acids, particularly lysine [192]. A study that examined the nutrient profile concluded that the contents of the nut are sufficient to support the growth of probiotics, making it a suitable prebiotic [193]. The phytochemical profiles of both the jugo bean and the cowpea are not well characterized; however, the cowpea is also rich in protein, and the protein-storing globulins, known as vicilins, were characterized as quite different to those in the common pea (*Pisum sativum* L.), due to greater emulsion-forming ability, meaning it is similar to the jugo bean in its ability to be manufactured into a milk product [194]. Both of these legumes may find a niche in the market as a milk substitute, superior in nutritional attributes compared to soy milk.

5. Conclusions

The dietary risk of CVD stems from the lack of phytochemical diversity in foods. The reduced phytochemical diversity of foods that are available on a grand scale in societies is a consequence of selection for crops with high yields of starchy grains or tubers that are sweet tasting. However, for a food item to be sweet and rapidly satiating, it requires that bitter components are minimally expressed. Because the slight bitter principle of foods derives from phytochemical richness, the staple foods in the modern diet are deficient in phytochemicals.

Most phytochemicals in wild crop relatives are associated with biological effects that are protective against the oxidative damage caused by the caloric load of foods. Empty calories power the body's cells, but the waste products of their metabolism are not adequately disposed of or neutralized by xenobiotics directly or via their biological effects. The most common positive biological effects from dietary phytochemicals include the induction of antioxidant genes, attenuation or cessation of inflammation and direct quenching of free radicals.

Foods that nurture the gastrointestinal system are also regarded as protective against CVD. This is due to the modulation of sugar released during the digestion of starches, the artefacts of digestion of soluble dietary fibre and the modulation of the gut microbiome to favour diversity of species.

South Africa is floristically diverse, and there are many endemic or naturalized species that demonstrate high potential as staple or culinary food crops. Because these species have not been phenotypically altered by thousands of years of selective breeding, they have retained the phytochemical diversity that serves not only an ecological benefit to the organism but confers protective effects to the consumer in the context of CVD prophylaxis. For this reason, South Africans should have these indigenous foods made available at economically viable prices, to incentivize a return to a holistic natural diet that could potentially turn the tide on the growing burden of CVD.

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