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## Strategies of Functional Foods for Heart Disease Prevention in Human Beings

**Abstract:** Functional food is used for modifying the key risk factors for heart disease. To obtain a better understanding of functional food crop for heart disease prevention, we conducted a systematic review for risk factors and prevention strategies for heart disease using the PubMed and so on database for the period 2001-2016. Major heart disease risk factors of dietary except heredity in human are low dietary fiber, obesity and high elements intakes. The countermeasures of heart disease prevention in humans are the functional foods with brown rice, whole wheat, barley grain/grass powder and its product, oat and its product, vegetables, fruits, and mushrooms for dietary, which associated with food type of ancient human beings. These are the reasons that Western countries have more coronary heart disease than that of stroke and diabetes for Asian countries, based on the loss of K and Mg as well as dietary fiber of major food from whole wheat to wheat flour. We can suggest that chronic disease especially heart disease of human beings was associated the five evolutionary stages of the major dietary guidelines, which was as follows: I-fruits or vegetables, II-grass or Cyperaceou, III-cereals (rice, wheat, millet, beans, barley and corn), IV-polished rice or wheat flour, V-white rice or wheat flour + grass powder, i.e. the most healthy major dietary guidelines for modern humans.

**Keywords:** functional food, dietary, heart disease prevention, human being.

### 1 Introduction

Heart disease is the main cause of mortality world-wide, costing U.S \$503 billion in 2010. Congenital heart disease (CHD) is a question for structure and function of heart at birth, however acquired heart diseases including the coronary (CHD), ischemic (IHD), hypertensive (HHD), rheumatic (RHD), pulmonary (PHD), hyperthyrod (HYHD),

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metabolic (MHD), infective etc. eight types heart disease. The depression is related with an increased risk of CHD and stroke [1]. More than 50% of global mortality rates of all heart diseases are preventable. Natural products play important roles against heart disease [2,3]. The diet and exercise can be very effective in reducing coronary risk, even outperforming drug therapy [4]. Liver X Receptor- $\alpha$  associated with CHD and neuro-degenerative diseases have been found to be regulated by the dietary components [5]. Children can develop habits which reduce their risk of heart disease, based on tobacco avoidance, healthy food choices, and regular physical activity [6]. The Mediterranean-style diet reduce greater cardiovascular diseases than low-fat diets, this diet including vegetables, fruit, whole grains, olive oil, and fish [7].

Functional foods are powerful tools for maintaining health and fighting against heart disease [8]. Their global market is about 73 billion euros with 8%–16% growth rate every year [9]. The main bioactive constituents for foods with heart disease prevention include angiotensin I, polyphenols (tea), flavonoids (buckwheat), flavanols (vegetables), catechins (green tea), anthocyanins (blueberry), phenolic acids (fruits), tannins (plant), resveratrol, saponin (panax notoginseng), sterols (barley), vitamins, polysaccharides (mushrooms), fiber, as well as K, Ca, and P [10]. Functional foods were used as bone health, heart disease, and arthritis [11]. A diet with high long-chain n-3 fatty acids intake may prevent cardiovascular mortality associated with increased resting heart rate [12]. Modifiable risk factors for coronary artery disease (CAD) were associated with diet with low calorie intake [13]. This article was expounded by a wide range of functional foods for heart disease preventing in China and discuss reasons caused heart disease and strategies preventing.

## 2 Major Heart Disease Risk Factors for Dietarey

### 2.1 Heredity is a Major Factor that Causes Heart Disease

Genetic factors may play an important role for heart disease development in cases not related to environmental factors [14]. Inhibiting microRNA-34 and microRNA-25 benefit heart disease [15,16]. 16 genes encoding structural proteins and transcription factors, which are associated with congenital heart disease in humans [17]. The expression levels of TCF21 and miR-224 were disturbed in human atherosclerotic lesions, which revealed the complex heritable mechanisms of CHD risk [18]. The apoE  $\epsilon$ 4 allele is a risk factor for CHD in China which revealed the complex heritable mechanisms of CHD risk [19].

NKX2-5 gene is associated with a small number of ventricular septal defect, and rs2277923 SNP is associated with the risk of sporadic atrial septal defect Yunnan population in China [20]. Tumor necrosis factor alpha 308G>A associated with the increased risk of RHD [21]. Homocysteine is an important risk factor for lots of cardiovascular diseases, but its removal is very important in cardiac development

[22]. A comprehensive list of 75 single nucleotide variations have been collected, and predisposed individuals associated with cardiac arrhythmias [23]. Four loci for CAD located in or near TTC32-WDR35, GUCY1A3, C6orf10-BTNL2 and ATP2B1, which are associated with the susceptibility for CAD of Han population in China [24]. 12 SNPs are associated with a lipid trait, 5 SNPs are associated with blood pressure, meanwhile, four most important pathways are linked to lipid metabolism and inflammation and so on activities in the genetic etiology of CAD [25].

## 2.2 Low Dietary Fiber of Polished Foods is Key Factors that Cause Heart Disease

The loss of fibre from brown rice to polished rice of China and world in 2010 is 3,964,955 tons and 13,926,233 tons, however whole grains to refined flour of wheat is 13,510,200 tons and 78,476,640 tons, respectively [26]. Dietary fiber is associated with lowering the risk of CHD, diabetes, cancers and other chronic diseases [27]. High carbohydrate intake of 70% from polished rice and 17% from refined products of wheat is associated with increased the risk of CHD in Chinese adults [28], and has significant correlation between wheat flour with high GI and CHD in China. The replacement of rice + noodles every day was associated with higher risk (26.11%), but rice + vegetables (-23.81%), fruit (-11.94%), or whole bread (-19.46%) every day was associated with lower risk of IHD death [29]. A large consumption of dietary fiber from cereals or vegetables is associated with lower risk of fatal IHD [30].

## 2.3 Obesity is A Key Risk Factor of Cause Heart Disease

Hypertension, diabetes, some cancer and heart disease are associated with obesity [26,31-34]. Obesity increases the risk of chronic diseases, such as heart disease, diabetes II, insomnia, some cancer and osteoarthritis [35]. More than 200 million hypertension in China was second major cause of heart failure [36]. The risk ratio each 5 kg/m<sup>2</sup> higher body-mass index was 1.27 for CHD and 1.18 for stroke after adjustment for confounders [37]. Adiponectin deficiency can increase fat, induced obesity, metabolic disorder, cardiac aberrance through decreased myocardial autophagy [38]. Hypertension is an important risk factor for CAD, its four loci (*SH2B3*, *GOSR2*, *YP17A1-NT5C2*, *CUCY1A3-GUCY1B3*) displayed study-wide significant association with CAD [39].

## 2.4 High Sodium and Phosphorus Intakes are the Major Factor of Cause Heart Disease

Hypertension and heart disease are frequently associated with Na. Fibroblast growth factor-23 can regulate renal phosphate reabsorption and vitamin D synthesis, affect renal Na retention, hypertension and heart hypertrophy [40]. Both low Na (<115 mmol) and high Na intakes (>215 mmol) consistent with a U-shaped association between Na intake and health, which is associated with increased mortality [41]. A higher urinary Na / K excretion ratio is remarkably associated with ventricular arrhythmias among well-controlled blood pressure [42]. QTLs with pleiotropic effects for *qK1/qMg1/ qCa1* region between markers Bmag0211 and GBMS0014 on chromosome 1H in barley was shown to have large additive effects in grains [43]. The variability of serum P is associated with coronary artery calcification and keeping serum P stable may decrease morbidity and mortality in patients [44]. Higher dietary P intake was associated with left ventricular mass [45]. Low urinary Mg excretion was associated with risk of IHD [46]. Women consumed more than 1400 mg of Ca daily had a higher risk of death from IHD but not stroke [47]. High serum transferrin saturation concentration was contrary inversely associated with CHD [48].

## 3 Natural Functional Food for Heart Disease Prevention

Heart disease is one of the most important diseases threatening human health. Prevention and control of heart disease rely on adopting a balanced diet, including mineral elements, protein, fats, and fiber from whole grains, vegetables and fruits.

### 3.1 Functional Food with High Dietary Fiber from Brown Rice or Whole Wheat Flour are the Key to Heart Diseases Prevention in Human Being.

In 2013, global rice yield and polished rice were 712.7 million tons and 477.5 million tons, but Chinese rice yield and polished rice were 202.75 million tons and 136.4 million tons, respectively. The loss of dietary fiber from brown rice to polished rice of China and throughout the world in 2013 were 4,056,746 tons and 13,981,979 tons, however whole grains to refined flour of wheat is 14,297,316 tons and 81,880,729 tons, respectively (See Table 1,2 and 3). Increasing consumption of cereal fiber when myocardial infarction was remarkably associated with lower cardiovascular mortality [49]. The loss of potassium from brown rice to polished rice of China and throughout the world in 2013 was 269,763 tons and 929,765 tons, however whole grains to refined flour of wheat is 835,128 tons and 4,782,778 tons, respectively (See Table 1, 2 and 3). Fibroblasts play a key role in cardiac function / dysfunction, regulating fibroblast K<sup>+</sup> channels can prevent fibrosis and atrial fibrillation [50]. The loss of magnesium from

brown rice to polished rice of China and the entire world in 2013 were 140,972 tons and 485,875 tons, however whole grains to refined flour of wheat is 247,010 tons and 1,414,626 tons, respectively (See Table 1,2 and 3). Compared with lower consumption, population in the highest Mg intake had a 34% reduction risk in mortality of cardiovascular disease [51], especially heart disease. The consumption of whole grains (wheat or rice) account for 1% but refined flour or polished rice account for 96% in China [26], however the consumption of whole grains (wheat or rice) account for 10% but refined flour or polished rice account for 85% in the world. Barley grass powder with higher GABA, Ca and K is the most ideal functional food promoting sleep [52]. Therefore, although whole grain (brown rice and wheat) with fiber, potassium and magnesium as well as B vitamins, make them for the useful food to foster heart health, but the replacement of major refined products (rice, wheat) with whole grains (brown rice, whole wheat) is very difficult.

**Table 1:** The Elements Concentration Loss from Brown Rice to Polished Rice Based on 202.75 Million Tons of Rice Yield in China and 712.7 Million Tons of Rice Yield of The World in 2013 [25] (<http://www.fas.usda.gov/>)

Elements	Elements content loss (%)	China (tons)	Globe (tons)
Strontium (Sr)	99.3	711,2	24,512
Chromium (Cr)	99.2	18,364	63,294
Magnesium (Mg)	61.8	140,972	485,875
Zinc (Zn)	61.0	7,007	24,149
Molybdenum (Mo)	60.6	350	1,206
Phosphorus (P)	57.9	399,036	1,375,320
Potassium (K)	55.9	269,763	929,765
Manganese (Mn)	55.0	2,982	10,278
Tin (Sn)	54.3	234	807
Nickel (Ni)	42.9	167	574
Iron (Fe)	31.7	1,113	3,838
Calcium (Ca)	31.2	9,168	31,599
Sodium (Na)	10.8	384	1,322
Sulphur (S)	9.1	17,102	58,944

**Table 2:** The Functional Ingredients Loss from Brown Rice to Polished Rice Based on 202.75 Million Tons of Chinese Rice Yield and 712.7 Million Tons of Rice Yield OF The World in 2013[25] (<http://www.fas.usda.gov/>)

Functional ingredients	Ingredients loss (%)	China (tons)	Globe (tons)
Dietary fibre	57.0	4,056,746	13,981,979
Total flavones	79.2	162,325	559,469
Total alkaloids	40.6	55,917	192,724
GABA	78.8	20,403	70,323
Pantothenic acid	32.0	972	3,350
Pyridoxine	68.0	704	2,426
Thiamine	83.0	502	1,731
Riboflavin	84.0	159	547

**Table 3:** The Nutrition Loss from Whole Grains to Refined Flour of Wheat Based on 121.7 Million Tons of Wheat Yield in China and 697 Million Tons of Global Wheat Yield in 2013[25] (<http://www.fas.usda.gov/>)

Nutrition components	Components loss (%)	China (tons)	Globe (tons)
Phosphorus (P)	91	931,646	5,335,536
Potassium (K)	77	835,128	4,782,778
Magnesium (Mg)	85	247,010	1,414,626
Calcium (Ca)	60	28,452	162,944
Zinc (Zn)	98	14,644	83,866
Manganese (Mn)	86	13,909	79,657
Iron (Fe)	75	5,708	32,690
Dietary fiber	89	14,297,316	81,880,729
Niacin	81	6,710	3,8428
Thiamine (VB1)	77	1,798	10,290
Pyridoxine (VB6)	72	1,138	5,517
Riboflavin (VB2)	67	407	2,314
Pantothenic acid	50	31	118

### 3.2 Functional Foods with Low Glycemic Index from Barley and its Grass Powder or Oat are the Key to Heart Diseases Prevention in Human Being

Women who eat foods with high glycemic index (GI), such as wheat flour, may be at greater risk for heart disease [53]. A QTL (*CslF6*) explaining 31% of the genet of  $\beta$ -glucan was located on 7HL, and naked barley for functional foods had significantly lower GI than oats [54]. The consumption of barley  $\beta$ -glucan alters microorganisms associated with a reduced risk of cardiovascular disease [55]. The wholegrain oat can be prebiotics and have low GI (40) [56]. Mean dietary GI was 56.2 approximately normal, however mean GI of major foods were 87 for polished rice and 86 for wheat flour, but 55 brown rice and 41 whole wheat flour as well as 25 pearl barley [57]. Tsangpa for barley products is taken as a baiyao, based on lower rate of heart disease and colon cancers occur in Tibet than that of expected [58]. The potential magnitude of health-related cost savings by health claims for soluble fiber of barley products and CHD [59].  $\beta$ -glucan of barley reduces the risk of CHD; arabinoxylan and resistant starch can ameliorate glycemic control [60]. Barley spaghetti for flavan-3-ols and soluble fiber as well as  $\beta$ -glucan enrichment reached USFDA requirements, which could allow these products for health claims “good source of dietary fiber”, “may reduce the risk of heart disease” [61]. USA and UK allowed health claim that oats  $\beta$ -glucan can reduces risk of heart disease and plasma cholesterol levels [62]. The intake of five bioactive substances controlled in whole grains (wheat, barley, oat) and their fractions is associated with a decreased risk of CHD and diabetes, which includes  $\beta$ -glucans, arabinoxylans, alkylresorcinols, tocols and phytosterols [3]. Whole grains (barley, oats) with high in viscous fiber can reduce the risk for CHD, serum low-density lipoprotein cholesterol, and blood pressure; meanwhile improving glucose and insulin responses [63]. Barley grass powder every day resulted in heart disease prevention, improved sleeping, lustihood, regulated blood sugar and pressure, enhanced immunity and liver function, detoxification acne skin, prevention of constipation, repair memory, improved gastrointestinal function, reduced gout and hyperuricemia disease, bone injury recovery, alleviated nerve dermatitis, anti-cancer, anti-aging, losing weight and reducing blood fat, anti-inflammatory and so on [26,64]. The reason is that the product is rich in nutritional and functional components, compared with brown rice, its total flavonoids and alkaloids were 2.1 times and 10.7 times, respectively; especially  $\gamma$ -aminobutyric acid for 37.8 times and potassium for 13 times, calcium for 55 times, iron for 30.2 times of brown rice [64].

### 3.3 Functional Foods with High Bioactive Components from Vegetables or Fruits are the Key to Heart Diseases Prevention in Human Being

The increased consumption of fruits and vegetables was deemed to be protecting humans against cancer, diabetes, heart and brain vascular diseases, which due to

the effect of  $\alpha$ -tocopherol, ascorbic acid,  $\beta$ -carotene, polyphenols and anthocyanins [65]. The dietary capsaicin can control cardiac hypertrophy and fibrosis in pressure overburden mice [66]. Ginger is a good functional food for treatment of hypertension and heart disease [2]. Garlic can protect the heart against myocardial infarction, hypertrophy, arrhythmia, cardiotoxicity and so on, based on  $H_2S$  and NO (nitric oxide) in cardiomyocytes and endothelial cells [67]. Some results support that the health effects of canola oil on CHD, insulin sensitivity, inflammation, and cancer cell growth [68]. Consumption of white vegetables with high potassium related to decreased risk of CHD and stroke [69]. Mortality from IHD and circulatory as well as cerebrovascular diseases was significantly lower in vegetarians with plenty of vegetables and fruits than in omnivorous populations [70]. An increased consumption of whole grain foods and fruits as well as vegetable leads to a reduced risk of multimorbidity [71]. Walnut area of Yunnan province in China reached 2646667 hectares, output and its value in 2013 have reached 680000 tons and 16 billion yuan; Consumption of walnut with high polyphenols related to decreased risk of CHD and other chronic diseases [72]. Olive and olive oil can prevent CHD and certain cancers based on their abundant monosaturated fatty acids and phenolic compounds [73]. Olive fruit contains four hydrophilic and one lipophilic phenolic compounds with cardiotonic, anti-hypertensive, antioxidant, anti-carcinogenic, anti-inflammatory, anti-microbial, laxative, anti-dyslipidemic, and antiplatelet [74]. Oral *Cordyceps sinensis* remarkable attenuates the heart injuries in chronic kidney disease rats [75]. The risk of myocardial infarction and cardiovascular disease is associated with chromosome 9p21 SNPs, which appears to be altered by the sufficient raw vegetables and fruits [76]. The magnanimous fruit and vegetable intake can reduce the risk of CHD by 17% [77]. *Capsella bursapastoris* is used as reduction of blood pressure, inhibition of inflammation, anti-cancer and diuretics [78], based on its bioactive components such as glycosides of quercetin, chrysoeriol, kaempferol, and isorhamnetin [79]. The proanthocyanidin in grape seed can offer cardiac protection against IHD [80].

### 3.4 Functional Foods with High Bioactive Components from Vegetables or Fruits are the Key to Heart Diseases Prevention in Human Being

Potassium such as in banana is important in physiological homeostatic control of cardiac function [81]. Selenium (Se) is a biomarker of CHD, meanwhile Se supplementation is very important to patients undergoing cardiac surgery [82]. Increasing the contractility of heart muscle cells by boosting intracellular Ca handling is an effective therapy for heart failure, however miR-25 overexpression causes declining cardiac function [16]. Troponin is integral to contraction of skeletal and cardiac muscle, and polymer paper to detect heart disease [83]. Supplementary Ca intake related to risk of CHD [84]. Dietary Mg intake was inversely related with reduced risk of CHD and IHD [46,85]. Decreasing dietary salt intake reduces CHD deaths in

the four counties (Tunisia, Syria, Palestine, and Turkey), however a comprehensive strategy can save money (\$13.28 billion) and lives (419250) [86]. Garlic and onion may be the organopolysulfides and quercetin mechanism in the treatment of chronic diseases [87].

### 3.5 Mushrooms is One of the Most Important Ways of Heart Diseases Prevention

*Ganoderma tsugae* possess the cardioprotective activity and ganoderic acids against cardiac insults [88]. *Agaricus brasiliensis* polysaccharide includes glucose (78.38%), arabinose (10.46%) and mannose (8.51%), which was propitious to some cardiovascular diseases [89] and used to treat heart diseases as well as prevent cancer [90]. *Lentinus edodes* is the treatment of chronic diseases involving heart disease, cancer, hypertension, diabetes, hyperlipidemia, hepatitis and so on, based on bioactive components such as lentinan, eritadenine, and lectins [91]. Cordyceps can treat heart disease, arrhythmias, hyperglycaemia, hyperlipidaemia, hyposexuality, and so on, based on three bioactive components (3'-deoxyadenosine, cordycepic acid and polysaccharides) [92]. Some mushrooms with abundant potassium without sodium can suit for functional foods of hypertension and patients with heart disease [90].

## 4 Discussion and Future research Questions

### 4.1 Large-Scale Chronic Disease Differences for Rice Versus Wheat Agriculture

Asian countries have more cases of stroke and diabetes than that of CHD, whereas the opposite is true in Western countries, based on 10 Asian countries and the United Kingdom as well as the United States [93, 94]. Although similar yields between rice and wheat in the world in 2013, but the loss of dietary fiber from whole wheat to wheat flour is 5.9 times than that of brown rice to white rice, however the loss of potassium and magnesium from whole wheat to wheat flour are 5.1 times and 2.9 times than that of brown rice to white rice, respectively (See Table 1, 2, 3). Higher potassium and magnesium as well as dietary fiber are associated with decreased risk of CHD; polished rice is major food of Asian populations, but wheat flour is major food of Western populations. Higher consumption of polished rice is related to a remarkable increased risk of diabetes II for Asian populations [95], but functional rice with high resistant starch is an important ways for diabetes preventing in China and Asia [96,97]. The Near East Fertile Crescent is the center of origin, diversity, and domestication for barley, whereas Tibet in China is one of domestic centers of cultivated barley [98]. This is one reason that Western countries have more CHD than that of stroke and diabetes for Asian countries, based on the loss of K and Mg as well as dietary fiber of major food from whole wheat to wheat flour, whereas another reason that Asian countries have more stroke and diabetes than

that of CHD for Western countries, based on Asian diabetes outbreak is rooted in brown rice and barley with low GI (25) for major food of the ancient humans into polished rice and white flour with high GI (87) as staple food of modern humans [64]. In addition, farming rice makes lots of cultures, whereas farming wheat more independent [99]. In the future research, we will discover that coevolution between heart disease and food structure of human being for Asia and Western countries.

#### **4.2 Chronic Disease especially Heart Disease for Modern Humans Associated with Food Structure of Ancient Humans**

The dietary flexibility of early hominins to include foods consumption from grasses, sedges, and succulents in tropical savannas and deserts represents a remarkable ecological and behavioral distinction from extant great apes as well as the last common ancestor [100]. Utilization of functional foods for dietary of chronic disease preventing in human being includes whole grains (brown rice, wheat flour, barley, buckwheat, oats, and others) or functional rice with high resistant starch food, functional vegetables (bitter melon, garlic, onions, broccoli, cabbage, and others), functional fruits (malnut, blueberries, strawberries, watermelon, olive oil, and others), mushrooms, green tea, coffee, and barley grass powder [26,32,33]. We can guess that chronic disease especially heart disease of human being was associated with the five evolutionary stages of the major dietary, which was as follows: I-fruits or vegetables, II-grass or *Cyperaceou*, III-cereals (rice, wheat, millet, beans, barley and corn), IV-polished rice or wheat flour, V-polished rice or wheat flour+barley grass powder. In the future research, we will discover that correlation evolution between heart disease and five food structure of human being.

#### **4.3 Origin of Functional Crop Evolution is Closely Related to Chronic Diseases for Dietary of Human Being**

Functional crop (brown rice, vegetables, fruits, and mushrooms) for preventing heart disease is not only similar to cancer [33] and hypertension [32] as well as diabetes prevention [26] in China and in the world, but also further support that Southwest China (especially Yunnan Province) is one common sphere that the coevolution of functional crop is closely related to the chronic diseases of human.

The Near East Fertile Crescent is not only one of the earliest domestication of crop in the world, but also the center of origin and diversity of wild wheat and barley [26], the cradle for human civilization. Barley grass powder is a remarkable decrease in fasting blood sugar, total cholesterol, low-density lipoprotein cholesterol, but a remarkable increase in high-density lipoprotein cholesterol levels [101]. The diet of *Theropithecus* for a common large-bodied primate was making up of grasses or

sedges, which occurred with hominins in East and South Africa [102]. The human's evolution of an enlarging brain, a contracting large intestine, and prolonging small intestine necessitated a require for nutritionally dense foods (Armelagos 2014). In future research, it is necessary to discover the origin and evolution of functional crop associated with chronic diseases of human evolution.

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