

Participation Of Banana Intolerance in Atherosclerosis Review Of the Literature

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Abstract

The main cause of atherosclerosis is not completely understood. Besides the classical risk factors, food intolerance and its microbiota promote inflammation. IgG antibodies against antigens and microbial genomes have been detected in atherosclerotic lesions.

It has been suggested that fruits despite their benefits in terms of nutrients and anti-oxidative properties may also act as “enemies” provoking diseases through immunity pathways. The current production of fruits involves the use of conservatives, insecticides, fungicides, herbicides, acaricides, surface disinfectants etc. hostile to human body.

Banana contains microorganisms which may use our “ecosystem” to build colonial biofilms called plaques in order to survive. Their metabolites create acidic environment resulting in illnesses and even death.

The primary outcome of this computerized search was that there is a direct and indirect association between banana intolerance and arteriosclerosis. There is limited information about fruit antigens and microbiota and their interactions with the host. Biofilms and immunity complexes could link banana with atherosclerosis. The banana contains nutrients good for us and for our intrinsic “habitants” and microflora which interacts and modulates the host microbiota. Plaques are reconstructed by living “microbes” fighting for home and food.

Banana’s antigenic load triggers the production of immunocomplexes which are deposited on the vascular walls and initiate atheroma formation.

Extensive studies on the biology and “dietology” of diseases should be conducted to further clarify the “gaps” of this issue.

Key words: banana intolerance, inflammation, atheroma, coronary artery disease, oxidative stress, microbiota, biofilm formation, infection, antigens

Introduction

The predisposing risk factors of atherosclerosis (smoking, genetic disorders of lipid and lipoprotein metabolism, environmental factors, obesity, hypertension, hyperlipidemia, diabetes mellitus, increased plasma homocysteine, ageing) have been recognized[1-9]. However, their pathogenetic mechanisms cannot be completely linked to the root-aetiology of atherogenesis. In various studies there were confounding agents and in all likelihood the illness seemed multifactorial[10].

The improvement of diagnostic tools and microscopical mapping of the plaque morphology led to the discovery of the missing ideology of disease expression. The causal mechanisms of atherosclerosis were also defined as infectious and inflammatory[11-24]. Infections and the existence of pathogens in atheromas were screened by laboratory techniques. The implanted alien microbial populations confined in a host ecosystem competes for nutrients and settlement[25]. The plaque existence is driven by physicochemical characteristics of living organisms. It is a place of nutrient exchange between the colonizers and the

host, a site of quorum sensing between different molecules and cells. The immunological and inflammatory reactions of the host manifest the presence of the foreigners. Microbial ecosystems are universally confronted and implanted. They survive and are affected by our dietary habits in the food chains.

The immunity system attacks exogenous and endogenous antigens by creating antibodies and immune-complexes which are deposited in the vascular wall contributing to atherosclerosis[26]. IgG antibodies against pathogens determine the severity of endothelial damage. Immuno-complexes formed after the exposure to antigens and microbes were found in plaques and in the blood circulation. It is a rescue mechanism of the innate immunity system to destroy microorganisms and intruders[27].

In the effort to solve the global problem of angiopathy, food was initially studied as a “stranger”-trigger factor of coronary artery disease[28]. The chronic inflammation resulting from food processing the human organization and the destructions caused by the immunological answers of the host are new associated links of the presence of the disease.

In one trial the IgGs against all food categories of patients with coronary artery disease were searched using commercial kits. The most common intolerances detected were in bananas, dairy products and eggs. However, there was a statistically significant difference for banana intolerance and its association with the serious forms of ischemic heart disease[26].

This led to the review of the literature and the analysis of the way's banana intolerance mediates the atheroma creation. This review deals with the solution of the atherogenesis enigma for purposes of future targeted therapies. It emphasizes the microbial and antigenic infra-structure of banana fruit and its possible association with vascular changes and blockage.

Aim and Methodology

A computerized search was performed in Pub Med and Medline regarding banana intolerance and atherosclerosis including results from 1978 until up to 2020. The key words used were: banana, intolerance, inflammation, coronary artery disease, arteriosclerosis, oxidative stress, plaque, microbiota, biofilm, antigens.

We found one meta-analysis of prospective studies and one systematic review.

With the words "banana intolerance" we found 12 articles. Using veil combinations "banana intolerance and inflammation", "banana intolerance and atherosclerosis", "banana intolerance and oxidative stress", "banana intolerance and microbiota", "banana intolerance and plaque" no articles were noted.

With the key words "banana consumption and inflammation" there were 8 articles. With the words "banana consumption and atherosclerosis" 1 article was written. With "banana consumption and oxidative stress" 7 articles, with "banana consumption and microbiota" 2 articles, with "banana consumption and plaque" 4 articles were announced.

With "banana consumption and coronary artery disease" none was reported.

With the words "banana antigens" there were 209 articles noted but with "banana antigens and atherosclerosis" none.

We included all published articles such as cohort studies, objective screening projects, case reports, cross-sectional surveys, post-hoc analyses, experimental research studies, systematic screening analyses, single-center prospective studies, studies on rats, review articles on sepsis and on food chemical composition, randomized crossover studies about malnutrition and the increased risk of infections, randomized controlled trials, experimental laboratory studies.

One prospective study mentioned the food intolerances in relation to coronary artery disease. The methodologies used for detection of either hypersensitivity or intolerances associated to angio-changes hid some biases. Nutritional support, bioactive food particles, side effects of malnutrition were addressed.

Animal studies emphasized the effect of food consumption on gut microbiota, the deficiency of enzymes in the metabolic pathways and the metabolic disorders as risks of atherosclerosis, the toxicity of diet and drugs were documented as well as the host immunity defenses.

Screening projects in Intensive Care Units were conducted in order to monitor the appropriate nourishment of patients, controlling other comorbidities in an attempt to extent early treatment of diseases and prevention of unfavorable outcomes.

Allergies or intolerances to foods have been documented with other methods e.g. standardized questionnaires, skin tests, hypersensitivity tests, detection of serum antibodies Ig-E, RAST and immunoblotting inhibition analyses. The methods are not 100% predictive of food adverse reactions, meaning that food ingestion and metabolism and its side effects cannot yet clearly confirmed.

The gastrointestinal fermentation of food and the consequences were mentioned. The socio-demographic characteristics, economy and lifestyles (including diet) and their relation to prevention, cure and control of diseases were also addressed among countries.

Classical and New Mechanisms Of Atherosclerosis

Atherosclerosis is a chronic inflammatory disease of the vessels and not only the accumulation of lipids and apoptotic cells on the vascular wall[11].

The clinical and epidemiological characteristics of the disease are not fully justified by the multiple classical risk factors. *Cigarette smoking* is hazardous to cardiovascular system through mechanisms of oxidative stress, inflammation and endothelial dysfunction[1, 2]. *Genetic disorders of lipid and lipoprotein metabolism and environmental factors* influence the expression of atherosclerosis e.g. dietary habits[3]. Obesity which includes abnormality of metabolic pathways, autophagy and alterations of gut microbiota predisposes to cardiovascular diseases[4]. *Hypertension* causes damages to tissues and organs. High blood pressure depends on intrinsic factors (: renin-angiotensin-aldosterone system, the immune system, estrogen and testosterone sex hormones, metabolic disorders) and extrinsic factors (e.g. nutrition). It is implicated in initiating and progressing atherosclerotic lesions[5]. *Hyperlipidemia* means elevated serum cholesterol, triglycerides and Low-Density Lipoprotein levels. Statin therapy and diet rich in flavonoids reduces this cardiovascular risk[6]. *Diabetes mellitus* predisposes to atherosclerosis. It is known that hyperglycemia promotes inflammation, cellular oxidative stress, changes of the gut microbiota and microRNA expression causing plaque generation[7]. *Increased plasma homocysteine* reduces the levels of vascular protein S-nitrosylation and NO which regulate the cardiovascular system[8]. *Ageing*: time -related impairment of vascular functions is mostly related to thickening of the vessel walls, oxidation and inflammation[9].

The Mediterranean lifestyle consisting of low-fat vegetarian diet, less quantity of animal products and moderate exercise prevents or treats cardiovascular diseases[29].

Novel mechanisms of *atherosclerosis include infections* leading to inflammation and alterations of the lipid metabolism, deposition of cholesterol on the endothelium[12].

Microorganisms such as *Chlamydia pneumoniae* and *Cytomegalovirus* (: intracellular pathogens), *Helicobacter pylori* were detected within the plaques. They activate T cells, involved in the destabilization of the intima[12, 13]. Different microbial populations run simultaneously metabolic procedures having the ability to build neoplastic tissues (: biofilm, plaques, tumors)[14]. Antimicrobial interventions, dissection of human genes, protease inhibitors, vaccinations, acoustic or bioelectrical systems applied to prevent bacterial surface adherence and their bio-membranes are effective in controlling and killing bacteria and biofilm-mediated chronic diseases[15-18].

Microbial antigens, DNA, elevated antibodies, immune complexes and living organisms were found within plaques[18,19]. *Helicobacter pylori*, *Chlamydia pneumoniae* DNA were detected in carotid artery plaques by cultures and polymerase chain reaction[19]. When endothelial cells are infected, active hydroxyl radicals are formed intracellularly, interleukins (IL-6) are produced, increased adhesion of monocytes and coagulant activity of endothelial cells altogether start atheromatosis[20]. Bacterial and viral infections may cause acute coronary events[21]. Immunological and inflammatory pathways link the endovascular infection with atherothrombosis and atherogenesis[18, 19, 21].

Chronic inflammation resulting from food processing the human body, leads to chronic diseases[22]. Microorganisms of the food enter the oral cavity invoking periodontitis, destruction of teeth and then invade the blood circulation [23, 24].

Periodontitis has been linked to cardiovascular disease, type 2 diabetes, systemic reactions (: platelet aggregation, hyperlipidemia, production of active inflammatory mediators, atheroma creation) [30, 31]. The presence of microorganisms such as *Aggregatibacter actinomycetem comitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Prevotella nigrescens* and *Tannerella forsythia* were detected on dental biofilm plaque using the PCR method[23]. The same kinds of bacteria found on dental plaques were also detected in blood cultures and in atherosclerotic plaques[23]. *Prevotella nigrescens* and *Porphyromonas gingivalis* were related with carotid atherosclerosis[32]. Periodontal treatment and oral hygiene reduces systemic inflammation, C-reactive protein and atherosclerosis, improves the coagulation status, the biomarkers of endothelial cells activation, endothelial function, arterial blood pressure, and overall health status[31, 33].

Virulent microbes secrete substances and enzymes (e.g. proteases), modulate immunological reactions resulting in the formation of dental plaque which resembles the atherosclerotic one. It is a well-organized community in a uterus-infrastructure made of polysaccharides, proteins and DNA (extracellular space)

woven by the bacteria (: dysbiotic microbial biofilm). Periodontitis initiates systemic and chronic inflammatory diseases through the interactions of micro-organisms with the host megallo-organism and "metastasizes" extra-orally[34].

Polyphenols and Flavonoids isolated from plant species inhibit the substances produced by the bacteria, their growth, the periodontitis and the biofilm (: plaque) formation[35]. When the dental plaque is reduced mechanically or chemically, local and systemic diseases (: intracardiac vegetations, rheumatoid arthritis, chronic obstructive pulmonary diseases, chronic infections, neoplasias, atherosclerosis etc.) are prevented, the oral and overall health is improved and the glycemic index of people with type 2 diabetes mellitus[34,36].

The bacteria enter the bloodstream through the oral cavity or other gates e.g. through lines and dialysates of hemodialysis, migrate to different places and damage the endothelium[37]. They weaken the intima of vessels, proliferate, create their biological colony, and build the plaque. They release endotoxins and participate in pathophysiological procedures, including amyloidosis, malignancies, atherosclerosis, chronic infectious and autoimmunity diseases, endocarditis, mortality. Biofilm formation in combination with an eliminating immune response leads to inflammation and cardiovascular diseases[38,39].

A destructive immune-inflammatory response is a modern translation of risk to atherosclerosis besides the classical risk factors. Dietary deficiencies have crucial impact upon periodontal and cardiovascular diseases. Macro and micronutrients (vitamins, minerals etc.) regulate the functionality of enzymes during the metabolic processes in human cells and gene transcription factors (e.g. pro-inflammatory and anti-inflammatory nuclear factors) [40]. Enzyme activities can be affected by the food deficiencies causing intolerances and coronary artery disease[26].

Furthermore, bacteria, viruses, fungi, proteus, parasites and other microorganisms live within the intestinal tract influencing health, growth and development. The microbial communities can be affected by dietary habits, environmental and maternal factors[41]. Bacteria can exist in planktonic form or in biofilm that allows them to survive under hostile conditions. The bacterial colonies cause chronic inflammations including tissue damages, and they contribute in the cross-correlation between local infections and systematic diseases such as atherosclerosis[42]. Biofilms are resistant to antibiotics[39]. The relationship between infections and immune system, bacterial products as activators of the immunity responses, microbial metabolites are considered cardiovascular risk factors[42, 44].

Atheroma is immunological response to exogenous and endogenous antigens, causing inflammatory changes in the arterial wall and cholesterol accumulation. Antigens may be the constituents of food or its microbial load[26]. Antibodies, activated macrophages, products of oxidation, biofilms lead to atherosclerosis[27]. Diverse bacterial genomes (*H. pylori*, *N. meningococcal*, *S. aureus*, *S. pneumoniae*, *S. epidermidis* and *E. coli*) and T-cells are present

in atherosclerotic plaques. T-cells react to bacteria starting endothelial dysfunction, thrombus and atheroma formation [45, 49].

Humoral immunity and the reactions against bacterial antigens can play an important role in the process of atherogenesis. Heat Shock Proteins (HSPs), proteins expressed by cells after exposure to stressful conditions and their cytotoxicity have been identified. Microorganisms produce HSPs mediating the creation of plaque through immunity pathways [46]. Antibodies against *Escherichia coli* HSP and *Chlamydia* HSP from patients with atherosclerosis were detected on human endothelia. *The immunocomplexes (: Ab-Ag) are deposited on tissues and cause inflammatory damages* [47].

Pathogenic load defined as the number of positive antibodies and immunoglobulin G against cytomegalovirus, chlamydia pneumonia, *helicobacter pylori*, hepatitis A virus and herpes simplex virus-1 have been measured. *IgG against pathogens is a determinant of severity of endothelial dysfunction* [48]. The microbial DNA (especially of *Chlamydia pneumonia* and the Cytomegalovirus) activates the immune system cells via receptor TLR-9 [49, 50]. Lipopolysaccharide receptors of macrophages (involved in microbiological recognition) result in cellular immunological responses to products of microorganisms and to specific antigens of oxidation. Inflammatory factors e.g. cytokines, toll like receptors, accumulation of immune cells exert atherogenic effects [51]. *The lipoproteins constitute an endogenous immune system binding and destroying microorganisms with their byproducts through the formation of immunological complexes (Ab-Ag). Such complexes (: antibody-antigen) can block the blood supply causing ischemia, destroy vascular cells and create unstable plaque* [52].

In summary, *antigens and microorganisms* found in plaques or blood trigger the immunity reactions (: activation of lymphocytes, production of cytokines, antibodies against HSPs or oxidized LDL, activated macrophages and lipoproteins, elevated fibrinogen etc.) connecting inflammation with atherosclerosis [52, 53].

Connection Of Banana Intolerance with Arteriosclerosis (: Immunological and Infectious Mechanisms)

References to banana describe both its usefulness and deleterious actions.

In investigations of hypersensitivity or intolerance reactions as *trigger factors for abdominal angioedema attacks* they reported tomato, green salad, fish, citrus fruits, apple, onion, garlic, cheese, chili, kiwi, milk, tree nut, peanut, strawberry, pineapple, shrimps, bread, banana, leek, chicken, chamomile and alcohol. However, the disease mechanisms remain unknown [54]. Banana, rhubarb, curcumin, peppermint oil and ginger were searched as bioactive foods which could be applied in hospital patients. *Malnutrition, infections, gastrointestinal events increase morbidity and mortality* [55].

Bananas have been used as components in beverages to augment their value and stimulate the growth of beneficial gut microflora

[56]. Lipid transfer protein (LTP) is a plant allergen causing IgE mediated adverse reactions. However, banana seemed safe for the LTP-allergic patients [57]. *Antibodies against banana allergens were demonstrated* by serological tests, detecting IgE antibodies [58]. In one study banana, cacao, egg, hazelnuts were recognized as foods responsible of the migraine attacks of patients aged from 7 to 18 years. Oligo-antigenic diet had a significant improvement of the migraines to some patients [59].

The existing bibliography promotes banana consumption. It is evaluated for its nutrients and effects on plasma antioxidants, markers of oxidative stress, inflammation and function of the immunity system. Especially in the elderly, immunosenescence and malnutrition can contribute to increased risk and severity of infections [60]. Banana, berries, apples consumption increases cellular antioxidant activity and reduces the risk of neoplasias [61]. Banana meal enhances the resistance to oxidative modification of LDL and protects from atherogenesis [62]. Banana contains prebiotic indigestible carbohydrates and increases the bifidobacterial levels of fecal microbiota. Consequently the pathogenic microbiota is downregulated [63]. *Although the fruit is benign, oral cariogenic bacteria* such as *Streptococcus mutans*, *Streptococcus sorbinus*, *Lactobacillus* spp. and *Actinomyces* spp. can decompose its carbohydrates into acids and create biofilms, lesions and plaques [64]. This fact can be interpreted as follows: the banana is a good fruit, but when it is consumed, "bad" bacteria metabolize it for their needs and for the benefit of their biological colonies. We assume that plaques are biofilm colonial clusters.

Vegan diet prevents cardiovascular diseases [65]. Banana contains phenolics, carotenoids, biogenic amines and phytosterols, protecting the body against oxidative stresses and chronic diseases [66, 67]. Bananas contain sucrose, fructose, glucose, fibers, tryptophan, and B-complex vitamins. The vitamin B6 regulates blood glucose levels. The consumption of banana products prevents diseases linked to digestion and glucose/insulin metabolism or treats type 2 diabetes [68, 69]. The B6 and B12 vitamins as well as potassium and magnesium minerals found in them neutralize excessive acidity. It has iron content curing anemia. Its products exert beneficial effects on glycemic control, lipid metabolism, and blood pressure [69]. Banana can limit the risk of death from strokes [70].

Although the above knowledge is true, there is evidence that banana intolerance results in diseases through immunity pathways and secondly the hostile microorganisms carried in or near the fruit may work in a vicious cycle of inflammation. In a recent prospective study, patients with coronary artery disease were checked for food intolerance with the use of commercial kits Food Detective/Golden test. The banana, egg, milk was most prevalent. There was a statistical evidence of *correlation of banana intolerance with the severe form of atherosclerosis*. A percentage of population defends against banana (: its microbiota or substances) [26].

A possible explanation of the above study is the fact that some individuals cannot digest banana, opposing to its foreign

substances and microbiome and producing antibodies. These are connected with the antigens, creating immune complexes which are deposited on all organs, on the endothelia starting inflammatory reactions and chronic diseases. The *atheroma is a response of the immune system to antigens, causing endothelial damages*. Immunity receptors recognize dangerous molecules and antibodies IgG are generated. These are detected in atherosclerotic lesions. Anti-food IgG is pathogenetically involved in the development of obesity and atherosclerosis. Antibodies and products of oxidation and apoptosis contribute to the formation of the plaque [71]. Banana allergens may evoke allergy syndrome caused by the presence of cross-reactive IgE [72]. The immunological defensive responses favor the atheroma formation, the maturation and exacerbation of arteriosclerosis[11]. Oral allergy syndrome (OAS) includes hypersensitivity symptoms, mouth and throat itching, anaphylaxis. Patients with ragweed allergy may show OAS symptoms with banana [73]. *Intolerance or allergy reactions against banana lead to the creation of immune-complexes and inflammatory procedures*. Banana is “innocent” as a fruit but the host organism (: consumer) weaknesses fight it and incriminate it.

Several food proteins induce gastrointestinal inflammation and pancreatitis. Immune-related cells such as mast cells, eosinophils, neutrophils, and T cells are involved in the adverse reactions to food (: IgE mediated, non-IgE mediated, and mixed). *Consumption of banana as a possible cause of pancreatitis is also noted* [74]. When pancreas is not functioning correctly, enzymatic deficiencies result in intolerances and metabolic disorders (: risk factors to atherosclerosis). Banana seems to be a factor triggering abdominal angioedema probably due to intolerance and not due to Ig-E mediated hypersensitivity [54]. Increased IgG4 response to foods including banana were detected in IgG4-Related Disease (:a systemic fibro-inflammatory condition, characterized by high serum IgG4 and IgG4-positive plasma cells in the diseased organs) [75]. Ig-Gs united to Ags are circulating and deposited in various sites such as vascular walls initiating plaques, or in pancreas causing diabetes (: risk factor to atherosclerosis), causing thickening of the vessels and hypertension due to inflammation and eventually ageing of the cardiovascular system due to oxidation [75].

Diet contains microbiota which means in other words that food is not sterile neither is banana. The bacteria of food can build in us biological colonies e.g.neoplasias, plaques. It is a necessity for their survival [14, 76-77]. *Banana illnesses depend on the microorganisms that invade it through the food (: soil – water-air)and also depend on the antigens e.g. fertilizers, pesticides the fruit is exposed* [73]. Analytically, the scenario of all diseases depend on the power supply and the struggle of the consumer with it.

Food components lead to atherogenesis by the induction of hypercholesterolemia and by modulation of the gut microbiome. Intestinal microbes influence the expression of genes in the enterocytes related to immune function and lipid metabolism.

The intrinsic flora, dysbiosis and a numerical increase of pathogens results to cytokine release, damage of the intestinal barrier and increase of atherogenic metabolites, inflammation through immunity pathways, cardiovascular side effects[78].

Banana contains its microflora stimulating and interacting with oral and gastrointestinal microflora. The microorganisms are necessary for the digestion, metabolism and absorption of food. Diet should strengthen the benign gastrointestinal flora, alter bodily acidity (pH) as well as the incidence of illnesses. Individuals cannot consume all food categories because of intolerances or allergies to their constituents and microbes, lack of metabolic enzymes. Eating banana also means bodily “contamination” with pathogenic intruders. *Banana contains its ownbacteria that produce metabolites* [79]. The microflora of the consumer dissolves banana starch into glucose, fructose, sucrose and acids are produced[80]. Approximately 164 lactic acid bacteria (e.g. Lactobacillus plantarium, Lactobacillus, Weissella) were isolated from bananas in Taiwan which affect the incidence of banana diseases (e.g. fusarium disease), its sugar content and acidity (: sugar to acid ratio) [81]. *The banana can become ill depending onthe ground, feed and fertilizers used*. Modifying the texture of soil (: bacterial burden, number of actinomycetes, bacilli numbers, the proportion of bacteria to fungi), we can improve the health of the fruit, its quality and indirectly the health of the consumers [82]. Pesticides pollute grasslands, plantations through the food and water [83]. Bacterial and fungal communities in the soil, organic matter, interactions between bacteria and fungi in the ground and within the fruit correlate with banana diseases and depletion [76].

Generally, the amount and the activity of enzymes a consumer secretes after a meal are influenced by the quality and quantity of food[84]. A cause of banana intolerance is the insufficient metabolism and absorption because of enzymatic deficiency and disturbance. Banana offers water andnutrition to human organism as well as to its microflora[85]. The good scenario is that it offers water, food and protection to friendly bacteria (e.g. lactobacillus). It contains starch resistant to gastric acid and intestinal amylases[86, 87]. The resistant starch competes the fecal microflora and protects Lactobacillus plantarium from gastric acids and bile[86]. This microorganism can live and work its ways through the host.

Consumption of fruits including banana has acidogenic potentiality because they are fermented with either oral or extra oral bacteria to sugars and acids [80]. Fructo-oligosaccharides (: oligosaccharides constituted of fructose and glucose chains) present in banana are non-absorbable, having prebiotic effect and stimulating the nonpathogenic intestinal microflora. The banana starch is consumed by intestinal microbiota for anaerobic cellular energy production[85]. Their final metabolites are the carboxylic acids, the lactic acid etc. The chemical composition of plants characterizes their bacteriostatic features. For example, kinds of mint contain essential oils battling the Staphylococcus epidermidis ATTC 35984 which creates bio membranes [88].

However, banana presents bacterio-feeding and inflammatory characteristics.

Banana fibers are used for the production of surgical sutures because of their powerful inflammatory reactions resulting in healing processes [89]. The fibers reinforce the intestinal bacteria (lactobacilli, bifido-bacteria). *Lactobacilli* excrete antimicrobial substances and uniteto cells. Banana starch along with these lactobacilli decreases pH, increases the production of lactic acid and short chain fatty acids from the intestinal microbiota (: a source of energy for the intestinal cells) and inhibits the population of others e.g. salmonella typhimurium SA2093 [90]. The plant fibers include polysaccharides, oligosaccharides and inulin which are fermented with intestinal microbiota influencing its composition and activity [91].

Dickeya MS1-Erwinia chrysanthemi is a bacterium that forms biofilm and pollutes banana plantations[92]. The biological colonies (: bio-membranes) built by this microorganism are constituted of bacterial cells and extracellular matrix of polysaccharides made by the bacteria. Their colonies, extracellular proteases and toxins harm banana causing its decay and indirectly illnesses of the consumers [93]. The quantity and quality of microbiota and their efforts for survival (=dysbiosis) is the root of diseases. Microorganisms produce useful metabolites (: vitamins, potassium etc.) or dangerous molecules (: alcohol, acids) in the large bowel, serum, blood, fetus, urinary tract, cardiovascular system etc. Disorder of the metabolism of choline by bacteria, involves overproduction of trimethylamine precursors involved in atherosclerosis, increased production of hydrogen sulfide, ammonia and bile acids leading to inflammatory diseases. Microbial production of phenylalanine, tyrosine and tryptophan-indole derivatives contribute to the pathogenesis of chronic liver and kidney disease, cardiovascular diseases, psychiatric and neurological illnesses etc. The knowledge of microbial metabolism-metabolites and dietary changes can prevent diseases [44].

The pathogenesis of banana diseases is explained by the harmful bacteria isolated from the fruit such as *Vibrio harveyi*, *V. owensii*, *V. sinaloensis*-like, *V. campbellii*, *V. shilonii*, *Vibrio* sp. and *Photobacterium damsela*. They had virulent genes and whips and could adhere to cellular lines, forming organic colonies [94]. Because of the fact that microorganisms compete to each other, they introduced rhizobacteria in the soil in order to protect plants from pathogenic bacteria. Banana root contains organic acids which help rhizobacteria to colonize and form biofilms. Studies of *Bacillus amyloliquefaciens* NJN-6 colonizing the root of banana and their behavior; ability to create bio membranes are useful for the treatment of diseases [95]. Epiphytic and endophytic bacteria were detected on leaves. *Mycosphaerella fijiensis* causes fungal disease of banana. 648 bacterial species in vitro were found to compete against it, influencing the formation of mycelium and the morphology of the fungus spores. Microorganisms either act synergistically or antagonistically to each other [96].

Banana diseases mimic human disease. The biomembranes

responsible for infections are the key-solution to arteriosclerosis. The pathogens are attached to vascular endothelial cells or locations of vascular damage and start the "proliferating" procedures. Microorganisms, cell adhesion molecules (: proteins controlling links, cell migration, proliferation, survival and apoptosis), development of connections-adhesion either between cells or between cells and components of the extracellular infrastructure are involved. Selectins, integrins, immunoglobulins (: adhesion proteins) participate in the interaction between leukocytes and vascular endothelium, play a role in the integrity of tissues, inflammation, the creation and progression of atherosclerotic plaque [97]. Various antigens stimulate immune responses causing inflammation and the development of atherosclerotic plaques. Antigens may be the dietary ingredients or its microflora [26]. Immunomodulating treatments will target those mediators of inflammation, preventing cardiovascular diseases [98].

Bacteria are living in various sites in the form of a biofilm. Disturbance of homeostasis of biofilm and increase in the number of acid-forming bacteria lead to the development of the diseases. The etiopathogenesis of atheroformation is explained by the biofilmic colonization and the metabolic bacterial activities[99]. Besides the classical risk factors, microorganisms and antigens also promote atherogenesis. The inflammatory response against pathogens or antigens of food may have an important role in the creation and stability of atherosclerotic plaque. Banana's foreign microorganisms enter the host changing the flora of the internal ecosystem (: oral, gastrointestinal, cardiovascular) and thrive for a living. Especially the oral and gut microbiome is associated with the infectious state of the body and diseases. There is a complex relationship between microbiota with the classical risk factors of atherosclerosis, obesity, insulin resistance, fatty infiltration of the liver, blood clotting disorder mechanisms, construction of plaques[100].

Biological battles are observed in nature and in mankind. The health of plants, animals and humans is a matter of balance. We use friendly microorganisms to fight the "evil" ones. The atheroma is not formed only by lipids and cellular debris[101]. The activation of the immune system, inflammation, monocytes, macrophages, cytokines during plaque formation represent procedures against various stimuli. These responses to foreign matters change the endothelium and its function. Elevated monocytes, activated T-lymphocytes, oxidized LDL cholesterol, increased production of peroxides, activated macrophages, cytokines (: IL-1, IL-6, gamma interferon) and Lp (a) lipoproteins have proved to be immune responses while the atherosclerotic plaque is created sub-endothelially. In the process of inflammation the levels of CRP (: acute phase protein), fibrinogen and the erythrocyte sedimentation rate are increased. Medications (statins, aspirin, ACE inhibitors, antibiotics) work as anti-inflammatory drugs. Microorganisms have been detected on atherosclerotic plaque or blood, e.g. *Helicobacter pylori* or *Chlamydia pneumonia*. Reactions against proteins (: heat shock) and oxidized LDL are explained by the immunity pathways[53].

Banana intolerance and consumption to cardiac patients means eating pathogens and antigens. The body produces antibodies which bind to antigens. These complexes are circulating and deposited on the endothelium. Endothelial dysfunction and inflammation is initiated ending in atherogenesis. It also means alteration in total acidity. A megalorganism is better to be alkaline than acidic. Within alkaline environment, no disease is present. Ph of blood below 7 equals death. Atheromatic plaque is a form of highly diverse biofilm built by the endogenous microorganisms[102]. It is necessary to understand its composition so that we proceed to the appropriate treatment using methods such as enzymatic lyses [103, 104]. Fibrinolytic therapy with tissue plasminogen activator (: alteplase) was used in vascular occlusions. The rheological improvement was due to the reduction of plasma viscosity[105].

All plaques are biofilms resistant to antibiotics. Antimicrobial peptides (: AMPs made up of 10–50 amino-acid) have been considered crucial in human immunity. They act against Gram-positive and Gram-negative bacteria, fungi, eradicating biomembranes. The anti-biofilm molecules (: herbal compounds, lantibiotics etc.) interfere in the quorum sensing pathways, adhesion mechanisms, disruption of extracellular DNA, and the messengers involved in biofilm formation[106, 107].

Dietary changes can fight biofilms and infections of the vascular system. Proanthocyanidins (PACs) from cranberries have properties against *Escherichia coli*, *P. aeruginosa* and their biofilms[108]. Diet with stevia, xylitol, probiotics, vegan food, mint resulted in less caries and plaque development[109]. The Mediterranean diet with olives, nuts, fruits, vegetables, fish, and minimal consumption of animal products changes our microbiome, displacing the aciduric and acidogenic bacteria[109, 110].

Atherosclerosis affects all organs and fetus in pregnancy. Maternal hypercholesterolemia enhances fetal lesions and postnatal atherogenesis[111]. It equals inflammation and may be associated with banana intolerance leading to immunocomplexes (: IgG-Ag) deposited on the endothelium. The microbiota of this fruit may build the arteriosclerotic biofilm.

We need to understand better the food related microbiology and immunology, so that we apply therapeutic nutrition.

Conclusions

All food categories cannot be consumed by all consumers due to intolerances or allergies. Research through the literature gives rationale to the relationship between banana intolerance and consumption with arteriosclerosis. It is necessary to explore banana microflora and constituents for the benefit of immunity system and biological microenvironment without causing metabolic disorders or inflammation. It is also mandatory to search the microbiota of the host and the ways it works for a living.

What we have seen in terms of the atherosclerotic mechanisms and banana suggests that banana intolerance and consumption may mediate atherogenesis and growth of plaques. The host organism attacks the “foreigner - banana” resulting as a boomerang to its own destruction.

Banana diseases depend on the soil and its microbial populations. The relationship between the soil and banana are not clear. The soil is the “food” source of banana and its soil-borne diseases.

Atherosclerosis is associated with nutrition and its feed-borne diseases. Under circumstances banana’s living microorganisms can build the biological colonies of the plaques for their safety or the microorganisms of the host can digest banana producing metabolites and reconstruct colonies for their survival producing plaques and destroy the human body.

Dietary biological “microenvironment” and antigenic content may be the key-translation to atheroma formation. There is limited information about fruit antigens and microbiota and their interactions with the host. Antigens may be the ingredients or microflora of diet. Research focusing on adverse immune and microbiological responses to food could clarify the underlying mechanism of banana-induced atherosclerosis. Biofilms and immune-complexes could link banana with inflammation and atherosclerosis. Plaques are built by living “microbes” fighting for home and food.

The banana nutrients are good for us and for our intrinsic “habitants”. Banana is a benign fruit but the host organism (: consumer) weaknesses attack and incriminate it.

Extensive studies on the microbiology and dietology of diseases should be conducted to further enlighten the “gaps” of this issue.

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Author contributions

Angeliki or Aggeliki Tsantsaridou had the idea and wrote this particular article. George Valsamakis revised it and corrected it. The rest of the authors also contributed to drafting the manuscript.

References

- Siasos G, Tsigkou V, Kokkou E, Oikonomou E, Vavuranakis M, Vlachopoulos C, et al. Smoking and atherosclerosis: mechanisms of disease and new therapeutic approaches. *Curr Med Chem*. 2014;21(34):3936-3948.
- Messner B, Bernhard D. Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. *Arterioscler Thromb Vasc Biol*. 2014;34(3):509-515. Doi: 10.1161/ATVBAHA.113.300156
- Hegele RA. Gene-environment interactions in atherosclerosis. *Mol Cell Biochem*. 1992;113(2):177-186.
- Lovren F, Teoh H, Verma S. Obesity and atherosclerosis: mechanistic insights. *Can J Cardiol*. 2015;31(2):177-183. doi: 10.1016/j.cjca.2014.11.031
- Colafella KMM, Denton KM. Sex-specific differences in hypertension and associated cardiovascular disease. *Nat Rev Nephrol*. 2018;14(3):185-201. doi: 10.1038/nrneph.2017.189
- Cappello AR, Dolce V, Iacopetta D, Martello M, Fiorillo M, Curcio R, et al. Bergamot (Citrus bergamia Risso) Flavonoids and Their Potential Benefits in Human Hyperlipidemia and Atherosclerosis: an Overview. *Mini Rev Med Chem*. 2016;16(8):619-629.
- Yuan T, Yang T, Chen H, Fu D, Hu Y, Wang J, et al. New insights into oxidative stress and inflammation during diabetes mellitus-accelerated atherosclerosis. *Redox Biol*. 2019;20:247-260. Doi: 10.1016/j.redox.2018.09.025
- Chen Y, Liu R, Zhang G, Yu Q, Jia M, Zheng C, et al. Hypercysteinemia promotes atherosclerosis by reducing protein S-nitrosylation. *Biomed Pharmac*. 2015;70:253-259. doi: 10.1016/j.biopha.2015.01.030
- Thijssen DH, Carter SE, Green DJ. Arterial structure and function in vascular ageing: are you as old as your arteries? *J Physiol*. 2016;594(8):2275-2284. doi: 10.1113/jphysiol.2016.05.007
- Orhan IE et al. Naringenin and atherosclerosis: a review of literature. *Curr Pharm Biotechnol*. 2015;16(3):245-251.
- Zhu Y, Xian X, Wang Z, Bi Y, Chen Q, Han X. Research Progress on the Relationship between Atherosclerosis and Inflammation. *Biomolecules*. 2018;8(3). pii: E80. Doi: 10.3390/biom8030080
- Leowattana W. Chronic infections and atherosclerosis. *J Med Assoc Thai*. 2001;84 Suppl 3:S650-S657.
- Froberg MK, Seacotte N, Dahlberg E. Cytomegalovirus seropositivity and serum total cholesterol levels in young patients. *Ann Clin Lab Sci*. 2001;31(2):157-161.
- Apostolou P, Tsantsaridou A, Papasotiriou I, Toloudi M, Chatziioannou M, Giamouzis G. Bacterial and fungal microflora in surgically removed lung cancer samples. *J Cardiothorac Surg*. 2011;6:137. Doi: 10.1186/1749-8090-6-137
- Kebschull M, Demmer RT, Papapanou PN. "Gum bug, leave my heart alone!"--epidemiologic and mechanistic evidence linking periodontal infections and atherosclerosis. *J Dent Res*. 2010;89(9):879-902. Doi: 10.1177/0022034510375281
- Freebairn D, Linton D, Harkin-Jones E, Jones DS, Gilmore BF, Gorman SP. Electrical methods of controlling bacterial adhesion and biofilm on device surfaces. *Expert Rev Med Devices*. 2013;10(1):85-103. doi: 10.1586/erd.12.70
- Huang LM. Recent advances in the study, prevention, and treatment of infectious diseases. *J Formos Med Assoc*. 2000;99(2):92-99.
- Kuppuswamy VC, Gupta S. Antibiotic therapy for coronary heart disease: the myth and the reality. *Timely Top Med Cardiovasc Dis*. 2006;10:E2. Review.
- Kaplan M, Yavuz SS, Cinar B, Koksai V, Kut MS, Yapici F, et al. Detection of Chlamydia pneumoniae and Helicobacter pylori in atherosclerotic plaques of carotid artery by polymerase chain reaction. *Int J Infect Dis*. 2006;10(2):116-123.
- Visseren F, Verkerk MS, van der Bruggen T, Marx JJ, van Asbeck BS, Diepersloot RJ. Iron chelation and hydroxyl radical scavenging reduce the inflammatory response of endothelial cells after infection with Chlamydia pneumoniae or influenza A. *Eur J Clin Invest*. 2002;32(s1):84-90.
- Albert NM. Inflammation and infection in acute coronary syndrome. *J Cardiovasc Nurs*. 2000;15(1):13-26.
- Minihane AM, Vinoy S, Russell WR, Baka A, Roche HM, Tuohy KM, et al. Low-grade inflammation, diet composition and health: current research evidence and its translation. *Br J Nutr*. 2015;114(7):999-1012. Doi: 10.1017/S0007114515002093
- Padilla EC, Lobos GO, Jure OG, Matus FS, Descouvieres CC, Hasbún AS, et al. Isolation of periodontal bacteria from blood samples and atheromas in patients with atherosclerosis and periodontitis. *Rev Med Chil*. 2007;135(9):1118-1124.
- Tonetti MS, Van Dyke TE. working group 1 of the joint EFP/AAP workshop. Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *J Periodontol*. 2013;84(4 Suppl):S24-S29. doi: 10.1902/jop.2013.1340019
- Dobretsov S, Rittschof D. Love at First Taste: Induction of Larval Settlement by Marine Microbes. *Int J Mol Sci*. 2020;21(3). pii: E731. doi: 10.3390/ijms21030731
- Angeliki Tsantsaridou, Vissarion Panagiotis Papathanasiou, Gerasimos Dimisianos. Association of Food Intolerance with Coronary Artery Disease. *Journal of Food and Nutrition Research*. 2019;7(1):71-81.
- Park SJ, Kim JY, Teoh CL, Kang NY, Chang YT. New targets of molecular imaging in atherosclerosis: prehension of current status. *Anal Sci*. 2015;31(4):245-255. doi: 10.2116/analsci.31.245
- Hughes MF, Lenighan YM, Godson C, Roche HM. Exploring Coronary Artery Disease GWAS Targets With Functional Links to Immunometabolism. *Front Cardiovasc Med*. 2018;6(5):148. doi: 10.3389/fcvm.2018.00148
- Mirzaei H, Di Biase S, Longo VD. Dietary Interventions, Cardiovascular Aging, and Disease: Animal Models and Human Studies. *Circ Res*. 2016;118(10):1612-1625. doi: 10.1161/CIRCRESAHA.116.307473
- Guiglia R, Lo Russo L, Coccia E, Di Liberto C, D'Angelo M, Indovina G, et al. The association between periodontal diseases and cardiovascular diseases: a narrative review. *Panminerva Med*. 2008;50(4):327-337.
- Ford PJ, Raphael SL, Cullinan MP, Jenkins AJ, West MJ, Seymour GJ. Why should a doctor be interested in oral disease? *Expert Rev*

- Cardiovasc Ther. 2010;8(10):1483-1493. doi: 10.1586/erc.10.109
32. Yakob M, Söder B, Meurman JH, Jogestrand T, Nowak J, Söder PÖ. *Prevotella nigrescens* and *Porphyromonas gingivalis* are associated with signs of carotid atherosclerosis in subjects with and without periodontitis. *J Periodontol Res*. 2011;46(6):749-755. Doi: 10.1111/j.1600-0765.2011.01398.x
 33. Tonetti MS, Van Dyke TE; working group 1 of the joint EFP/AAP workshop. Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *Periodontol*. 2013; 84(4 Suppl):S24-9. doi: 10.1902/jop.2013.1340019. PMID: 23631582
 34. Kriebel K, Hieke C, Müller-Hilke B, Nakata M, Kreikemeyer B. Oral Biofilms from Symbiotic to Pathogenic Interactions and Associated Disease -Connection of Periodontitis and Rheumatic Arthritis by Peptidylarginine Deiminase. *Front Microbiol*. 2018;30(9):53. doi: 10.3389/fmicb.2018.00053
 35. Kariu T, Nakao R, Ikeda T, Nakashima K, Potempa J, Imamura T. Inhibition of gingipains and *Porphyromonas gingivalis* growth and biofilm formation by prenyl flavonoids. *J Periodontol Res*. 2017;52(1):89-96. doi: 10.1111/jre.12372
 36. Sabharwal A, Gomes-Filho IS, Stellrecht E, Scannapieco FA. Role of periodontal therapy in management of common complex systemic diseases and conditions: An update. *Periodontol*. 2000. 2018;78(1):212-226. doi: 10.1111/prd.12226
 37. Verma S, Indumathi VA, Gurudev KC, Naik SA. Bacteriological Quality of Treated Water and Dialysate in Haemodialysis Unit of A Tertiary Care Hospital. *J Clin Diagn Res*. 2015;9(10):DC14-DC16. doi: 10.7860/JCDR/2015/14681.6692
 38. Du LY, Sun XL, Yu WX, Ren JY, Gu XM, Zhou YM. Research progress in the pathogenic mechanisms of *Porphyromonas gingivalis* fimbriae. *Zhonghua Kou Qiang Yi Xue Za Zhi*. 2018;53(10):703-707. doi: 10.3760/cma.j.issn.1002-0098.2018.10.011
 39. Mitra S, Drautz-Moses DI, Alhede M, Maw MT, Liu Y, Purbojati RW. In silico analyses of metagenomes from human atherosclerotic plaque samples. *Microbiome*. 2015;3:38. doi: 10.1186/s40168-015-0100-y
 40. Dommisch H, Kuzmanova D, Jönsson D, Grant M, Chapple I. Effect of micronutrient malnutrition on periodontal disease and periodontal therapy. *Periodontol*. 2000. 2018;78(1):129-153. doi: 10.1111/prd.12233
 41. Lim ES, Wang D, Holtz LR. The Bacterial Microbiome and Virome Milestones of Infant Development. *Trends Microbiol*. 2016;24(10):801-810. doi: 10.1016/j.tim.2016.06.001
 42. Li DY, Tang WHW. Gut Microbiota and Atherosclerosis. *Curr Atheroscler Rep*. 2017;19(10):39. doi: 10.1007/s11883-017-0675-9
 43. Marcinkiewicz J, Strus M, Pasich E. Antibiotic resistance: a "dark side" of biofilm associated chronic infections. *Pol Arch Med Wewn*. 2013; 123(6):309-313
 44. Heianza Y, Ma W, Manson JE, Rexrode KM, Qi L. Gut Microbiota Metabolites and Risk of Major Adverse Cardiovascular Disease Events and Death: A Systematic Review and Meta-Analysis of Prospective Studies. *J Am Heart Assoc*. 2017;6(7). pii: e004947. doi: 10.1161/JAHA.116.004947
 45. van der Meer JJ, vander Wal AC, Teeling P, Idu MM, vander Ende A, de Boer OJ. Multiple bacteria contribute to intraplaque T-cell activation in atherosclerosis. *Eur J Clin Invest*. 2008;38(11):857-862. doi: 10.1111/j.1365-2362.2008.02031.x
 46. Ghayour-Mobarhan M, Rahsepar AA, Tavallaie S, Rahsepar S, Ferns GA. The potential role of heat shock proteins in cardiovascular disease: evidence from in vitro and in vivo studies. *Adv Clin Chem*. 2009;48:27-72.
 47. Mayr M, Metzler B, Kiechl S, Willeit J, Schett G, Xu Q. Endothelial cytotoxicity mediated by serum antibodies to heat shock proteins of *Escherichia coli* and *Chlamydia pneumoniae*: immune reactions to heat shock proteins as a possible link between infection and atherosclerosis. *Circulation*. 1999;99(12):1560-1566.
 48. Prasad A, Zhu J, Halcox JP, Wacławski MA, Epstein SE, Quyyumi AA. Predisposition to atherosclerosis by infections: role of endothelial dysfunction. *Circulation*. 2002;106(2):184-190.
 49. Tobias P, Curtiss LK. Thematic review series: The immune system and atherogenesis. Paying the price for pathogen protection: toll receptors in atherogenesis. *J Lipid Res*. 2005;46(3):404-411.
 50. Hammann L, Glaeser C, Hamprecht A, Gross M, Gomma A, Schumann RR. Toll-like-receptor (TRL)-9 promoter polymorphisms and atherosclerosis. *Clin Chim Acta*. 2006;364(1-2):303-307.
 51. Miller YI, Viriyakosol S, Binder CJ, Feramisco JR, Kirkland TN, Witztum JL. Minimally modified LDL binds to CD14, induces macrophage spreading via TLR4/MD-2, and inhibits phagocytosis of apoptotic cells. *J Biol Chem*. 2003; 278(3):1561-1568.
 52. Ravnkov U, McCully KS. Infections may be causal in the pathogenesis of atherosclerosis. *Am J Med Sci*. 2012; 344(5):391-394. Doi: 10.1097/MAJ.0b013e31824ba6e0
 53. Jaber J, Murin J, Kinová S, Gavorník P, Ghanem Wisam MA, et al. The role of infection and inflammation in the pathogenesis of atherosclerosis. *Vnitř Lek*. 2002;48(7):657-666.
 54. Steiner UC, Kölliker L, Weber-Chrysochoou C, Schmid-Grendelmeier P, Probst E, Wüillemin WA, et al. Food as a trigger for abdominal angioedema attacks in patients with hereditary angioedema. *Orphanet J Rare Dis*. 2018;13(1):90. doi: 10.1186/s13023-018-0832-4.
 55. Kuchnia AJ, Conlon B, Greenberg N. Natural Bioactive Food Components for Improving Enteral Tube Feeding Tolerance in Adult Patient Populations. *Nutr. Clin Pract*. 2018;33(1):107-120. doi: 10.1177/0884533617722164
 56. Gonczewicz A, Misiewicz A, Owczarek L, Jasińska U, Skąpska S. The Effect of a Newly Developed Oat-Banana Fermented Beverage with a Beta-glucan Additive on LDL Gene Expression in *Streptococcus thermophilus* TKM3 KKP 2030p. *Curr Microbiol*. 2016;73(6):773-780.
 57. Asero R, Mistrello G, Roncarolo D, Amato S. Detection of some safe plant-derived foods for LTP-allergic patients. *Int Arch Allergy Immunol*. 2007;144(1):57-63.
 58. Brehler R, Theissen U, Mohr C, Luger T. Latex-fruit syndrome": frequency of cross-reacting IgE antibodies. *Allergy*. 1997; 52(4):404-410.
 59. Guariso G, Bertoli S, Cernetti R, Battistella PA, Setari M, Zacchello F. Migraine and food intolerance: a controlled study in pediatric patients. *Paediatr Med Chir*. 1993;15(1):57-61.
 60. Hunter DC, Skinner MA, Wolber FM, Booth CL, Loh JM, Wohlers M, et

- al. Consumption of gold kiwifruit reduces severity and duration of selected upper respiratory tract infection symptoms and increases plasma vitamin C concentration in healthy older adults. *Br J Nutr*. 2012; 108(7):1235-1245.
61. Wolfe KL, Kang X, He X, Dong M, Zhang Q, Liu RH. Cellular antioxidant activity of common fruits. *J Agric Food Chem* 2008;56(18):8418-8426. doi: 10.1021/jf801381y
 62. Yin X, Quan J, Kanazawa T. Banana prevents plasma oxidative stress in healthy individuals. *Plant Foods Hum Nutr*. 2008;63(2):71-76. doi: 10.1007/s11130-008-0072-1
 63. Mitsou EK, Kougia E, Nomikos T, Yannakoulia M, Mountzouris KC, Kyriacou A. Effect of banana consumption on faecal microbiota: a randomised, controlled trial. *Anaerobe* 2011;17(6):384-387. doi: 10.1016/j.anaerobe.2011.03.018
 64. Faustova MO, Ananieva MM, Basarab YO, Dobrobolska OV, Vovk IM, Loban' GA. Bacterial factors of cariogenicity (literature review). *Wiad Lek*. 2018;71(2 pt 2):378-382.
 65. Wright N, Wilson L, Smith M, Duncan B, McHugh P. The BROAD study: A randomized controlled trial using a whole food plant-based diet in the community for obesity, ischaemic heart disease or diabetes. *Nutr Diabetes*. 2017;7(3):e256. doi: 10.1038/nutd.2017.3
 66. Singh B, Singh JP, Kaur A, Singh N. Bioactive compounds in banana and their associated health benefits - A review. *Food Chem* 2016; 206:1-11. Doi: 10.1016/j.foodchem.2016.03.033
 67. Sun J, Chu YF, Wu X, Liu RH. Antioxidant and antiproliferative activities of common fruits. *J Agric Food Chem*. 2002;50(25):7449- 7454.
 68. Ana Luisa Falcomer, Roberta Figueiredo Resende Riquette, Bernardo Romão de Lima, Verônica C. Ginani, and Renata Puppin Zandonadi. Health Benefits of Green Banana Consumption: A Systematic Review. *Nutrients*. 2019;11(6):1222. 2019;11(6). pii: E1222. doi: 10.3390/nu11061222
 69. Olvera-Hernández V, Ble-Castillo JL, Betancur-Ancona D, Acevedo-Fernández JJ, Castellanos-Ruelas A, Chel-Guerrero L. Effects of modified banana (*Musa cavendish*) starch on glycemic control and blood pressure in rats with high sucrose diet. *Nutr Hosp*. 2018; 35(3):588-595. doi: 10.20960/nh.1506
 70. Levine SR, Coull BM. Potassium depletion as a risk factor for stroke: will a banana a day keep your stroke away? *Neurology*. 2002; 59(3):302-3.
 71. Wilders-Truschnig M, Mangge H, Lieners C, Gruber H, Mayer C, März W. IgG antibodies against food antigens are correlated with inflammation and intima media thickness in obese juveniles. *Exp Clin Endocrinol Diabetes*. 2008;116(4):241-245.
 72. A K G Hassan, Y P Venkatesh. An Overview of Fruit Allergy and the Causative Allergens. *Eur Ann Allergy Clin Immunol*. 2015;47(6):180-187.
 73. Nuray Bayar Muluk, Cemal Cingi. Oral Allergy Syndrome. *Am J Rhinol Allergy*. 2018;32(1):27-30. doi:10.2500/ajra.2018.32.4489
 74. Murli Manohar, Alok K Verma, Sathisha Upparahalli Venkateshaiah, Hemant Goyal, Anil Mishra. Food-Induced Acute Pancreatitis. *Dig Dis Sci*. 2017; 62(12):3287-3297. doi: 10.1007/s10620-017-4817-2
 75. Emma L Culver, Ellen Vermeulen, Mateusz Makuch, Astrid van Leeuwen, Ross Sadler, Tamsin Cargill. Increased IgG4 Responses to Multiple Food and Animal Antigens Indicate a Polyclonal Expansion and Differentiation of Pre-Existing B Cells in IgG4-related Disease. *Annals of the Rheumatic Diseases*. 2014;74(5).
 76. Shen Z, Penton CR, Lv N, Xue C, Yuan X, Ruan Y, et al. Banana Fusarium Wilt Disease Incidence Is Influenced by Shifts of Soil Microbial Communities Under Different Monoculture Spans. *Microb Ecol*. 2018;75(3):739-750. doi: 10.1007/s00248-017-1052-5
 77. Getz GS, Reardon CA. Diet, Microbes, and Murine Atherosclerosis. *Arterioscler Thromb Vasc Biol*. 2018;38(10):2269-2271. doi: 10.1161/ATVBAHA.118.311513
 78. Fatkhullina AR, Peshkova IO, Dzutsev A, Aghayev T, McCulloch JA, Thovarai V, et al. An Interleukin-23-Interleukin-22 Axis Regulates Intestinal Microbial Homeostasis to Protect from Diet-Induced Atherosclerosis. *Immunity*. 2018;49(5):943-957.e9. doi: 10.1016/j.immuni.2018.09.011
 79. Luna M, García S, García O, Trigos Á. Serratia a new metabolite obtained from *Serratia marcescens*, a bacterium isolated from the microflora associated with banana plantations. *Nat Prod Res*. 2013;27(1):49-53. doi: 10.1080/14786419.2011.650638
 80. Beighton D, Brailsford SR, Gilbert SC, Clark DT, Rao S, Wilkins JC, et al. Intra-oral acid production associated with eating whole or pulped raw fruits. *Caries Res*. 2004;38(4):341-349.
 81. Chen YS, Liao YJ, Lan YS, Wu HC, Yanagida F. Diversity of Lactic Acid Bacteria Associated with Banana Fruits in Taiwan. *Curr Microbiol*. 2017; 74(4):484-490. doi: 10.1007/s00284-017-1213-2
 82. Zhong ST, Shen ZZ, Sun YF, Lyu NN, Ruan YZ, Li R, Shen QR. Effects of continuous application of bio-organic fertilizer on banana production and cultural microflora of bulk soil in orchard with serious disease incidence. *Ying Yong Sheng Tai Xue Bao*. 2015;26(2):481-489.
 83. Dromard CR, Bouchon-Navaro Y, Cordonnier S, Guéné M, Harmelin-Vivien M, Bouchon C. Different transfer pathways of an organochlorine pesticide across marine tropical food webs assessed with stable isotope analysis. *PLoS One*. 2018;13(2):e0191335. doi: 10.1371/journal.pone.0191335
 84. Sethuramalingam TA, Haniffa MA. Effect of formulated diet on digestive enzymes of *Labeo rohita* (Ham.). *Indian J Exp Biol*. 2002;40(1):83-8.
 85. Sabater-Molina M, Larqué E, Torrella F, Zamora S. Dietary fructooligosaccharides and potential benefits on health. *J Physiol Biochem*. 2009;65(3):315-328. doi: 10.1007/BF03180584
 86. Hongpattarakere T, Uraipan S. Bifidogenic characteristic and protective effect of saba starch on survival of *Lactobacillus plantarum* C1F17AN2 during vacuum-drying and storage. *Carbohydr Polym*. 2015;117:255-261. doi: 10.1016/j.carbpol.2014.09.065
 87. Lehmann U, Jacobasch G, Schmiedl D. Characterization of resistant starch type III from banana (*Musa acuminata*). *J Agric Food Chem*. 2002; 50(18):5236-5240.
 88. Ludwiczuk A, Kieltyka-Dadasiewicz A, Sawicki R, Golus J, Grażyna Ginalska. Essential Oils of some *Mentha* Species and Cultivars, their Chemistry and Bacteriostatic Activity. *Nat Prod Commun*. 2016;11(7):1015-1018.
 89. Dorfman S, Dorfman D, Leonardi R, Maroso J, Cardozo J, Durán A. Comparison of hemp and cotton fiber implants in muscle rat tissue. Study of the inflammatory response. *Invest Clin*. 1994;35(1):35-40.
 90. Uraipan S, Brigidi P, Hongpattarakere T. Antagonistic mechanisms

- of symbiosis between *Lactobacillus plantarum* CIF17AN2 and green banana starch in the proximal colon model challenged with *Salmonella Typhimurium*. *Anaerobe*. 2014;28:44-53. doi: 10.1016/j.anaerobe.2014.05.002
91. Slavin J. Fiber and prebiotics: mechanisms and health benefits. *Nutrients*. 2013;5(4):1417-135. doi: 10.3390/nu5041417
 92. Chen X, Yu C, Li S, Li X, Liu Q. Integration Host Factor Is Essential for Biofilm Formation, Extracellular Enzyme, Zeamine Production, and Virulence in *Dickeya* spp. *Mol Plant Microbe Interact*. 2019;32(3):325-335. doi: 10.1094/MPMI-04-18-0096-R
 93. Huang N, Pu X, Zhang J, Shen H, Yang Q, Wang Z, Lin B. In Vitro Formation of *Dickeya* spp. Biofilm. *Curr Microbiol*. 2019;76(1):100-107. doi: 10.1007/s00284-018-1593-y
 94. Hatje E, Minniti G, Stewart MJ, Neuman C, Knibb W, Katouli M. First description of 'Chalky back' phenomenon in banana prawns (*Fenneropenaeus merguensis*) and its possible association with *Vibrio* and *Photobacterium* species. *FEMS Microbiol Lett*. 2016;363(4). pii: fnw019. doi: 10.1093/femsle/fnw019
 95. Yuan J, Zhang N, Huang Q, Raza W, Li R, Vivanco JM, Shen Q. Organic acids from root exudates of banana help root colonization of PGPR strain *Bacillus amyloliquefaciens* NJN-6. *Sci Rep*. 2015;24; 5:13438. doi: 10.1038/srep13438. PMID: 26299781
 96. Ceballos I, Mosquera S, Angulo M, Mira JJ, Argel LE, Uribe-Velez D, et al. Cultivable bacteria populations associated with leaves of banana and plantain plants and their antagonistic activity against *Mycosphaerella fijiensis*. *Microb Ecol*. 2012;64(3):641-653.
 97. Golias C, Batistatou A, Bablekos G, Charalabopoulos A, Peschos D, Mitsopoulos P, Charalabopoulos K. Physiology and pathophysiology of selectins, integrins, and IgSF cell adhesion molecules focusing on inflammation. A paradigm model on infectious endocarditis. *Cell Commun Adhes*. 2011;18(3):19-32. doi: 10.3109/15419061.2011.606381
 98. DeCarvalho JF, Pereira RM, Shoenfeld Y. Vaccination for atherosclerosis. *Clin Rev Allergy Immunol*. 2010;38(2-3):135-40. doi: 10.1007/s12016-009-8145-y
 99. Chałas R, Wójcik-Chęcińska I, Woźniak MJ, Grzonka J, Świąszkowski W, Kurzydłowski KJ. [Dental plaque as a biofilm - a risk in oral cavity and methods to prevent]. *Postepy Hig Med Dosw*. 2015;69:1140-1148.
 100. Knaapen M, Kootte RS, Zoetendal EG, de Vos WM, Dallinga-Thie GM, Levi M, et al. Obesity, non-alcoholic fatty liver disease, and atherothrombosis: a role for the intestinal microbiota? *Clin Microbiol Infect*. 2013;19(4):331-337. doi: 10.1111/1469-0691.12170
 101. Aukrust P, Yndestad A, Waehre T, Gullestad L, Halvorsen B, Damås JK. Inflammation in coronary artery disease: potential role for immunomodulatory therapy. *Expert Rev Cardiovasc Ther*. 2005;3(6):1111-1124.
 102. Ferrera I, Massana R, Balagué V, Pedrós-Alió C, Sánchez O, Mas J. Evaluation of DNA extraction methods from complex phototrophic biofilms. *Biofouling*. 2010;26(3):349-357. doi: 10.1080/08927011003605870
 103. Zenz W, Muntean W, Beitzke A, Zobel G, Riccabona M, Gamillscheg A. Tissue plasminogen activator (alteplase) treatment for femoral artery thrombosis after cardiac catheterisation in infants and children. *Br Heart J*. 1993;70(4):382-385.
 104. Werner RG, Bassarab S, Hoffmann H, Schlüter M. Quality aspects of fibrinolytic agents based on biochemical characterization. *Arzneimittelforschung*. 1991; 41(11):1196-1200.
 105. Hagen R. Fibrinolytic therapy in sudden deafness with recombinant tissue-type plasminogen activator. Hemorheologic and therapeutic effects]. *Laryngorhinootologie*. 1991;70(7):353-358.
 106. Chung PY, Khanum R. Antimicrobial peptides as potential anti-biofilm agents against multidrug-resistant bacteria. *J Microbiol Immunol Infect*. 2017;50(4):405-410.
 107. Roy R, Tiwari M, Donelli G, Tiwari V. for combating bacterial biofilms: A focus on anti-biofilm agents and their mechanisms of action. 2018; 522-554.
 108. Ulrey RK, Barksdale SM, Zhou W, van Hoek ML. Cranberry proanthocyanidins have anti-biofilm properties against *Pseudomonas aeruginosa*. *BMC Complement Altern Med*. (2014)
 109. Kishta-, Derani M, Neiva GF, Boynton JR, Kim YE, Fontana M. The antimicrobial potential of stevia in an in vitro microbial caries model. *Am J Dent*. 2016; 29(2):87-92.
 110. D. Beighton. Can the Ecology of the Dental Biofilm Be Beneficially Altered? *Adv Dent Res*. 2009; 21(1):69-73. doi: 10.1177/0895937409335641
 111. Palinski W, Napoli C. The fetal origins of atherosclerosis: maternal hypercholesterolemia, and cholesterol-lowering or antioxidant treatment during pregnancy influence in utero programming and postnatal susceptibility to atherogenesis. *FASEB J* 2002;16(11):1348-1360.