

REVIEW

Foods of the Mediterranean diet: tomato, olives, chili pepper, wheat flour and wheat germ

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Keywords

Mediterranean diet • Flavonoids • Wheat germ • Chili pepper • Tomatoes • Olives

Summary

Mediterranean people, which follows a diet rich in minimally-processed plant-based foods, are believed to live longer and healthier lives than many other populations in the Western world. Epidemiological and clinical data suggest that the Mediterranean diet has beneficial effects for several chronic diseases, such as cardiovascular diseases, obesity, cancer and diabetes. Although the mechanisms of action of the Mediterranean diet are not completely clear, the synergistic effects of a number of its components and their bioactive phytochemicals exert antioxidant, anti-inflammatory, anti-microbial and anti-cancer effects. The Mediterranean diet includes daily consumption of whole cereals, fruit, vegetables and legumes

in moderate proportions, weekly consumption of white meat in low to moderate proportions and occasionally sweets and chocolates in small amounts. Since olive oil is the main lipids source, it has special significance for health. Healthy fruit and vegetables, rich in phytochemicals, are a major proportion of this diet and contribute to the overall nutritional value and bioactivity of its components. Here we review the nutritional and health benefits of wheat germ, tomatoes, olives and chili pepper; items at the base of Mediterranean diet food pyramid that provides beneficial molecules, such as polyphenols, vitamins and flavonoids, and exert anti-inflammatory, anti-microbial and anti-oxidative actions.

Introduction

The Mediterranean diet is currently considered one of the healthiest diets in the world [1-3]. It features daily intake of nuts, vegetables, fruit, olives, olive oil, legumes and whole grains. Rich in antioxidants, fiber, vitamins, minerals, phytosterols, probiotics, omega 3 and omega 6 fatty acids, it has value for human health and wellbeing [1-3]. *Mediterranean diet* is a term coined for the dietary pattern of the people of the southern European countries in 1960s. This population was observed to have a high adult life expectancy, and low rate of diet-related chronic diseases and of certain cancers. The food pattern is typically represented in the form of a pyramid [1]. Indeed, regular consumption of whole grains, vegetables, fruit and legumes with plenty of olive oil and moderate weekly consumption of white meat and low consumption of red meat were the main features of their diet. Although it is still unclear why this diet affords health benefits, epidemiological and clinical studies have produced much evidence that it has lipid-lowering effects, scavenges free radicals thereby reducing oxidative stress, suppresses inflammation and platelet aggregation, restricts specific amino acids thereby inhibiting nutrient-sensing pathways, modulates and regulates growth factors and hormones involved in oncogenesis, and shapes the gut microbiota and corresponding metabolites, thereby influencing overall metabolic health [1-5]. Further research is needed to define the specific effects

Mediterranean diet's nutrients, and how their modification can modulate the microbiome, energy intake and expenditure, thus influencing cells, tissue and organ health during aging.

In addition, the Mediterranean diet is abundant in fresh fruit and vegetables and relies heavily on olive oil as lipid source. Low to moderate consumption of dairy products, red meat, fish, seafood, poultry and eggs [1-3] is another feature. Various studies report that portion-controlled consumption of the components of the diet is beneficial in preventing non-communicable diseases, including chronic and inflammatory diseases such as obesity [4-6], cardiovascular disease [7], diabetes [8, 9], metabolic syndrome [4] and cancer [10] and has a positive impact on autoimmune diseases [11, 12]. The diet has been observed to reduce inflammation and enhance mobility and vitality in patients with rheumatoid arthritis [12] and to decrease the risk of other autoimmune diseases including multiple sclerosis [11]. Among the several foods typical of the Mediterranean diet, wheat, tomatoes, chili pepper and olives proved to have high beneficial effects by many studies. Thus, in this review we focused on the beneficial properties of these specific foods.

Whole grain cereals

Since ancient times, cereals have remained the major staple food across the globe. Cereals are an important

content of every diet, providing carbohydrates, dietary fiber and bioactive molecules with antioxidant, anti-cancer and anti-thrombotic action [13, 14]. Cereals and their derivatives, such as bread and pasta, contribute 55-60% of the total calories of the Mediterranean diet and are therefore indicated at the base of the food pyramid [15]. Unlike refined cereals, whole grain cereals maintain bran, germ, thus containing several bioactive molecules that promote health and mitigate metabolic disorders [16].

WHOLE WHEAT

Wheat is not only an important cash crop but also one of the most widely consumed staple foods in the world. Besides being a major source of starch, dietary fiber and energy, wheat provides substantial amounts of protein (60-70% of which is gluten), B vitamins, carotenoids, phenolic acids, benzoxazinoids, tocopherols, alkyl-resorcinol, phytosterols, biogenic amines and lignans [13-15]. The high fiber content of whole wheat helps digestion and bowel movements, thereby decreasing the risk of intestinal cancer [17]. Phenolic compounds, vitamin E and carotenoids with antioxidant properties help scavenge free radicals, thereby protecting against their deleterious effects.

Wheat polyphenols and antioxidants prevent or decrease the development of several chronic diseases, among which colon and breast cancer, type 2 diabetes and cardiovascular diseases [18-21]. Different varieties of bread wheat and wild-type wheat have been explored for their chemical constituents and bioactive compounds. Some bioactive compounds, such as phenols, antioxidants and vitamin E, are present in almost all types of wheat, however wild-type wheat contains more bioactive compounds. For instance, a comparative study of *Triticum monococcum* ssp. *Monococcum*, *Triticum aestivum* (bread wheat) and *Triticum durum* Desf. (durum wheat) revealed that the first had significantly higher total phenolic, ferulic acid and p-coumaric acid contents than bread and durum wheat, indicating its antioxidative activities and potential health benefits in reducing and preventing cardiovascular disease, diabetes and cancer, in addition to its valuable nutritional properties [22].

The main antioxidants of wheat grain are terpenoids and phenolic acids, such as hydroxycinnamic acid derivatives. They are not present in white wheat flour, while they are concentrated mainly in the bran and germ of wheat [21]. Examples are synapic and p-coumaric acids and dehydromers and dehydrotrimers of ferulic acid [23]. The phenols are bound to the cell wall of the

bran by ester bonds. The highest antioxidant activity occurs in the aleurone layer of the wheat grain [24]. Other antioxidants in wheat bran are flavonoids, carotenoids (mainly lutein) and lignans [25, 26]. In addition to this, wheat contains many vitamins. Indeed, wheat is rich of vitamin B1 (thiamin), B2 (riboflavin), B3 (niacin), B6 (pyridoxine) and B9 (folate) [27].

WHEAT GERM

Wheat germ is usually removed with the milling process, although it is rich in nutrients [17]. Indeed, wheat germ contains a high amount of proteins and carbohydrates, as well as water and lipids. Moreover, as well as whole wheat, wheat germ contains bioactive molecules such as antioxidants (e.g., flavonoids, polyphenols, tocopherols, tocotrienol i.e. vitamin E), carotenoids, plant sterols and biogenic amines [18] (Tab. I).

Biogenic amines have several beneficial effects for human health, especially on fat metabolism, blood pressure and neurotransmitters regulation, but they can cause food poisoning if assumed in excess [19, 20]. Examples are putrescine, spermine, spermidine and histamine. Indeed, they are used as industrial food quality parameters in the Chemical Quality Index [19]. Several research studies proved that these polyamines have an antioxidant activity, preventing damages to cellular membrane and nucleic acids [18]. Wheat germ is rich in polyamine, especially if compared to other foodstuffs [21].

Another significant bioactive compound of wheat is gamma-oryzanol, a phenolic compound with antioxidant activity. Moreover, it participates in lipid metabolism, lowering lipid uptake and improving blood lipid levels [22]. Gamma-oryzanol have been tested in various diseases, such as diabetes, hyperlipidemia and cancer, for its beneficial effects [23-27].

Vegetables and fruit

Bran cereal fiber, fruit, vegetables and tea have a special place in the Mediterranean diet as they inhibit the onset and progress of cardiovascular disease and cancer by virtue of their antioxidant, anti-genotoxic, anti-inflammatory properties.

TOMATOES

Tomatoes both raw and cooked are extensively consumed in the Mediterranean region. Tomatoes are low

Tab. I. Classification of bioactive phytochemicals in whole wheat and wheat germ.

Classification	Bioactive compounds	Bioactivity	References
Polyamines	Putrescine, spermine, and spermidine	Healthy metabolic function, antioxidants	[18, 19]
Phenolic acids	Hydroxy benzoic acid and hydroxy cinnamic acid derivatives e.g., γ -oryzanol, ferulic acid	Antioxidants, lower lipid absorption, anti-cancer, anti-inflammatory	[22]
Tocopherol	Alpha tocopherols and tocotrienols	Cardioprotective	[23]
Carotenoids	Carotenoids, lutein	Anti-cancer, anti-proliferative	[24]
Phenolic lipids	Alkylresorcinols such as 5-alkenylresorcinol	Antioxidant, anti-genotoxic and cytostatic activities	[22]

in fats, rich in vitamins A and C, folate, potassium, carotenoids and polyphenols [28]. Dietary consumption of ripe red tomatoes (rich in polyphenols such as lycopene, flavanones and flavones and carotenoids such as phytoene, β -carotene and lycopene) has beneficial chemoprotective, anti-inflammatory, anti-genotoxic and anti-proliferative effects [29]. Tomato has been studied for its biologically active compounds (Tab. II).

Rich in phytochemicals with anti-proliferative, anti-mutagenic, anti-cancer, anti-inflammatory, and anti-oxidative properties, tomatoes inhibit the onset and progression of chronic diseases, such as cardiovascular disease and cancer. For instance, lycopene and vitamins C and E reduce oxidative stress and the risk of chronic diseases [34, 35]. Specifically, blood concentrations of lycopene are reported to be inversely correlated to the incidence of heart disease [37]. Tomato intake is also inversely correlated with atherosclerosis by virtue of its anti-inflammatory properties [38]. Lipophilic compounds in tomatoes modulate LDLs and the corresponding atherogenic processes in endothelial cells, thereby reducing the risk of cardiovascular disease and atherosclerosis [39].

Tomato products have shown protective effects against lung and prostate cancer [40, 41]. This may be because polyphenols and carotenoids prevent tumorigenesis by impeding the initiation and progression of cancer [34]. Moreover, flavonoids such as quercetin foster chromatin remodeling, thereby inhibiting epigenetic changes that promote cancer [34].

Because tomatoes are rich in carotenoids, tomato consumption promotes intercellular signaling pathways, modulates immune reactions, regulates the cell cycle, induces apoptosis, and interacts with many physiological systems, thereby playing an important role in protecting against chronic diseases [42]. One of the most studied carotenoids of tomato is lycopene. It is stably released during cooking when the plant cell wall is disrupted by heating [43].

In the Mediterranean diet, absorption of lycopene, a non-polar compound, is favored by olive oil. Since lycopene has many useful properties, it has been extensively studied. Figure 1 summarizes some interesting studies on lycopene bioactivity.

OLIVES

Olive trees, olives and olive oils have special significance in the Mediterranean region, providing an important food and nutrient source for the indigenous popu-

lations of the region. The fruit of the olive tree is processed to obtain table olives which are consumed daily in a moderate amount. Olives contain nutritional and non-nutritional components such as carbohydrates, proteins, lipids, minerals, water and phenols [62]. Phenolic compounds occur in almost all parts of olives in different concentrations. The major phenolic compounds are acids, alcohols, flavonoids and secoiridoids [63, 62]. The hydroxytyrosol derivatives, ligstroside, oleuropein and verbascoside are the most abundant biologically active phenolic alcohols of the olive fruit along with tyrosols [63]. They are produced by hydrolysis of oleuropein in the unripe fruit, removing the typical bitter taste of untreated olives [64, 65]. Besides being precursors of hydroxytyrosol, ligstroside and verbascoside, oleuropein has cardioprotective, anti-hypertensive, antioxidant and anti-inflammatory properties [66]. Hydroxytyrosol has been proposed for the treatment of diseases, such as lymphedema and COVID-19 [67-71]. Olive fruits are also rich in flavonoids such as quercetin-3-rutinoside, apigenin-7-rutinoside, apigenin-7-glucoside, luteolin-7-glucoside and luteolin-5-glucoside [72].

Since the phenolic compounds of olive fruits are high in hydroxytyrosol and flavonoids, they have anti-carcinogenic, anti-proliferative and antioxidant activity [73]. Hydroxytyrosol has been shown to scavenge free radicals and activate glutathione reductase and superoxide dismutase [74, 75]. It also has anti-inflammatory properties through inhibition of prostaglandin E, nitric oxide and inflammatory cytokines release [76]. It plays a cardioprotective role by reducing oxidative stress [19, 64], and has cancer preventing properties, significantly suppressing tumor proliferation in skin and breast tissue [77]. Hydroxytyrosol, oleuropein, ligstroside and verbascoside are also useful in the treatment of osteoarthritis [78], in neuroprotection and for wound healing (Fig. 2) [79].

CHILI PEPPER

Epidemiological data regarding chili pepper, a significant constituent of the Mediterranean diet, is still scarce. Chili pepper (*Capsicum annuum*) belongs to the highly diverse and globally distributed genus *Capsicum* of the Solanaceae family, in which domesticated species such as *C. baccatum*, *C. pubescens*, *C. chinense* and *C. frutescens* are also present. Although chili pepper is best known for its pungent flavor, it has significant amounts of carotenoids, provitamin A, vi-

Tab. II. Bioactive compounds of tomato and their health effects.

Classification	Bioactive compounds	Bioactivity	References
Phenolic acids	Caffeic, chlorogenic, synapic, p-coumaric and ferulic acids	Reduction of oxidative stress	[30, 31]
Flavonoids	Quercetin, rutin, kaempferol, chlorogenic acid and naringenin	Antioxidant, anti-cancer	[32, 33]
Carotenoids	Lycopene, α -carotene, β -carotene, γ -carotene, δ -carotene, phytoene, phytofluene, neurosporene and lutein	Antioxidant	[34]
Vitamins	A, B, C and E	Antioxidants, radical scavenging	[35]
Glycoalkaloids	α -tomatine and dihydroxy tomatine	Toxic to pathogens	[36]

Fig. 1. Health benefits of lycopene.

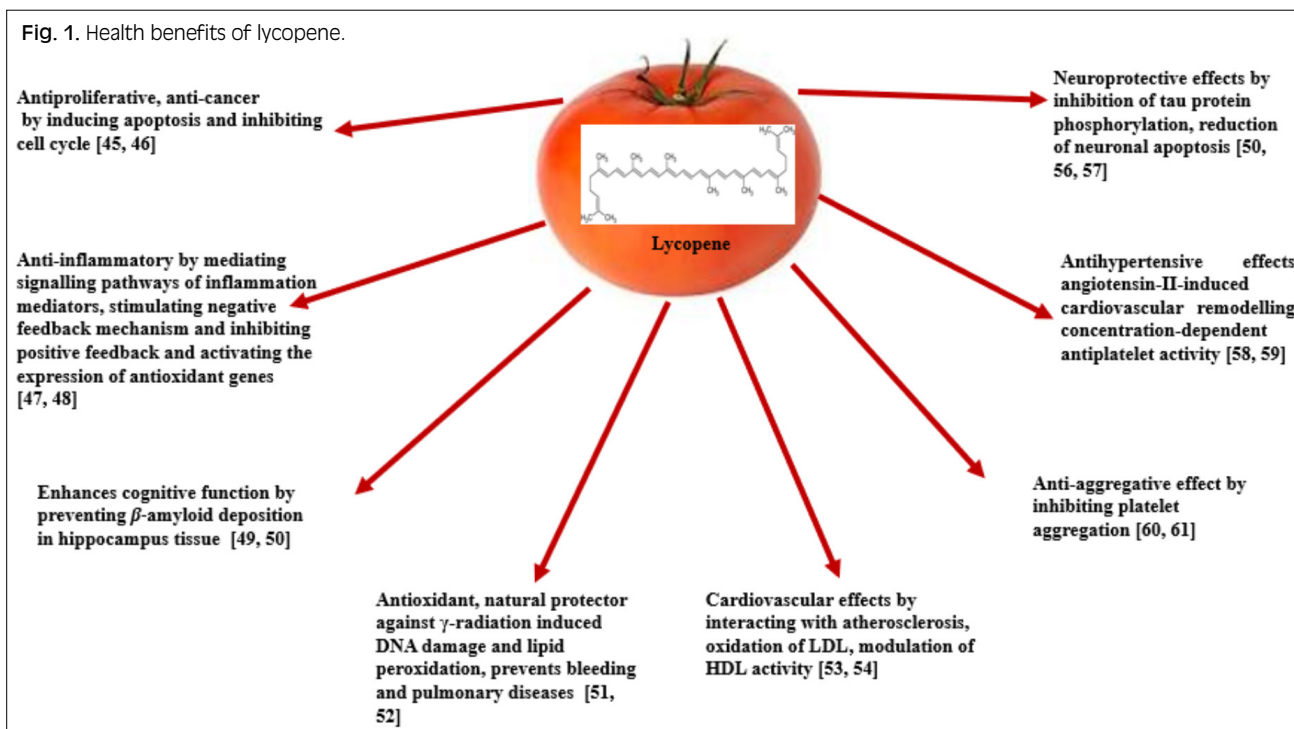
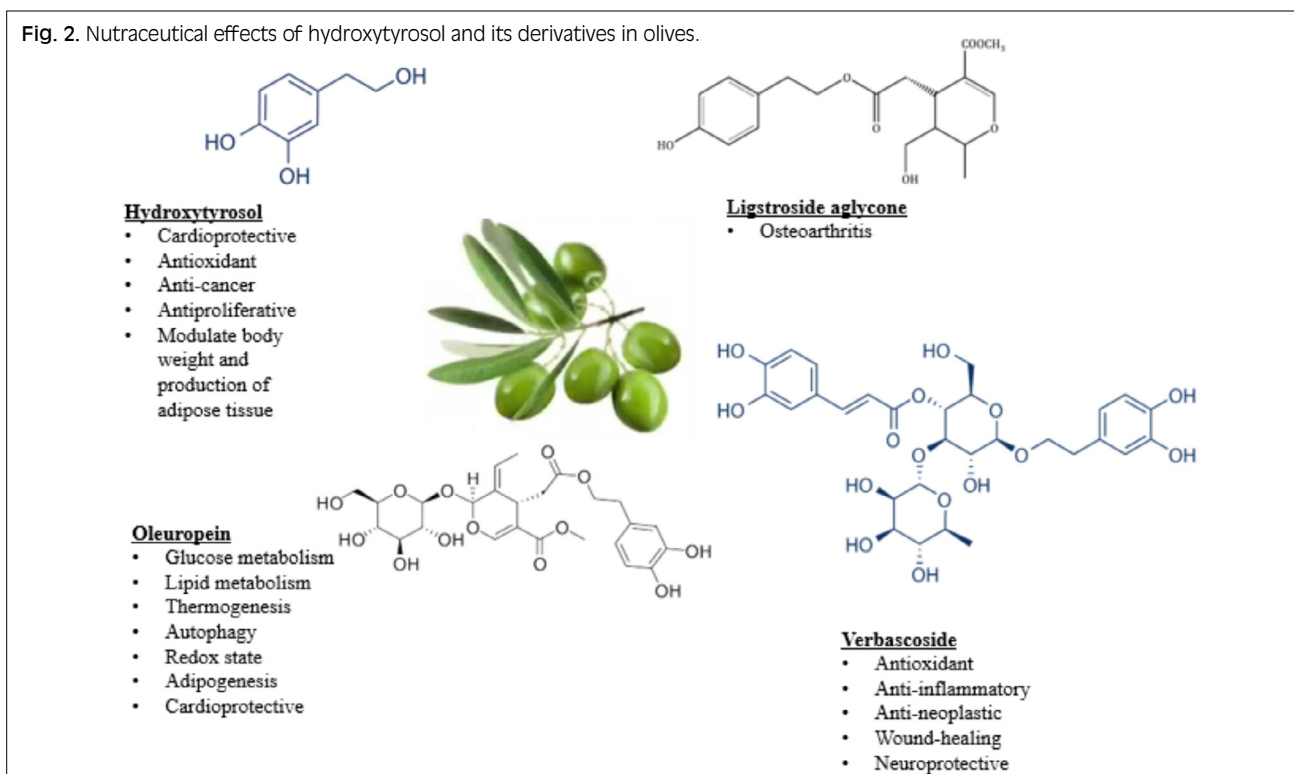


Fig. 2. Nutraceutical effects of hydroxytyrosol and its derivatives in olives.



tamins K, E and C and phenolic compounds such as capsaicinoids, quercetin and luteolin (Fig. 3), which act synergistically to confer antioxidant, anti-inflammatory, anti-cancer, anti-microbial, antiseptic and immunomodulatory properties [80-82]. This makes chili pepper particularly useful in scavenging free radicals and promoting good health.

Chili pepper have been used for the treatment and prevention of several conditions, such as toothache, wound

healing, sore throats, cough, parasitic infections and rheumatism. Creams containing capsaicin and capsi-cum are commercially available for intractable pain and HIV-linked neuropathy [82]. Antioxidant carotenoids (α - and β - carotenes), vitamin C and pro-vitamin A in capsicum peppers support immune function and combat inflammation, thereby easing rheumatism, asthma attacks and arthritis [83]. Chili pepper has been studied for its biologically active compounds (Tab. III).

Tab. III. Biologically active metabolites of chili pepper.

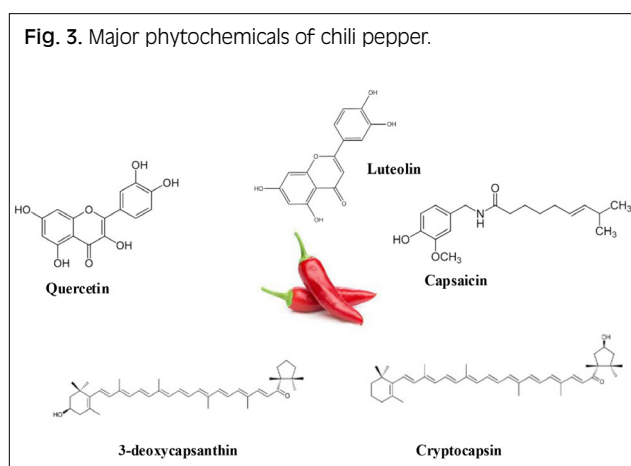
Biological activity	Metabolites	Target cell/organism/disorder	Mechanism	References
Anti-proliferative	Quercetin	Glioblastoma multiforme	Regulates several proteins participating in cell signal transduction	[84]
Antimicrobial	Capsaicin	<i>Bacillus</i> , <i>Micrococcus</i> sp., <i>E. coli</i> , <i>Pseudomonas</i> sp., <i>Citrobacter</i> sp., <i>Salmonella typhimurium</i> , <i>Pseudomonas aeruginosa</i>	Affects membrane stability	[85, 86]
Antiviral	Capsaicin	Guinea pig cutaneous herpes simplex virus	Disrupts virus-neuron connections	[87]
Insecticidal	<i>Capsicum frutescens</i> extracts	<i>A. aegypti</i> mosquitoes	Extract acts as repellent	[88]
Anthelmintic and larvicidal	<i>Capsicum annuum</i> leaf extract essential oils	Cercaria of <i>Schistosoma mansoni</i>	Kills larvae	[89]
Cardiovascular effects	Capsaicin (10-300 µg/kg)	Mongrel dogs	Temporary increase in mean systemic blood pressure	[90]
Anti-inflammatory	Carotenoids	Egg albumin-induced inflammation of rat hind paw	Reduces inflammation	[91]
	Capsaicin	Osteoarthritis	Pain relief	[92]

Conclusion

The Mediterranean diet is rich in fresh fruit, vegetables and cereals that not only are economical but a healthy choice for a long life. These ingredients at the base of the pyramid are recommended for daily consumption. Rich in phytochemicals such as vitamins, carotenoids, flavonoids and phenols, these dietary items may be responsible for the beneficial effects of the Mediterranean diet. Indeed, the Mediterranean population is believed to live longer and healthier than many other population in the Western world, with low incidence of non-communicable diseases such as obesity, cardiovascular diseases and cancer. It therefore stands to reason that the Mediterranean diet holds promise for healthy people with a healthy lifestyle and also for people with chronic health conditions.

Acknowledgements

This research was funded by the Provincia Autonoma di Bolzano in the framework of LP 15/2020 (dgp 3174/2021).



Conflicts of interest statement

Authors declare no conflict of interest.

Author's contributions

MB: study conception, editing and critical revision of the manuscript; ZN, Kristjana D, Kevin D, BA, VV, GM, AI: literature search, editing and critical revision of the manuscript. All authors have read and approved the final manuscript.

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How to cite this article: Naureen Z, Dhuli K, Donato K, Aquilanti B, Velluti V, Matera G, Iaconelli A, Bertelli M. Foods of the Mediterranean diet: tomato, olives, chili pepper, wheat flour and wheat germ. *J Prev Med Hyg* 2022;63(suppl.3):E4-E11. <https://doi.org/10.15167/2421-4248/jpmh2022.63.2S3.2740>

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