

## LETTER TO THE EDITOR

## Functional Foods are a Useful Adjunction to Antihypertensive Drug Treatment

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## DEAR EDITOR

We thank Dr. Mitsiou you for her letter [1], which contributes to the improvement of the clarity of the associated Editorial.

First, of course there are false claims of several functional foods. However, pomegranate juice (PJ) was shown in rather small but indisputable clinical studies (Prof. Aviram is engaged with PJ for the last 15 years), that they possess anti-hypertensive, antioxidant, and antidiabetic effects to the degree that these can halt or even reverse atherosclerosis [2]. Moreover, it is the responsibility of the attending physician to explain to the hypertensive patient (mainly those with hypertension combined with diabetes, metabolic syndrome or smoking) that this is an adjunctive therapy on top of other no-pharmacological interventions or drug treatments for hypertension [2]. There are no data so far that functional foods compromise the adherence of the patient to antihypertensive drug treatment, if their utility is explained by the physician.

Second, the reduction of ACE activity has been shown in diabetic wistar rats [3] and in humans; even after two weeks administration of PJ [4]. A 36% decrement in serum ACE activity was recorded and a dose-dependent inhibitory effect (31%) of PJ on serum ACE activity was observed also in vitro [4]. Another possible mechanism, besides ACE activity reduction, of reduction in blood pressure (BP) might be the effect of polyphenols that PJ has on K/Na exchange in the kidney [5]. It has been shown that rats in the oral administration of polyphenols improves the restoration of renal

Na<sup>+</sup>, K<sup>+</sup>-ATPase properties during the recovery from hypertension to normotension in rats [5].

Third, there are no data on the effect of PJ to the tissue ACE, main site of action of ACE inhibitors. PJ was shown to reduce serum ACE activity by more than 36%. Thus, the partial inhibition of ACE by PJ does not restrain the combination with ACE inhibitors, angiotensin II receptor blockers (ARBs), or direct renin inhibitors (aliskiren) [6, 7]. The double (one scale being PJ and the other ARB or aliskiren) blockade of the renin-angiotensin system is not expected to be associated with more adverse events than monotherapy, without an increase in benefit, as this was detected in the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET) study [7], because the ACE inhibition with PJ is partial [2].

Fourth, several studies suggest that the regular consumption of foods and beverages rich in flavonoids is associated with a reduction in the risk of several disease states ranging from hypertension to coronary heart disease, stroke and dementia, improving thus CV health. Increasing blood flow with dietary polyphenols is one potential way for improving vascular function in large and medium arteries (heart, brain, kidneys, etc) [8]. The major polyphenols shown to have these effects in humans are primarily from cocoa, wine, grape seed, berries, tea, tomatoes, soy, and pomegranate [8]. There has been a significant paradigm shift to polyphenol research during the last decade, and looks very promising. Fasting blood glucose levels which were decreased significantly by PJ and known compounds in pomegranate, such as punicalagin and ellagic, gallic, oleanolic, ursolic, and uallic acids, have been identified as having anti-diabetic actions [8]. Moreover, recent research suggests pomegranate flowers and juice may prevent the diabetic sequelae via peroxisome proliferator-activated receptor-gamma binding and NO production. PJ compounds such as oleanolic, ursolic, and gallic

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acids are associated with antidiabetic effects. Pomegranate fractions and their active compounds hold a sizable antidiabetic potential [9]. Avoidance of diabetes by itself, especially when combined with BP reduction, is a major contributor to the reduction of CVD risk and the improvement of CV (metrics) health status.

To sum up, PJ is a useful adjunction to antihypertensive treatment especially in "complicated" hypertensives with diabetes, metabolic syndrome or/and smoking.

#### CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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