Are we in the polyphenols era?

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Website: www.phcogres.com

DOI: 10.4103/0974-8490.81966

Sir,

Polyphenols constitute a group comprising about 8000 different molecules, among which flavonoids are the most studied family. Polyphenols are potent antioxidants abundant in medicinal plants, fruits, vegetables and particularly in derived food products such as chocolate, tea and wine. This more 'natural' approach to antioxidant supplementation seems to be promising, since the antioxidant capacity of these compounds is not simply related to direct scavenging of reactive oxidant species (ROS), but also to inhibition of enzymatic sources of oxidative stress and augmentation of endogenous non-enzymatic and enzymatic antioxidant systems. Benefits from polyphenol-rich medicinal plants, foods and beverages are likely to arise from multiple pathways, and the antioxidant property appears to be only one of these.[1,2]

Despite these promising data, further questions remain to be solved. First of all, it remains unclear how potent are the antioxidant properties of polyphenols and which molecules in this class are the most potent ones *in vivo*. Further, it needs to be clarified whether these compounds possess other properties beyond their chemical antioxidant ones in specific pathophysiological conditions. As well, the amount of active constituents present in medicinal plants, food and beverages show remarkable variability due to genetic and agronomic factors, post-harvest handling, and subsequent processing or formulation steps. Such problems could apparently be overcome by using standardized formulations for supplementation, but except a few cases (like silymarin, green tea etc) this field still awaits exploration for the majority of the products. Unfortunately, the human studies on polyphenolics done to date are of such variable design, quality and results that no definitive conclusions about degrees of effectiveness in the treatment or prevention of diseases can yet be made. Better quality multifaceted clinical trials are therefore necessary. At this moment, strong evidence obtained with long-term randomized controlled clinical trials is still lacking, and no conclusion on the efficacy and safety of flavonoid supplementation in pathophysiological conditions can be reached.[3,4]

Nevertheless, polyphenols are more promising than other direct synthetic antioxidants, whose clinical efficacy is limited by the disadvantageous biochemical alterations.[5] Thus, rather than considering the conventional antioxidant hypothesis for polyphenols, we need more hypothesis-driven and rigorous clinical trial designs, guided by a deeper understanding of the complex physiology of ROS including other possible interrelated and independent mechanisms.

Therefore, the future research should more clearly address the differences between different kinds of polyphenols, in order to identify which type of intervention would constitute the most feasible and effective approach for prophylactic and therapeutic purposes. Additionally, definitive research should aim to clarify whether these encouraging results can be translated into reduction or amelioration of disease conditions.

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