LAY ABSTRACT

The diet can influence health not only by supplying essential nutrients, but also by providing alternative micronutrients that, by affecting specific metabolic pathways, can act as pharmaceutical-like compounds under appropriate conditions. In this direction the overall objective of this project is to study the possibility that hypertension and associated conditions, as obesity, diabetes, and cardiovascular disease in general, could be treated or prevented by the consumption of certain fruits and vegetables. Hypertension is a highly prevalent cardiovascular risk factor in the USA with nearly 60 million people having elevated blood pressure (BP) (28% of the adults according to the US NHANES). Untreated hypertension is important, accounting for about 30% of hypertensive people in the USA. These figures are rather similar in different population around the world, and are not expected to be different in California. An increase in the systolic or diastolic BP increases the risk of developing heart disease, kidney disease, arteriosclerosis, eye damage, and stroke. These complications are normally the end result of chronic high BP. Accordingly, the diagnosis of high BP in an individual is important so that efforts can be made to normalize the BP. Beyond the use of antihypertensive drugs, lifestyle (including diet) is a relevant strategy to maintain BP levels. Thus, specific modifications of dietary habits in a population can have a major impact on BP and cardiovascular disease. To set parameters to improve diets, it is important to understand how food components (macro and micronutrients) can interact with biological systems to enhance health.

Increasing evidence demonstrates that diets rich in fruits and vegetables promote health, and that these health benefits can be causally linked to the presence of specific compounds. In the context of cardiovascular health, flavanols are a family of plant-made compounds that have received particular attention. Flavanol-rich plant-derived foods and beverages include wine, tea, apples, cocoa, and various other fruits, nuts and berries.

Several pharmaceutical drugs are successfully used in the treatment of hypertension by inhibiting the renin-angiotensin system (RAS), including ACE-inhibitors (enalapril, captopril, etc.); and ARB-blockers (losartan, irvesartan, etc.). It is the hypothesis of this project that the mentioned dietary flavanols could act as inhibitors of RAS, thus combating hypertension. In this direction, recent dietary and clinical intervention studies in humans and animals indicate that foods and beverages that are rich in flavanols, e.g. tea, cocoa, wine, etc., can lower BP and provide cardiovascular benefits. However, how these effects are produced in the organism is unknown, making it impossible to design dietary strategies that provide the desired health benefits. In this regards, some relevant questions are the following: are all fruits and vegetables equivalent? If not, should the recommended 5-10 servings a day be restricted to specific fruits and vegetables? Can a compound isolated from the plant and put in a pill provide the same benefits of an equivalent amount of the compound present in the food?

The present plan is aimed at generating experimental data that will allow advances in the search for answers to the above questions. Experimentally, we proposed a first part of the study in which the effect of a particular flavanol, epicatechin, will be assayed in rats that develop hypertension after a treatment with an inhibitor of vasodilation. It is expected that the results will provide information about the specific action of epicatechin on BP, and the biochemical mechanisms involved in such inhibition. The second part of the study will use the results of the first part to define dose and time of treatment, to assay food containing epicatechin. This part will allow expanding the results obtained with the purified compound to the use of whole foods, and from that qualify if there is some difference in consuming these test foods. Finally, because studying the animals it is difficult to identify molecular mechanisms, the effects of epicatechin and epicatechin-containing foods on the production of vasodilating agents (nitric oxide) and in the regulation of RAS will be evaluated in cell cultures.

In summary, the results obtained in this study performed in animal and cell models will provide relevant information on the possibility that flavanol-containing foods can benefit cardiovascular health by lowering BP. Although the obtained answers will not provide definitive recommendations, they are expected to be relevant to continue this health relevant research under the frame of a more comprehensive program on dietary flavanols and their effects on hypertension and cardiovascular health.