

# Letter to the Editor

## The combination of hydralazine and isosorbide dinitrate: the only antioxidant treatment recommended in the guidelines

Dear Editor,

We read the article 'Cardiovascular diseases: oxidative damage and antioxidant protection' by Zhang et al with great interest<sup>1</sup>. In this article, it was focused on the well-known antioxidant vitamins of ascorbic acid (vitamin C), beta-carotene (vitamin A) and alpha-tocopherol (vitamin E). However there is no clinical trial demonstrating preventing effects of supplemental vitamins from the cardiovascular diseases. Only 200 mg/day of vegetables, 200 mg/day of fruits and 35-40 mg/day of fiber containing food are recommended in the guidelines<sup>2</sup>. As a matter of fact bilberry, high bush blueberry, blackberry, strawberry, raspberry, kale, spinach, Brussels sprout, alfalfa and broccoli show higher total antioxidant capacity (TAC) than the fruits and vegetables including well-known antioxidant vitamins such as grapefruit, melon, kiwi onion, lettuce or red pepper<sup>3</sup>. This paradoxical situation is associated with the non-vitamin antioxidants of polyphenols and anthocyanins. The studies demonstrated that the contribution of polyphenols and anthocyanins to TAC was much higher than those of the Vitamin A, C and E<sup>3</sup>.

The solely antioxidant therapy which is recommended in guidelines is the combination of hydralazine and isosorbide dinitrate (Hyd-ISDN)<sup>4</sup>. In the V-Heft and A-Heft trials, it has been shown that Hyd-ISDN combination reduced mortality rates in patients with heart failure<sup>4,6</sup>. It was revealed that hydralazine and nitrates reduced superoxide production by inhibiting NADPH-Oxidase, thereby improved nitroso-redox balance both in the endothelial cells and also in the cardiomyocytes<sup>7-9</sup>. Furthermore hydralazine precludes nitrate tolerance emerging in long lasting nitrate therapies<sup>8</sup>. We demonstrated that Hyd-ISDN decreased oxidative stress and reduced sarcoplasmic reticulum calcium leak and restored calcium content in an experimental model of nitroso-redox imbalance<sup>9</sup>. Thereby, Hyd-ISDN normalized impaired sarcomere length shortening. It seems that this combination leads to positive effects through decreasing oxidative stress.

Therefore, in a review addressing oxidative stress in cardiovascular diseases, we believe that discussing also Hyd-ISDN might be useful for researchers dealing with oxidative stress.

### Conflict of Interest

The Authors declare that there are no conflicts of interest.

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