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### Abstract

Many human activities, including waste disposal and the use of synthetic phosphate fertilizers, increase the concentration of cadmium (Cd) in the environment and harm plants and human health. Therefore, it is imperative to find effective solutions to overcome this problem. As plant biostimulants, *trans*-zeatin-type cytokinin (*tr*-Z) and silymarin (Sm) can act as anti-heavy metal agents, effectively ameliorating Cd damage to plants. In a pot trial, the impacts of foliar treatment with *tr*-Z (40  $\mu$ M), Sm (400  $\mu$ M), or *tr*-Z + Sm (25 +250  $\mu$ M, respectively, applied sequentially) on biomass production, yield, photosynthetic efficiency, osmoregulators, antioxidative defense system, and transcript levels of enzyme-related genes of chili pepper under normal or Cd (500  $\mu$ M) stress were investigated. Cadmium stress elevated the levels of superoxide ( $O_2^{\bullet-}$ ), hydrogen peroxide ( $H_2O_2$ ), electrolyte leakage (EL), malondialdehyde (MDA), and Cd, while negatively affecting biomass production, photosynthetic efficiency, and defense system components. Exogenous *tr*-Z and/or Sm attenuated the Cd-induced negative impacts on plants, highlighting that the integrative *tr*-Z + Sm treatment was more efficient than the single treatments. The *tr*-Z + Sm treatment decreased contents of roots, shoot, and fruit Cd by 66–91%, and reduced levels of  $O_2^{\bullet-}$  and  $H_2O_2$ , MDA, and EL by 45%, 73%, 51%, and 72%, respectively, correlated with increased *tr*-Z and Sm contents by 38–66%. Exogenous *tr*-Z + Sm increased biomass production by 99–134%, photosynthetic efficiency attributes by 31–169%, and antioxidants (ascorbate, proline, glutathione, and phenolics) by 33–123%. The levels of proteins and total leaf and fruit capsaicin were higher in Cd-stressed plants treated with *tr*-Z + Sm. Furthermore, the co-application of *tr*-Z + Sm up-regulated the activities of superoxide dismutase (SOD), glutathione reductase (GR), ascorbate peroxidase (APX), and catalase (CAT) enzymes by 38–43%, and maximized transcript level of genes-encoding enzymes in stress-exposed plants. As a result, the integrative *tr*-Z + Sm treatment is highly recommended to mitigate Cd stress impacts in chili pepper plants.