There is increasing interest in studying the health effects of complex mixtures of environmental agents. Several large environment-wide association studies (EWAS) have estimated the association between multiple exposures and health outcomes. However, these studies have thus far only considered a small set of confounding variables in their regression models. When the exposure is multivariate and may include interactions between agents and the number of potential confounding variables is large (p ≥ n), it is challenging to properly adjust for confounding and maintain model parsimony. In this paper we demonstrate that approaches for confounder adjustment when estimating the health effects of exposure to a single agent are inadequate in the multivariate exposure setting. Then we develop a new approach rooted in the ideas of Bayesian model averaging to adjust for confounding when estimating the health effect of simultaneous exposure to multiple agents including interactions. We introduce an informative prior that assigns likely confounders a higher probability of being included into the model. Our approach can be formulated in terms of a penalized likelihood which leads to an easy to implement tuning approach, removing the need for computationally expensive tuning approaches such as cross validation. Through a simulation study we demonstrate that the proposed approach is effective at identifying parsimonious models that are fully adjusted for observed confounding even as the exposure increases in dimension. We applied the proposed approach to an EWAS study that uses data from the National Heath and Nutrition Examination study to identify mixtures of nutrients and pesticides associated with lipid levels.