Differential Cerebrovascular Toxicity of Various Tobacco Products: A Regulatory Perspective

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Editorial

Blood-Brain Barrier (BBB) is a dynamic anatomical interface that separates brain parenchyma from blood circulation and is principally constituted by the cerebral microcapillary endothelial cells [1,2]. BBB is composed of distinct structural and functional organization through the presence of inter-endothelial tight junction complexes, abundant expression of nutrient and efflux transporters including metabolically active sites. While the TJ complexes tightly seal the paracellular gaps and contribute to high resistance of BBB [3], the presence of specific nutrient transporters and receptor systems selectively regulate the delivery of metabolic substrates, nutrients and macromolecules to the brain. In addition, efflux transporters belonging to the ABC superfamily prevent the brain permeation of blood-borne neurotoxic chemicals including xenobiotics and eliminates the accumulation of toxic metabolites within the brain parenchyma [1]. Taken together, the BBB serves as a physiological, transport and metabolic barrier that critically regulates ion, molecular and cellular flux into the brain, thus maintaining the CNS microenvironment for optimal neuronal transporters including metabolically essential for regulatory bodies to set standards on the tobacco products for improving public health [15]. Recent studies from our laboratory and others have challenged the safety of these reduced or low-exposure products. For example, recently we investigated the toxic impact of mainstream TS (whole) extracts from various tobacco products on BBB endothelium in vitro [16]. Our data revealed a strong positive correlation between the TS-induced BBB endothelial dysfunction (through increased oxidative stress) and total tar and nitric oxide content of various tobacco products (such as regular full flavor 3R4F, Ultra low nicotine, Ultra-Light 1R5F, and Nicotine-Free). Mainly, smoke extracts from Nicotine-Free and Ultra low nicotine cigarettes were found to be more toxic at BBB endothelium compared to regular products [16].

In summary, rigorous analysis of the safety (or toxicity) profiles of various tobacco products on cerebrovascular function in experimental and clinical studies is critically required to set up regulatory control. In addition, such studies would provide mechanistic insights into the molecular mechanisms underlying tobacco smoke associated BBB neurotoxicity.

References


15. FDA (2012) Food and Drug Administration Center for tobacco products, guidance for industry reporting harmful and potentially harmful constituents in tobacco products and tobacco smoke under section 904 (a) (3) of the Federal Food, Drug, and Cosmetic Act.