TITLE OF THESIS : ***« Toxicity of ethylbenzene and m-xylene alone and in a binary mixture in a model of human bronchial epithelial cells (BEAS-2B) exposed to an air-liquid interface.»***

ABSTRACT :

Benzene, toluene, ethylbenzene and xylenes (o-, m-, p- xylenes) make up a ubiquitous mixture, generally referred to as BTEX, known for its toxic effects. These volatile organic compounds (VOCs) are commonly found in indoor air and occupational environments. Most in vitro toxicological studies focus on the mechanisms of action of benzene and its substitute, toluene. Very few experimental toxicology studies have characterised the mechanisms of action of m-xylene and ethylbenzene, let alone the binary mixture. The result is incomplete data on the consequences of human exposure to these two VOCs. In this context, the aim of the research work is to study the acute toxicity of ethylbenzene and m-xylene, alone and in a binary mixture, on human bronchial epithelial cells exposed to the air-liquid interface (ALI). The cells were exposed to VOCs alone and in a mixture at their ELV-8h and ELV-15min for 1 hour, followed by 5, 23 and 47 hours of incubation in order to characterise the kinetics of the following toxic effects: cytotoxicity, biotransformation of xenobiotics, antioxidant defence system, inflammatory response and apoptosis. Biological responses to exposure to ethylbenzene and m-xylene are specific, whether alone or in a binary mixture. Ethylbenzene does not appear to be metabolised in BEAS-2B cells because it inhibits gene expression of the xenobiotic metabolising enzymes (EMX) studied. It does not induce antioxidant defence systems or apoptosis. However, a slight inflammatory response was observed after exposure to VLCT-15min. For its part, m-xylene is metabolised in BEAS-2B cells, inducing several EMX. It also upregulates certain enzymes involved in the antioxidant defence system, as well as markers of inflammation and apoptosis. With regard to co-exposure to the binary mixture, an inhibition phenomenon was observed, resulting in the inhibition of the toxic action mechanisms studied. In conclusion, the results of this project have provided new information on the toxicity of ethylbenzene and m-xylene. They also show the importance of conducting ALI exposures to mixtures of toxicants, as the responses observed cannot necessarily be predicted by conventional hypotheses such as additivity. These results may contribute to a better understanding of the effects of these compounds on human health.