Fetal alcohol spectrum disorders (FASD) in the honey bee (*Apis mellifera* L.): anatomical, physiological, and social consequences.

Fetal alcohol spectrum disorder (FASD) is an incurable, nongenetic disease that can occur in individuals whose mothers consume alcohol during pregnancy. Alcohol is toxic to the developing foetus, quickly passing through the placenta, and the foetus is unable to metabolize it, leading to long-lasting consequences. Children with FASD may experience low birth weight, microcephaly, and various neurobehavioural problems. These defects are irreversible, and there is no safe level of alcohol consumption during pregnancy. The cost of treating FASD in the U.S. reaches $4 billion annually.

Research has shown that ethanol causes developmental anomalies not only in humans but also in other species, including fish and rodents. In fish, such as zebrafish and mud frogs, exposure to ethanol during the foetal period has been found to lead to abnormalities in craniofacial structure and cognitive impairment. In rodents, the impact of FASD on motor skills and problem solving has been studied, whereas primates have been used to analyse responses similar to human behaviours. However, research on vertebrates is costly and poses ethical challenges, prompting scientists to seek models among invertebrates. Currently, nematodes (*Caenorhabditis elegans*) and fruit flies (*Drosophila melanogaster*) are used as models for FASD research, but the lack of social behaviours in these species limits their applicability.

Owing to their complex social interactions, the honeybee (*Apis mellifera*) could serve as an excellent model for FASD research. Although many studies have investigated the effects of alcohol on this species in adult individuals, there is limited information on how alcohol exposure during development affects the lives of adult bees. To date, only one study has shown that alcohol administered during the larval stage can negatively impact larvae by reducing their survival rates and body weights after pupation.

In the proposed project, I plan to comprehensively assess the impact of alcohol exposure during the larval development of honeybees on their adult lives, with a focus on physiology, behaviour, and anatomy. To test the main hypothesis that alcohol exposure during the larval period leads to FASD in adult bees, I plan to conduct a series of experiments on honeybee individuals raised on diets containing alcohol (0%, 3%, and 6%). For this purpose, I will cultivate worker and drone larvae in vitro and add an alcohol solution to larvae raised naturally in the hive (in each experiment, I plan to include both groups). These components are implemented in all the experiments, which are divided into four main groups. I We will test how exposure of honeybee larvae to alcohol affects their adult lives in terms of **(1)** lifespan, body asymmetry, and reproduction (3 experiments); **(2)** worker behaviour, including brood care, communication, initiation of foraging, and aggression (one experiment over 4 seasons); **(3)** alcohol tolerance, risk of addiction, and levels of alcohol dehydrogenase in haemolymph (3 experiments); and **(4)** effects on learning, memory, cognitive errors, and levels of octopamine, dopamine, and serotonin in haemolymph (2 experiments).

The results of this project may confirm whether honeybees can serve as a model for FASD research, offering unique opportunities due to the ease of breeding and social behaviours. Additionally, the significant phenotypic plasticity of honeybee and the availability of its entire genome make it a valuable model organism for studying FASD. Investigating the extent to which this species is suitable for FASD research could contribute to understanding the biological and social consequences of FASD and to developing methods to prevent its effects in humans.