Investigation of the therapeutic potential of natural flavour and fragrance materials in inflammatory oral diseases induced by *P. gingivalis* species.

Periodontitis and oral squamous cell carcinoma (OSCC) are two of the most serious oral diseases affecting populations worldwide. A significant contributor to the progression of both conditions is the bacterium *Porphyromonas gingivalis*, which promotes inflammation through its virulence factors. This bacterium can enter the bloodstream via bleeding gums, potentially spreading to other parts of the body. A key mechanism involved in the progression of these diseases is **pyroptosis**, a form of programmed cell death closely associated with inflammation. The inflammatory response is mediated by pro-inflammatory cytokines produced by fibroblasts and gingival epithelial cells. Current treatments often involve synthetic agents that, while highly effective, commonly exhibit toxicity to the human body. Consequently, increasing attention is being directed toward natural biological alternatives that could serve as safer substitutes. Among these are natural flavour and fragrance raw materials (FFMs), a group of aromatic compounds known for their diverse biological activities. FFMs include, among others, essential oils - volatile, plant-derived substances used in aromatherapy and the treatment of infections. These oils have demonstrated antioxidant, antibacterial, antifungal, and anti-inflammatory properties, making them promising candidates for the safer treatment of inflammatory oral diseases.

The rationale for conducting the research described in this project is the limited availability of literature on the potential effects of FFMs with activity against *P. gingivalis* on the pyroptosis pathway in human oral cavity cell lines. Although the molecular mechanisms of pyroptosis have been extensively studied, there is a lack of comprehensive data on the activity of FFMs - their fractions and individual bioactive compounds - in modulating pyroptosis mediators involved in inflammatory oral diseases.

The primary goal of the project is to identify the stages of the inflammatory pyroptosis pathway at which FFMs exert their modulatory effects, and to assess the extent to which they influence key mediators in primary oral cavity cells. A secondary objective is to evaluate the anti-proliferative and cytotoxic activities of FFMs against a human oral cancer cell line.

The most active FFMs against *P. gingivalis*, identified based on preliminary study results, will undergo chromatographic analysis to separate them into individual fractions and bioactive compounds. Subsequently, biochemical analyses of pyroptosis mediators will be conducted on human oral cavity cell lines under the influence of these compounds.

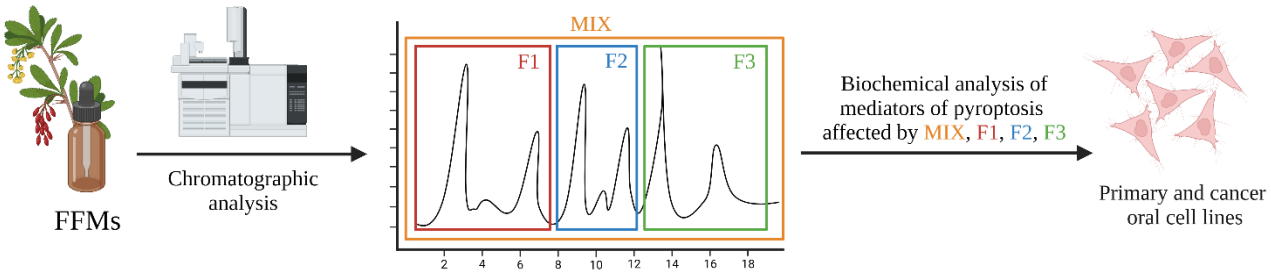

Fig. 1 Schematic plan of the study.

The results obtained from the planned studies will enhance our understanding of the role of FFMs, their fractions, and individual bioactive compounds in regulating pyroptosis mediators involved in the development of oral inflammatory diseases. This project is expected to uncover novel therapeutic applications of FFMs for treating such conditions, potentially offering safer and more effective treatment options in the future. Conversely, the findings may also inform regulatory decisions, including the restriction or removal of certain FFMs from the commercial market if they are found to be harmful.