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Sublingual Vaccination with an Oro-Dispersible Patch made with Natural Polymers: Optimization for Mucosal Protection

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Mucosae represent one of the preferential entry sites for pathogens. Consequently, the mucosal immune system has been shaped to act as the first line of defense to prevent microorganisms' invasions. By sublingual antigen administration, vaccination can be achieved with both systemic and local immune response induction, allowing both rectal and vaginal protection. However, buccal vaccines are usually administered as liquid form and previous studies revealed heterogeneous responses, mainly due to antigen dispersion. To overcome these issues and extend the time of contact between antigen and mucosa, we developed a patch made with natural biocompatible and biodegradable polymers for sublingual administration. First, we assessed the biocompatibility of the device *in vitro* and *in vivo,* by cytotoxic assay, histological analysis and pro-inflammatory cytokines quantification in mice tongues after patch administration. After antigen incorporation within the patch and administration to mice, we showed that our device allows increased contact time between antigen and sublingual mucosa, proving its mucoadhesive abilities. Finally, antibody quantification revealed that sublingual immunization stimulates humoral systemic response and induce IgA secretion in feces and serum, highlighting our patch *in vivo* bioactivity.

Our hypothesis is that our delivery system, by carrying and delivering antigens and adjuvant locally on the sublingual mucosa, would allow a stronger immune response compared to liquid administration. Indeed, the time of contact between antigens and mucosa could be prolonged by the patch, allowing a better penetration of antigens through the mucosa and thus an enhanced immune response.