World Academy of Science, Engineering and Technology
International Journal of Health and Medical Engineering
Vol:19, No:04, 2025

Development of a Thermosensitive Buccal Spray Loaded with an Antioxidant Polyphenols-Enriched Secondary Raw Material Produced from Virtuous Recovery of Grape Processing Waste: A Conscious Approach to Daily Oral Care

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Abstract : Oxidative stress is the key factor leading to both physiological processes of cosmetic interest (e.g., aging, photoaging) and pathological mechanisms affecting the skin and the mucosae (e.g., oral lichen planus, oral mucositis). These naturally occurring events or altered conditions are both characterized by an imbalance between the oxidative species and the physiological antioxidant defenses. In this view, the daily use of an antioxidant device could be a preventive strategy aimed at restoring any occurring imbalance. Nowadays, the use of natural and safe antioxidants is certainly preferable, and polyphenols are currently under the spotlight. Additionally, as polyphenols suffer from low bioavailability after oral intake, they could surely take advantage of a direct buccal administration. A further actual trend is related to sustainability and circular economy. Particularly, at present, sustainable efforts focus on the extraction of natural antioxidants from agri-food wastes, and recently, the waste black bentonite (BB), an inorganic waste coming from grape/must clarification, emerged as a rich source of polyphenols. Based on these considerations, the aims of this work were to develop and characterize a secondary antioxidant raw material starting from the waste BB and employ this excipient to produce a buccal thermosensitive spray intended for oral cavity wellness. To maintain a sustainable point of view, maceration with eco-friendly and unconventional extraction solvents was established as a method to recover polyphenols. Specifically, according to a waste-to-market approach, PEG200, a well-known safe and eco-friendly pharmaceutic and cosmetic liquid excipient, was selected to obtain a high-value-added secondary raw material directly useful to produce cosmetics, pharmaceuticals, and medical devices. The extract has been extensively characterized by HPLC-DAD and HPLC-MS analyses, DPPH, Bradford, and Folin–Ciocalteu assays as well as validated as a safe raw material of cosmetic interest through OECD-compliant in vitro tests. Then, it was directly inserted into a liquid formulation intended for daily oral care. The goal of the design process was to develop a user-friendly device that could be easily integrated into daily routines. To achieve this, a fluid formulation was designed using Pluronic F-127, a temperature-sensitive gelling polymer, which led to a fluid, sprayable, and easily administrable formulation at room temperature, but that transforms into a viscous gel once at body temperature, enhancing retention time and allowing polyphenols to effectively accumulate in tissues. The formulation incorporated a high concentration of extract (30% w/w), xylitol as a sweetener, preservatives (antimicrobial and antioxidant), and penetration enhancers (urea and sodium dehydrocholate). All components were dissolved in a citrate buffer (pH 5.5) to preserve and stabilize the polyphenols. The temperature-dependent gelation behavior has then been assessed by both in vitro and ex vivo tests and also the antioxidant power of the formulation was evaluated. Finally, the formulation has been proved through ex vivo test to be able to allow rapid polyphenol tissue accumulation as both the buccal and sublingual tissues were saturated after just 15 min of application.

Keywords : antioxidant, in situ gelling, oromucosal spray, polyphenols, waste recovery
Conference Title : ICDOH 2025 : International Conference on Dental and Oral Health
Conference Location : Venice, Italy
Conference Dates : April 03-04, 2025