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Process Improvement for the Production of Inert Pellets with Controlled Release Potential of Natural Actives and Supplements

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Keywords : *inert pellets; controlled release; natural actives; encapsulation; pharmaceutical technology.*

Highlights

Innovative process for producing inert pellets. Promising platform for controlled release of natural compounds and vitamins. Pellets showed uniform shape, smooth surface, and excellent flow properties. Future tests include dissolution, stability, and encapsulation efficiency analyses.

Resumo/Abstract

In the pharmaceutical context, pellets are defined as small, free-flowing particles obtained by agglomerating fine powders or granules of drugs and excipients using specific processing equipment. These multiparticulate systems have gained prominence due to their uniform size, good flow properties, and low friability, which favor greater dosage precision (Agrawal et al., 2022). For oral administration — the most widely used route owing to its practicality and patient compliance — the homogeneous distribution of active compounds in sustained-release forms enables controlled release, maintenance of stable plasma levels, and reduced dosing frequency, leading to improved therapeutic outcomes (Kohale et al., 2025). In this context, the technology of inert pellets coated with natural actives and vitamins has emerged as a promising strategy, supported by the biocompatibility, biodegradability, and lower toxicity of naturally derived excipients (Tiwari et al., 2024; Alwossabi et al., 2021). In addition to masking unpleasant tastes and odors, such systems enhance the stability of active compounds against environmental factors and allow modulation of the release profile through natural polymers, thereby improving bioavailability.

Pellet production methods can be grouped into four main categories: agitation, compaction, layering, and globulation (Mate et al., 2023). Among these, extrusion–spheronization stands out for producing spherical and uniform pellets, while solution or suspension layering is employed for progressive coating of inert cores. Other approaches include melt spheronization, which uses molten mixtures of drugs and excipients, and droplet formation techniques, such as spray drying and cryopelletization (Mate et al., 2023). In this study, the production process is being developed in partnership with a company and will be innovatively applied to obtain inert pellets made of sugar and microcrystalline cellulose, designed for the incorporation of natural active compounds.

The initial morphological characterization of the pellets was carried out using a stereoscopic magnifier, enabling the evaluation of shape, color, and particle uniformity (Patel et al., 2016). Future stages include detailed analyses by SEM, dissolution tests for orange oil and vitamin D₃ (quantified by GC-FID and LC-MS/MS, respectively), and assessment of vitamin C stability in two experimental groups (sealed flasks and environmental exposure), monitored by iodometric titration (Silva et al., 2017; Esteves et al., 2022; Zenebon et al., 2008; David et al., 2015; Toan et al., 2020; Becerra et al., 2025). Additionally, thermal stability (TGA), active–excipient interaction (FTIR), and particle size distribution analyses by mechanical sieving will be performed (Brand et al., 2018; Mallah et al., 2015; Bhujbal et al., 2020).

The initial morphological characterization of the pellets, conducted with a stereoscopic magnifier, indicated that the particles exhibit a uniform spherical shape, smooth surface, and homogeneous coloration. These attributes are favorable for the production of multiparticulate systems, as they contribute to consistent flow, low friability, and adequate homogeneity in active compound distribution — key aspects for controlled-release formulations.

The pellets present favorable morphology, with good sphericity and homogeneous surface, which are important characteristics for flow, uniformity, and controlled release of active ingredients.

The next stages include dissolution and stability tests of the vitamins and orange oil, along with complementary analyses by SEM, TGA, FTIR, and particle size distribution to validate the encapsulation efficiency.

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Agradecimentos/Acknowledgments

We thank the State University of Western Paraná (UNIOESTE) for providing the infrastructure, which was essential for the development of this work. We also thank the Sustainable Engineering Laboratory for their technical and scientific support during the experimental stages. Finally, we express our gratitude to Elementum Control Quality Laboratory for their partnership and collaboration, which made the execution of this research possible.