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QUALITY BY DESIGN APPLIED TO THE PRODUCTION OF THE HERBAL MEDICINE FROM *Monteverdia ilicifolia* (Mart. ex Reiss.) Biral

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With the advancement of quality tools, new opportunities have emerged to study and optimize processes that were previously not systematically controlled. In this context, Quality by Design (QbD) stands out as a strategic approach to ensure the efficacy, safety, and quality of herbal medicines, such as those derived from *Monteverdia ilicifolia* (Mart. ex Reiss.) Biral, commonly known as "Espinheira Santa", which is recognized for its antidyspeptic, antacid, and gastric mucosa-protective properties [(1)]. This study aimed to evaluate the extraction and spray-drying processes for obtaining an Espinheira Santa herbal medicine using QbD principles. Through process mapping and risk assessment, potentially critical factors were identified and subsequently challenged by means of Design of Experiments (DoE). For the extraction step, a 12-run Plackett–Burman design (8 factors) was conducted; for scaling-up, a Central Composite Design (CCD) with 7 runs (2 factors) was applied; and for the spray-drying step, a Rotational Central Composite Design (RCCD) with 17 runs (3 factors) was carried out. The response variables studied in each design were those related to Critical Quality Attributes (CQAs), that is, attributes that impact efficacy and safety [(2)]. The effects (linear, quadratic, and interaction) were estimated, and the models were evaluated by ANOVA using the statistical software RStudio Version 4.4.0. Factors showing significant effects (p-value < 0.1) were identified as critical [(3)]. In the extraction step, the following factors were significant for at least one CQA: “extraction type” (decoction or infusion), “drug-to-extract ratio” (1% to 6%), “herbal drug form” (cut or powdered), “vessel type” (glass or metal), “water quality” (purified or distilled), “exposure” (open or closed), “boiling time” (2 or 5 min), “stirring” (0 to 600 rpm), and “extraction time” (10 to 30 min). In the spray-drying step, maltodextrin addition (0 to 60%), feed rate (3.5 to 7.5 mL/min), and inlet temperature (120 to 200 °C) were significant for at least one CQA. In conclusion, the QbD approach enabled the identification of critical factors associated with the extraction and spray-drying processes of Espinheira Santa, ensuring process capability.

Keywords: Espinheira Santa, Extraction, Design of Experiments, Scaling-up, Spray drying.

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