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Process Development of Non-ionizing, Microbial Remediation for Medicinal Cannabis Flower

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INTRODUCTION

The compact morphology and dense flower structure of cannabis make it more susceptible to microbial contamination, increasing difficulty in microbial control during cultivation and production. Microbial proliferation can lead to product losses and pose health risks, particularly to immunocompromised patients. While ionising irradiation is commonly used, non-irradiated product is preferred in some countries such as Germany. Advanced oxidation technologies, can alternatively be used to reduce microbial levels by disrupting microbial cell integrity.

AIMS

- **To plan and design a suitable approach for microbial remediation of medicinal cannabis flower using quality and risk management tools, ensuring regulatory compliance and product quality preservation.**
- **To establish the critical process parameters and define a process validation protocol in line with EU-GMP for the proposed microbial remediation method.**

METHOD

Phase I – QFD: Product Planning

Focus group discussions and Quality Function Deployment (QFD) were employed to define the product plan. A House of Quality (HoQ) matrix integrated competitor analysis, regulatory requirements, and desired characteristics to establish functional requirements.

Phase II – QFD: Product Design

A second HoQ matrix translated technical and quality requirements into engineering characteristics, leading to the selection of a closed-system setup with cold plasma ozone generation. Failure Mode and Effects Analysis (FMEA) was used to identify critical process parts and critical failure modes.

Phase III – Process Development and Validation

Critical Quality Attributes (CQAs) were identified based on the EU Pharmacopoeia Cannabis monograph, classified by criticality, and assessed through Failure Mode Effects Analysis (FMEA) to identify variables impacting CQAs. Critical Process Parameters (CPPs) were established, and a validation protocol was formulated through identification of EU-GMP requirements.

RESULTS

Phase I

QFD correlation through HoQ, prioritized a certifiable EU-GMP/CE design and selective microbial reduction, leading to the selection of a closed ozone system due to its positive trade-offs in penetrability and efficacy.

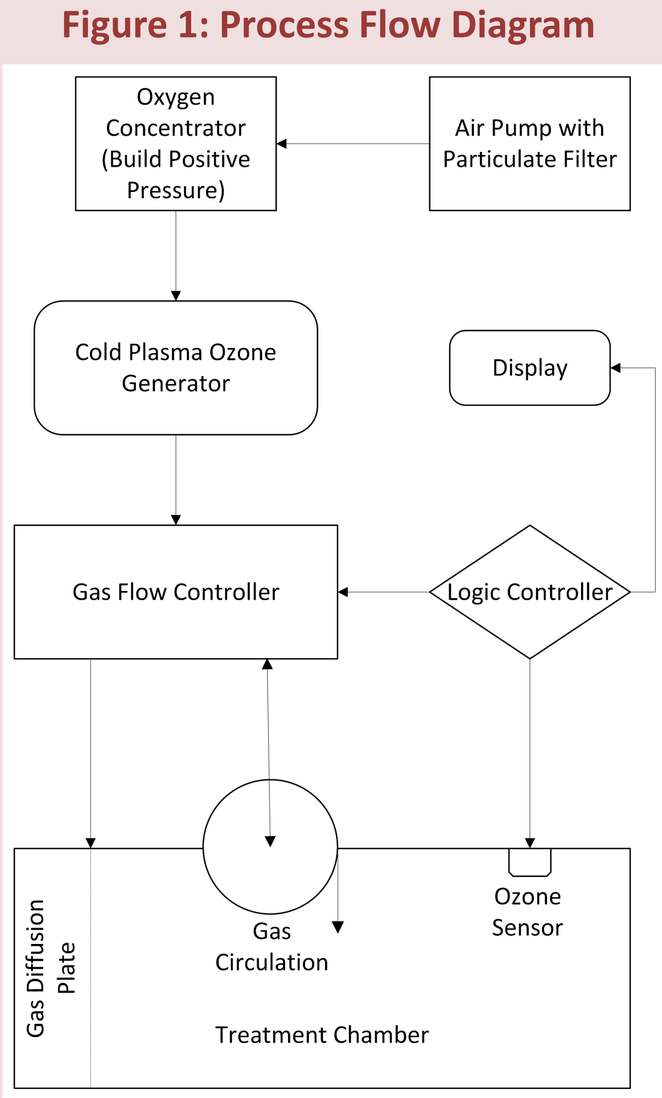
Phase II

The planning outputs were translated into specific design characteristics and critical parts. Design features included modular construction, ozone-resistant materials, and automated controls, and an FMEA risk assessment mitigated critical failure modes like ozone leakage through improved seals, exhaust systems, and safety controls.

Phase III

It was established that ozone concentration and cycle time are critical process parameters, as lower levels reduce microbial efficacy while higher levels increase oxidative byproducts. A suitable process validation protocol in line with EU-GMP was proposed.

Figure 1: Process Flow Diagram



CONCLUSION

Research on non-ionizing microbial remediation of medicinal cannabis remains limited. This study combined engineering and regulatory considerations to design a scalable, EU-GMP-compliant system, addressing material compatibility, process control, and risk mitigation. Focus groups, QFD, and FMEA guided product planning and design were undertaken. The process targets microbial reduction to acceptable levels, lowering bioburden and enhancing patient safety without significantly affecting product quality. Further studies are required to refine and validate the process toward a commercially viable solution for pharmaceutical cannabis and other applications requiring microbial control.