S U M M A R Y

NUTRACEUTICS OBTAINED FROM HIVE PRODUCTS AND VEGETAL EXTRACTS –OBTAINING, CHARACTERIZING,COMPARATIVE ANALYSIS OF THE ECONOMIC IMPACT

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The doctoral thesis entitled "Nutraceuticals based on beehive products and plant extracts - obtaining, characterization, comparative analysis of the economic impact" aims to address the complexity and diversity of beehive products and plant extracts in terms of their therapeutic and nutritional benefits. The main aim of this work is to develop and characterize two innovative nutraceuticals, which combine beehive products with plant extracts, focusing in particular on the optimization of antioxidant activity for the management of body weight and diabetes. This scientific approach is motivated by the need to improve the quality of life through functional food solutions that respond to current health challenges and to explore their economic potential in the global market. Through this PhD thesis, it is aimed not only to advance scientific and technological knowledge in the field of nutraceuticals, but also to demonstrate the economic viability and market acceptability of the developed products, offering new perspectives for the functional food industry and improving public health. The thesis is structured in several chapters, each with the objective of deepening the understanding and optimizing the extraction and formulation technologies of nutraceuticals.

Chapter I "Beehive Products and Their Beneficial Effects on Human Health" *explores the chemical composition and health benefits of beehive products such as honey, pollen, propolis, and royal jelly. The research presented demonstrates the ability of these products to improve immunity, fight infection, and promote cardiovascular and digestive health. The original contributions of this chapter include identifying the specific mechanisms by which these products exert antioxidant and antimicrobial effects, providing a scientific basis for their therapeutic use.*

Chapter II, entitled "Plant extracts used for honey supplementation", *focuses on the use of medicinal plant extracts to improve the functional properties of honey. It has been shown that the addition of plant extracts such as lavender, echinacea, and ginger can enhance the antioxidant, antimicrobial, and antiinflammatory properties of honey. Original results include the development of innovative extraction methods that maximize the preservation of bioactive compounds, as well as the evaluation of synergistic effects between honey and various plant extracts.*

Chapter III "Obtaining, optimizing and characterizing plant extracts" *focuses on the complex and innovative methods of obtaining, optimizing and characterizing plant extracts, emphasizing the extraction of bioactive compounds from various plant sources. The processes detailed in this chapter combine principles of engineering and biochemistry to maximize the yield and quality of extracts, using plant materials selected for their therapeutic properties. Among the plant raw materials used in the study are propolis, pasture, lavender (Lavandula angustifolia), sage (Salvia officinalis), cinnamon (Ceylon), blackberry (Nigella sativa), chicory (Cichorium intybus), dandelion (Taraxacum officinale), ginger (Zingiber officinale) and green tea (Camellia sinensis). Propolis and grass are two of the beehive products with remarkable properties, intensively used in the development of nutraceuticals due to their multiple health benefits. Tested extraction methods include the use of variable solvents and advanced techniques such as ultrasoundassisted extraction and CO2 extraction,*

each with detailed specifications for optimal operating conditions to maximize efficiency. Also, the importance of the selection of plant materials and solvents in influencing the quality and efficiency of the extraction was highlighted, highlighting the importance of the source of the plant materials and the pre-extraction processing conditions. The qualitative characterization of the extracts included the assessment of antioxidant capacity and total polyphenol content, where cinnamon and propolis recorded superior values, reflecting their high potential in nutraceutical applications. Lavender, although frequently used for its calming properties, showed low values in antioxidant capacity, suggesting a selectivity in its use depending on the desired application.

Statistical data analysis included multiple regression and design of experiments (DOE) methods, which facilitated the identification of optimal extraction conditions for each plant material tested. This rigorous approach allowed not only to maximize the extraction efficiency, but also ensured the reproducibility of the results, crucial for the industrial applicability of these extracts in nutraceutical formulations. Extensive investigations into the extraction and characterization processes of plant extracts have revealed significant optimizations that directly contribute to increased stability and therapeutic efficacy of formulated nutraceuticals.

The chapter makes original contributions by developing new methods for evaluating the efficacy of plant extracts, using advanced characterization techniques such as spectroscopy and chromatography to detail the biochemical profile of the extracts. The impact of the extraction parameters on the bioactive profile of the extracts is explored in detail, with the aim of optimizing the conditions for the maximum obtaining of the compounds of interest.

In conclusion, Chapter III provides a robust scientific basis for understanding and optimizing the extraction processes of bioactive compounds from plants, contributing significantly to the field of phytotherapy through the proposed innovative methods and the rigorous application of scientific principles in the extraction and analysis of plant compounds. These findings open new perspectives for the strategic use of plant extracts in various medical and cosmetic applications.

Chapter IV: "Development, Optimization and Evaluation of Nutraceutical Products Based on Beehive Products and Plant Extracts" *explored the development, optimization and evaluation of nutraceutical products using beehive products and plant extracts. The main goal of the research was to transform theoretical knowledge and experimental results previously obtained into effective and innovative nutraceutical formulas, integrating principles from biochemistry, pharmaceutical technology and food engineering. Within the working methods, additional materials such as apple cider vinegar and acacia honey were used, and the application of rigorous analytical methods for the characterization of raw materials and extracts, such as the determination of antioxidant capacity and total polyphenols. A total of 16 nutraceutical recipes were developed and tested. These recipes are grouped into two main categories: diabetes management products and body mass management products. Each recipe explores different combinations of natural ingredients, including apple cider vinegar, honey, different herbs and extracts to maximize therapeutic and nutritional benefits.*

Using a combination of natural ingredients such as apple cider vinegar and acacia honey, along with various extracts, formulas have been developed that promote health through antioxidant and diabetes and weight management properties. Experimental results indicate a significant improvement in total polyphenols, with an increase observed from 187.23 mg GAE/ml to 195.24 mg GAE/ml in the formula including apple cider vinegar, honey and lavender after 48 hours of maceration. Antioxidant capacity was also optimized, with increased values after extended maceration periods, demonstrating the effectiveness of the extraction process in enhancing antioxidant properties.

A rigorous evaluation of the sensory characteristics of the nutraceutical products was also carried out to ensure their acceptability by consumers. The importance of this step was emphasized by the implementation of simulated in vitro gastrointestinal digestion tests, which demonstrated how different product formats (liquid and solid) influence the release and absorption of bioactive compounds. The results obtained indicated a remarkable efficiency of most of the recipes, with increased concentrations of polyphenols observed after 48 hours of maceration, suggesting that an

extended maceration process can amplify the beneficial properties of nutraceuticals. In addition, the antioxidant capacity analysis revealed the synergistic benefits of the ingredient combinations. Regression analysis and formulation optimization, using advanced machine learning techniques, facilitated the identification of ingredient combinations that maximize therapeutic efficacy and acceptability of end products. By fine-tuning the proportions and processing conditions, it was possible to develop formulations that improve the absorption and bioavailability of bioactive compounds, thus strengthening the positive impact of nutraceuticals on health.

Finally, after numerous tests and optimizations, two final recipes were selected, one for diabetes management and another for body mass management, both highlighting the efficiency and synergy of the ingredients used.

Chapter V "Comparative analysis of economic impact" *focuses on evaluating the economic impact of nutraceutical products derived from beehive products and plant extracts, highlighting their importance in the current market context. In this analysis, we explored the market dynamics, consumption trends and economic viability of these products in different regions, with a special focus on the national and European markets. By collecting and analyzing data from government institutions and international organizations, a clear picture of the evolution of the hive products market and consumer behavior could be obtained. The analysis included the assessment of production costs, selling prices, as well as consumer preferences and perceptions of these products, thus providing a solid basis for strategic decisions in the nutraceutical industry.*

A central element of the research was the survey of a sample of consumers, which contributed to understanding their attitudes and knowledge about the benefits of beehive products considered nutraceuticals. The results of the survey underlined an increased responsiveness of consumers towards natural products and highlighted the positive influence of information campaigns and marketing strategies on public perception.

In conclusion, this chapter adds to the specialized literature by providing a detailed and evidence-based perspective on the economic potential of nutraceuticals based on beehive products and plant extracts. The study demonstrates that, despite the challenges, there are significant opportunities for the growth and sustainable development of this market segment, given the global trend towards a healthy and sustainable lifestyle.

Detailed exploration of the synergistic interactions between bioactive compounds in beehive products and plant extracts has allowed the identification of new ways to enhance the efficacy of these nutraceuticals, paving the way to more effective alternative treatments for chronic disease management.

Chapter VI *of the PhD thesis draws general conclusions and provides recommendations based on research conducted on the use of beehive products in nutraceutical formulations. The results of chemical, biological, and nutritional analyzes demonstrate the potential of these products in promoting health and preventing some ailments, by capitalizing on their antioxidant and antiinflammatory properties.*

The results of the thesis confirm that the synergistic use of beehive products and plant extracts leads to significant improvement of antioxidant, antimicrobial and anti-inflammatory properties and demonstrate that nutraceuticals based on beehive products and plant extracts can play a crucial role in improving public health and in innovation in the industry functional foods, providing significant opportunities for advancement in health and wellness.