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## **TEZĂ DE ABILITARE**

### **CERCETĂRI ÎN DOMENIUL PLANTELOR MEDICINALE ȘI A MEDICAMENTULUI DE ORIGINE VEGETALĂ**

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## **ABSTRACT**

The habilitation thesis entitled "RESEARCHES IN THE FIELD OF MEDICINAL PLANTS AND PHARMACEUTICAL FORMULATIONS BASED ON HERBAL DRUGS" is a synthesis of the most important scientific, professional and academic achievements accomplished after obtaining the PhD title.

The thesis has been written based on several scientific publications and is divided in three main parts: scientific achievements, professional, academic accomplishments and long term plans and references.

The first part of the thesis gives details about the numerous achievements, that I have obtained in the field of medicinal plants and herbal drugs research.

The studies were structured according with the main research course, that I have been followed throughout this period:

- the scientific ground of plants therapeutic use, based on the correlation between identified and quantified active substances and the potential therapeutic effects;
- the proposal of new pharmaceutical formulations that contain semisynthetic compounds or standardized plant extracts and their quality assessment;
- the dynamics of active substances accumulation in herbal drugs dependent on climatic conditions, collecting time etc., with the goal of establishing the proper time of herbal drugs collection in order to obtain selective extracts with a high content of active substances;
- the achievement of a herbal drug/ active compounds database, regarding their use in different medical conditions such as (respiratory, psychiatric, endocrine, metabolic, locomotory, gastro-intestinal and dermic diseases);
- the quality assessment of different medicinal herbal formulations (tea).

The research activity was seen as a complex approach of herbal drugs pharmaceutical formulation design, starting with raw materials analysis, correlation of chemical composition with potential therapeutic effects and scientific justification of herbal products associations.

The scientific research was conducted based on specific pharmacognostical and phytochemical methods together with biological, biochemistry and pharmaceutical technology determinations.

The work was carried out using different herbal products/herbal substances, hinting at their botanical identity, purity and quality together with the potential therapeutic effects, that were dependent on the raw materials chemical composition.

With the view of therapeutic valorification of new medicinal plants or proving the scientific use of herbal products based on their traditional employment, I have performed different qualitative and quantitative analysis. The aim of my research was the determination of herbal products identity by means of macroscopic, microscopic examinations and chemical composition. For example, I have determined the specific anatomic element used to differentiate *Artemia* species, whenever they are found in pharmaceutical formulations such as tablets, medicinal tea or caps (aerial parts of *Artemisia absinthum* – non-glandular "T"like trichomes, aerial parts of *Artemisia abrotanum* – unicellular non-glandular wart like trichomes and pluricellular non-glandular, ample, short trichomes, aerial parts of *Artemisia dracunculus* – unicellular, non-glandular, star like trichomes); for *Clematis vitalba* L. I have described for the first time the anatomic peculiarities of stems, leaves and flowers observed on transverse sections and chloral hydrate mounted preparations respectively. For *Sideritis scardica* Griseb. (a species from Macedonia), I have identified several specific anatomic elements for stems, leaves and flowers; for common liliac buds I have observed pistil like glandular trichomes with unicellular/pluricellular foot cells. I have also pointed out the anatomic differences between *Ocimum basilicum* and *O. basilicum* var. *purpurascens*: pollen grain type (acolpate for aerial parts of *Ocimum basilicum* and tetracolpate, hexacolpate ones for aerial parts of *O. basilicum* var. *purpurascens*). The active compounds were identified based on qualitative chemical analysis, that was performed on different extractive solutions obtained with both apolar and polar solvents. For qualitative chemical analysis I have also used chromatographic methods (thin layer chromatography – TLC and high liquid pressure chromatography – HPLC). Based on these methods I have determined the phytochemical profile of different indigenous species (cultivated or from wild flora): *Artemisia abrotanum* L., *A. dracunculus* L., *Galium verum* L., *Clematis vitalba* L., *Thymus alpestris* Tausch ex. A. Kerner, *T. Montana*, *Oenothera biennis* L., *O. muricata* L., *Rhododendron kotschyi* Simk., *Achillea filipendulina*, *A. millefolium* var. *rubra*, *Peucedanum officinale*, *Ocimum basilicum* var. *purpurascens* etc.

For the purpose of obtaining new semisynthetical compounds from natural substances, my research focused on anthocyanins extraction from fresh fruits of *Ribes nigrum* and *R. rubrum*. In view of obtaining pharmaceutical formulations, used for different oligoelements deficiency treatment, these compounds were coupled with biological active ions. Based on my

research I have obtained three semisynthetic compounds - anthocyanin-lithium, anthocyanin-magnesium and anthocyanin-zinc. These new compounds were analysed by means of different methods, that had in view the confirmation of their chemical structure, quality assessment and their effects towards vegetaa/animal cells together with their pharmaceutical processing. For characterization of these new compounds, different methods specific for pharmacognosy, inorganic and organic chemistry, vegetable biology, pharmacology, biochemistry and pharmaceutical tehnology have been used.

The manufacture of new pharmaceutical formulations based on herbal drugs had in mind the importance of standardization of herbal extracts and the knowledge of the exact amount of active substance *per* administration that could foresee and supervise side-effects. From this point of view I have obtained different formulations, based on standardized herbal extracts with hypoglycemic, anti-inflammatory, antimicrobial, anti-pigmentation and anti-cellulite activity. All researches started with quality determination of herbal products and choosing of the optimum solvent type and extraction method, followed by extracts analysis, standardization, manufacture of pharmaceutical formulation and its quality assessment. For several extracts I have also determined the specific therapeutical properties.

For establishing the most favourable time of collecting the herbal products, some research also focused upon the dynamics of active substances accumulation dependent on climate conditions, vegetable organ and plant stage development. From this point of view, I have performed several qualitative and quantitative analysis on different vegetable organs collected from the same species in different periods of year and/or different places. Therefore, in order to obtain herbal extracts enriched in active substances from old man's beard (*Clematis vitalba*), one must use leaves and flowers collected in the month of June; common lady's mantle (*Alchemilla vulgaris*) flowers are rich in phenolcarboxylic acids, *Tilia* flowers are rich in flavonoids, phenolcarboxylic acids, mucilages compared to bracts; barley shoots (*Hordeum vulgare*) represent a source of chlorogenic acid, only if they are collected when they have 10 cm in length; fully developed leaves of *Ginkgo biloba* have a lower content of flavonoids (probably due to polymerization) and rosmarinic acid synthesis in sage leaves is negatively influenced by low temperatures and high humidity.

Taking into consideration that phytotherapy has become a necessity and numerous physicians recommend this kind of treatment, another course of my research hinted at bringing about a bibliographical database of herbal products and active substances with potential use in respiratory, neuropsychiatric, endocrine, locomotory, digestive, metabolic and dermic diseases.

Another objective of my research was the quality assessment of different herbal drugs formulations, since their abundance on the pharmaceutical market. However, their therapeutic use is not always justified by their composition and extraction method (mentioned by the producer). Many of these researches have been conducted together with students, that belonged to the pharmacognosy scientific circle.

Professional and academic achievements were materialized in publication of 14 papers in the field of pharmacognosy, phytochemistry, phytotherapy together with an electronic format material; publication of 148 articles/abstracts among which 12 ISI papers; coordination of 155 licentiate's degrees and 37 scientific student papers presented at different conferences.

The second part of the habilitation thesis presents the development plan of academic, professional and research career.

The future researches will consider the identification and isolation of new natural compounds with therapeutic use, the research extension upon exogenous species, the proof of scientific use based on the correlation between identified and quantified active substances from herbal products (that are used traditionally) and obtaining new pharmaceutical formulations, that contain standardized extracts. With respect to this part, I also mean to extend interdisciplinary co-operations for the purpose of the accurate mechanism of action and biodisponibility determination.

Regarding, the teaching activity, this hints the permanent growth of didactic style through a better quality of teaching and learning of pharmacognosy, as a theoretic base, that is utterly needful for understanding the vegetal/animal drug, as well as the medical conditions, that might benefit by this treatment.

The last chapter of the habilitation thesis includes references.