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**INTERDISCIPLINARY APPROACH TO
QUANTITATIVE STUDIES CHEMICAL STRUCTURE -
BIOLOGICAL ACTIVITY AND PHYSICO-CHEMICAL
STUDIES IN THE RESEARCH OF PHARMACEUTICAL
BIOACTIVE SUBSTANCES**

ABSTRACT

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SUMMARY

*"Man can only become man through education.
He's nothing but what education makes of him." (Immanuel Kant)*

Expertise in the fields of pharmacy, chemistry, biology, and law will be designed to coagulate information at all levels to provide current, forward-looking information in pharmaceutical-chemical-medical research of great scope and importance in both legislation and socio-economic development of the current staging.

The technical-economic paradigm in Europe has determined radical changes that make their mark in real life, in any field. Harmakorpi (2002) said that regional development is a stage in which regional actors with different visions and strategies play together.

Its own personal development policy envisages a set of planned measures that aim to record evolutions that will leave defining imprints in people's minds and souls.

This habilitation thesis aims to "coagulate a transdisciplinary thread" of information obtained through chemical research, with pharmaceutical applicability in the transparency of the use of other related fields, biology, medicine, bioinformatics.

Medicinal and aromatic plants are valued both for their therapeutic potential and for the diversity of their constituent chemical compounds. Many companies are increasingly interested in the production of cosmetics, dermato-cosmetics, phyto-pharmaceuticals. Consumers are increasingly concerned about the use of these products due to their reduced side effects, combination with various therapies, diets.

A pharmaceutical preparation generally has several associated components which under certain conditions may react with each other, causing degradation of the preparation under the influence of various factors arising from the structure of the preparation, either due to improper combination of substances in a preparation or possible reactions between component. These reactions may occur from the time of preparation of the drug and represent the group of pharmaceutical incompatibilities.

The extracts from *Urtica Dioica* represented a first foray into the multitude of types of extraction methods, following the active principles and characterizing the complex mixtures of compounds obtained and their physico-chemical characterization.

Hepatoprotective activity has been demonstrated using nettle seed extract with hepatic protective effect by increasing paraoxonase, arylesterase activity and liver catalase activity. The leaf extract has hepatoprotective activity by decreasing alanine aminotransaminase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP). Nettle extract has also been shown to express antiviral activity. The microbial activity of the plant was tested on various gram-positive and negative bacteria, inhibiting the bacteria: *Staphylococcus aureus*, *Enterococcus faecalis*, *Bacillus subtilis*, *E-coli*.

The main chemical compounds of nettle are: flavonoids, tannins, volatile compounds and fatty acids, polysaccharides, isolectins, sterols, terpenes, proteins, vitamins and minerals [19]. Among the most important flavonoids in nettle are: kaempferol, isorhamnetin, quercetin, isoquercetin, astragalin, rutin and 3-rutinoside and 3-glycosides.

The preparation of a pharmacologically finished product with a soap, followed a recipe by which the classic soap was obtained, to which the previously obtained extract was added. The soap contains distilled water, sodium hydroxide, animal fat, coconut oil, olive oil and nettle extract obtained previously.

Another branch of the exploitation of bio-active compounds used in medicine and pharmacology, is given by the group of fungi that offer a series of therapeutic areas.

Today, mushrooms are of great global interest. They occupy a central position among the lower organisms. In developed countries, mushroom cultivation has become one of the most important horticultural crops. They are available all year round and are used in huge quantities due to their nutritional value and pharmacological benefits.

Edible mushrooms are fleshy organisms full of fruit. They grow above and below ground and have a fine taste, aroma and texture, without being poisonous.

In this way, many wastes can be converted into food through organic recycling processes. *Pleurotus Ostreatus* mushrooms have the ability to biotransform organic compounds.

As an example, the regio- and stereoselective reduction of the carbonyl group of 4-methyl-3-methyl-5-heptadione, which gives rise to (4S, 5S) -5-hydroxy-4-methyl-3-heptanone with a purity of 96%

The substances of high interest in *Pleurotus Ostreatus* mushrooms are statins (lovastatin), with a predominant role, hypocholesterolemic, and pleuran (beta-D-glucan), with an antioxidant, antibacterial, dermatological and immunomodulatory role. These are the main compounds of the *Pleurotus* mushroom, which contributes, both in its natural and synthetic state, to maintaining the homeostasis of the human body. Statins are chemically keto-enol and through them, *Pleurotus Ostreatus* mushrooms show their role as cholesterol-lowering.

They are of several types, of which the most important are: Lovastatin, Pravastatin, Simvastatin.

Cholesterol molecules, along with phospholipids, are components of cell membranes, which function as signaling molecules. Cholesterol passes through the bloodstream in small packets called lipoproteins. These "packages" are made of fat (fat) inside and protein on the outside. Two types of lipoproteins carry cholesterol in the body: low-density lipoproteins (LDL or bad cholesterol) and high-density lipoproteins (HDL or good cholesterol), both of which are highly important in cholesterol transport, but high LDL levels lead to accumulation. cholesterol in the arteries. HDL carries cholesterol from other parts of the body back to the liver, which removes excess cholesterol from the body.

High blood cholesterol leads to coronary heart disease (accumulation inside the arteries). Increased levels of LDL cholesterol also increase the risk of heart disease, while high levels of HDL cholesterol in the blood are associated with a lower chance of developing heart disease. Over time, cholesterol buildup hardens the coronary arteries and narrows their caliber. This process limits the flow of oxygen-rich blood from the heart, which leads to clots and blockage of blood flow.

The main purpose of statins is to inhibit the activity of HMG-CoA reductase (3-hydroxy-3-methyl-glutaryl coenzyme A reductase or HMG-CoA) and thus reduce the synthesis of cholesterol in the liver.

The antibacterial, antioxidant, immunomodulatory and dermatological role of *Pleurotus Ostreatus* is performed by pleuran (beta-1,3 / 1,6-D-glucan), which is an insoluble polysaccharide.

In order to obtain the active compounds from the *Pleurotus Ostreatus* mushroom, as the extraction method, we used the extraction method with ethyl acetate in acidic medium, with alcohol and with water.

The antibacterial activity of *Pleurotus* extract in ethanol was tested on 7 reference bacterial strains: *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), *Proteus mirabilis* (ATCC 12453), *Klebsiella pneumoniae* (ATCC 35657), *Pseud 27*), *Streptococcus pyogenes* (ATCC 19615), *Candida albicans* (ATCC 10231) (MicroBioLogics - MediMark, France).

Spectroscopic methods were used to analyze the structure of bioactive compounds in *Pleurotus Ostreatus* fungi. These methods aim to identify the bonds that the studied compounds form, based on the absorption of light radiation. In order to analyze the pharmacological effect of these fungi, their activity on bacterial cultures was studied.

Among the spectroscopic methods used, we mention IR and UV / VIS spectroscopy, thin layer chromatography.

In the spectrum of the *Pleurotus Ostreatus* mushroom extract (Figure 28), the existence of a slightly more intense one was highlighted at a frequency of approximately 328 nm. Literature data confirm the absorption of the solvent (ethyl acetate) at this value.

In the UV / VIS analysis, Lovastatin was degraded after a short time. One of the possibilities of degradation is an oxidation reaction.

The antibacterial effect of *Pleurotus Ostreatus* extract against *Streptococcus pyogenes* and *Pseudomonas aeruginosa* was not reported at the test concentration.

This study exemplifies the importance of plants in infectious pathology, highlighting the antibacterial effect of extracts that although they cannot replace anti-infective chemotherapeutics in certain diseases can be used for their antibacterial and antifungal action in certain topical preparations or in combination with other substances enhancing their anti-infective properties.

Extraction, computational strategy and antibacterial activity of natural compounds from

Nuts, it involves a transdisciplinary relationship with aspects of bioinformatics.

Antioxidants extracted from walnut compounds can be used in living systems, for the antioxidant effect by chemical action on oxygen free radicals and also to increase the stability of food by preventing lipid peroxidation.

A new strategy in viral diseases is the identification and use of natural compounds, with low side effects but still uncertain mechanism.

The quantitative structure-activity relationship (QSAR) applied to small and very large synthetic and natural molecules determined and compared the molecular characteristics of several compounds isolated from nuts, namely: ellagic acid, pedunculagin and tellimagrandine. The ADMET characteristics of these natural compounds compared to synthetic antibiotics were also analyzed.

Generating high-precision biological activity (SAR) relationship models as antimicrobial drugs and exploring new perspectives for understanding the mechanisms of action using computational methods is not only a modern but cost-effective vision for research, development of new directions. In evidence-based medicine.

The antibacterial effect of the alcoholic extract of walnut kernel proves to have a good effect on bacterial cultures with potential negative effects on human health, which may help us in the future to produce many natural plant extracts that can lead not only to the replacement of antibiotics. to which bacteria will gain resistance.

In the ADMET and SAR study, the structures of ellagic acid and ofloxacin are highly similar, ellagic acid also follows Lipinski's rule of five, so we can say that ellagic acid has drug-like activity.

Molecular simulation comprises computational techniques used to model interactions between molecules and to provide information on the binding affinities of various ligands to specific target structures.

These techniques are used in fields such as combinatorial chemistry, drug design, computational biology, and structure-biological activity (QSAR), applied to molecular systems ranging from small molecule systems to macromolecular complexes.

Generation of QSAR models based on series of de novo compounds as well as drugs used in the clinic, for the treatment of two cardiovascular, neurological, microbial diseases.

QSAR models were used to evaluate the biological activity of these compounds, and in these studies we established the contributions of membrane ions to the antagonistic nature of these drugs for the specific receptor. The statistical validity of QSAR models is indicated by significant values of statistical parameters (q^2 , cross-validation R^2 and correlation coefficient R^2).

Expertise in the fields of pharmacy, chemistry, biology, and law will be aimed at coagulating information at all levels so as to provide current, up-to-date information in large-scale and important pharmaceutical-chemical-medical research in both legislative and socio-economic aspects of the current staging.