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1. Assessment of a Benzylamide Derivative of Maslinic Acid Effects on Human Keratinocytes

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Background: The skin is one of the largest organs of the body and various extrinsic and intrinsic factors can influence and can produce changes in time. These changes can lead to skin aging, various skin diseases and even skin cancer [1]. Natural compounds were used for their effect in skin pathologies since ancient times. Pentacyclic triterpenes are studied for their effects in different skin conditions, being often used in wound healing [2]. Among them, maslinic acid present in *Olea europaea* L. and also its derivatives proved to have antioxidant and anti-inflammatory effects [3] and are worth investigating for their effect on skin conditions. The present study was purposed to determine the cytotoxic and antimigratory properties of a benzylamide derivative of maslinic acid (Benzyl (2 α , 3 β) 2,3-diacetoxy-olean-12-en-28-amide) known as "EM2" on HaCaT human keratinocytes.

Materials and Methods: EM2 was tested in five concentrations, namely 1, 5, 10, 25 and 50 μ M. In order to evaluate the effect of the compound on human keratinocytes viability, MTT assay was performed. The effect was evaluated at different periods of time, 24, 48 and 72h. Scratch assay was used for determination of the antimigratory potential of the compound. Representative cells pictures were taken at 0, 3, and 24 h after stimulation with EM2.

Results: The results obtained indicated that EM2 increased HaCaT cells viability at 24, 48 and 72h post-stimulation, at all the five concentrations tested. Regarding the antimigratory potential, EM2 did not affect HaCaT cells migration capacity.

Conclusion: The data obtained indicate that the derivative EM2 did not affect HaCaT keratinocytes viability. Further studies are required in order to further investigate EM2 effects and the underlying mechanism.

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2. Cytotoxic Effect of Sea Buckthorn, Lemongrass and Basil on Human Colonic Tumor (HT-29) and non tumor (CCD-18Co) Cell Lines

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Medicinal plants are intensively studied for their cytotoxic properties. Thereby, Sea Buckthorn (*Hippophae rhamnoides*) presents anticancer properties due to flavonoids which inhibit PI3K-Akt-mTOR pathway, which is directly implicated in more than 20% cases of colon cancer because of mutation on PIK3CA gene [1]. Basil (*Ocimum basilicum*) presents a large spectrum of phenolic compounds, especially flavonoids, which highlight a special interest in cancer field. In vitro studies made obvious the cytotoxic potential in case of colon cancer [2], making it as a potential solution to be used in food and pharmaceutical industries as antioxidants with anticancerous proliferative characteristics. Lemongrass (*Cymbopogon citrus*) presents selective anticancer activity. Compounds such as hydrocarbon terpenes, aldehydes, alcohols, ketones and esters print a strong antioxidant activity, antimutagenic activity, anti-inflammatory activity used for the treatment of the gastro intestinal tract and for colon cancer [3]. Once plants have been tested for their cytotoxic effect, it is important to test them to ensure their cytoprotective or harmless effect on healthy cells. So, CCD-18Co cell line is a healthy human colon line, which can be used to test the safety of extracts.

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3. **Betulinic acid – conjugated magnetic nanoparticles. Design of a potential theranostic nanoplatform**

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Worldwide, cancer is one of the leading causes of death, due to the fact that affects different organs of the body. Nowadays there are no proper medicines to treat specific kinds of cancer and the side effects derived from conventional treatment systems, rise more and more problems. Nanotechnology could be an encouraging domain for the therapeutic and drug-related sections, to avoid as possible as many of the side effects: limited efficacy, toxicity for normal cells or drug resistance. A corroboration between plant extracts and metallic nanoparticles has been developed in the nanotechnology domain, in order to defet the limitations of chemical or physicochemical synthesis [1]. Metallic nanoparticles based on iron oxides were widely used in medical applications such as immunoassay, tissue repair, hyperthermia, MRI contrast enhancement, cancer therapy and targeted drug delivery [2]. In literature, there are many synthesis route to obtain iron oxide nanoparticles, but the most suitable method which is facil, economic, involve a plant extract and less waste production, is the green synthesis [3].

In the present study we propose a versatile nanoplatform with great potential for theranostic applications. The strategy employed refers to the production of a system based on magnetic iron oxide nanoparticles (magnetite and maghemite) loaded with betulinic acid and coated with silica. In the first stage, magnetite and maghemite will be obtained by mixing an aqueous extract based on leaves of green tea, with an aqueous solution containing both Fe^{2+} and Fe^{3+} ions, in the appropriate molar ratio, to obtain separately the desired forms of iron oxides. It is well known that betulinic acid possess a wide range of pharmacological effects including, anti-inflammatory, antiviral, hepatoprotective, antiangiogenic and antitumoral effects. These biological activities are presumably in a synergistic combination with other plant components. The silica inorganic coating represent the magnetic system. Silica coating provide good stability (chemical and colloidal) to the nanoparticles and facilitates their surface to be functionalized by grafting certain biological ligands. In conclusion, we believe that this magnetic nanoplatform will show extraordinary results after use in cancer therapy.

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4. Evaluation of *Allium ursinum* L. Extract Effects

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Background: *Allium ursinum* L., known as ramson or wild garlic is a medicinal plant belonging to the *Amaryllidaceae* family. Ramson is a perennial, herbaceous plant, widespread in Europe and North Asia, but native to Asia [1]. The main constituents present in ramson are the organosulphuric compounds (methiin, alliin, isoalliin, etc). *A. ursinum* is also known to contain phenolic acids, steroidal glycosides, lectins, polysaccharides, etc. Ramson has multiple beneficial effects, including antioxidant, antimicrobial, cardio-protective and antitumoral properties [2].

The aim of the present study was to investigate the total polyphenol content and the antioxidant activity of an ethanolic extract obtained from ramson leaves.

Materials and Methods: Ramson ethanolic extract was obtained from the leaves of the plant using the ultrasound technique. In order to determine the total polyphenol content, Folin–Ciocalteu method was employed. Gallic acid was used as a standard. DPPH assay was used to evaluate the antioxidant activity and vitamin C served as a standard. Different concentrations of the extract were evaluated, namely 50 µg/mL, 100 µg/mL, 250 µg/mL, 500 µg/mL și 1000 µg/mL.

Results: The ethanolic ramson extract had a total polyphenol content of 2.12 mg GAE/g dry vegetal product. The data obtained following DPPH assay indicated an antioxidant activity between 11.18% (for the concentration 50 µg/mL) and 13.92% (for the concentration 1000 µg/mL). The results indicate a low activity compared to that obtained in the case of the standard, vitamin C.

Conclusion: The results obtained showed that *Allium ursinum* L. ethanolic solution has a low antioxidant activity. Further studies will be performed in order to determine other properties of this extractive solution.

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5. Caco-2 Cell Monolayer Used for Identification of Biotransformation of Medical Herbes Contaminated with Mycotoxins

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Mycotoxins are secondary metabolites of fungi, the most dangerous being aflatoxins, ochratoxins and trichothecenes including deoxynivalenol. The toxic and carcinogenic effect on the liver, kidneys and intestines is researched and begins to be elucidated [1]. Medicinal plants are increasingly used for various properties, especially for the immunoprotective, anti-inflammatory and reparatory spectrum. However, this class of phytochemicals can also be exposed to mycotoxin contamination [2], thus, the curative properties can be modified and altered, so that a beneficial source can be transformed into a dangerous one. In order to analyze the beneficial or toxic effect of a compound, its biotransformation must also be investigated. Biotransformation analysis is carried out on in vitro or in vivo models. In order to minimize the use of laboratory animals and to avoid ethically questionable use of animals, in vitro methods are preferred.

Thus the Caco-2 cell line, under normal conditions, can be used to detect the anticancer character of phytochemicals, and in special conditions of differentiation (at high passages, over 50 and 21 days post-seeding) and transformation into monolayer cells can be used to analyze the ability of compounds to pass the enteric barrier and the effect of biotransformed compounds on it [3].

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6. Dietary by-product grape seeds extract: high content in catechins and proanthocyanidins with angiogenic modulator effects

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Grape seeds (GS) represent a valuable by-product material in winery and juice production, considered as a good source of antioxidant phytochemicals, thus being widely used as dietary supplement. GS are concentrated in polyphenols such as phenolic acids, flavan-3-ol, including proanthocyanidins and catechins [1]. Oxidative stress protection, anti-inflammatory, antimicrobial, antidiabetic effects and chemoprevention in cancer are documented for several types of grape seed extracts [2,3], but more data is still needed. We aimed to contribute by analysing a commercial source of grape seeds, concerning the polyphenolic phytochemical profile next to an *in vivo* evaluation of the angiogenesis modulator effect.

An ethanolic extract of the dried grape seeds was obtained by ultrasound assisted extraction. Polyphenolic content was assessed by HPLC and the antioxidant effect through DPPH assay. The chorioallantoic membrane (CAM) *in vivo* assay was used for the angiogenic evaluation.

A high content in polyphenols with epicatechin and catechin as main phytochemicals was obtained for the GS extract. Antioxidant effects for 1mg/ml GSE were similar to antioxidant standards such as quercetin at the same concentration. The CAM investigation indicated the GS extract in concentration of 50 μg/ml can interfere with the angiogenic process, by reducing the number of new capillaries during the rapid developmental period of the vascular plexus.

Dietary grape seeds are a good source of by-products for extracts, and a valuable source of catechins and proanthocyanidins, with highly antioxidative capacity that can also interfere with pathological angiogenic process.

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7. *Ganoderma lucidum*: Bioactivities of an unexpected ingredient in skincare products

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Ganoderma lucidum (Reishi, Linghzi) is a medicinal mushroom that grows on heartwood trees in various regions of China and Europe. The species has a millenia old reputation in Eastern Traditional Medicine. The main secondary metabolites identified in the fruiting body, mycelia and spores of the fungus are polysaccharides, triterpenes, sterols, glycoproteins, peptides, fatty acids, flavonoids and phenolic compounds [1]. *G. lucidum* exhibits an impressive array of medicinal properties, including anti-inflammatory, antioxidant, immunomodulatory, anticancer, antidiabetic, antibacterial, antiviral, antifungal, anti-aging, antiulcer, and hepatoprotective [2]. Recently, in addition to its use for the treatment or prevention of various diseases, *G. lucidum* has become a high-end ingredient of skincare products. The effects that motivate its topical use are the capacity to protect cellular macromolecules against the deleterious effects of reactive oxygen species, to protect the glycation of collagen, to protect fibroblasts against UV radiation, to inhibit the activity of enzymes that degrade the macromolecules of the extracellular matrix, and to increase collagen biosynthesis. *G. lucidum* extracts have a wound healing, antibacterial and anti-inflammatory effect [3]. A well studied effect is the tyrosinase inhibition, with applications as a skin lightening agent [1]. Moreover, cell wall polysaccharides have a moisturizing effect. Based on these effects, the development of topical products with *Ganoderma* extracts having an optimized bioavailability is essential for therapeutic and cosmetologic uses, and researches in this directions are scarce for the time being.

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8. Investigation of the immunomodulatory potential of *Origanum vulgare* L. volatile oil

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Introduction: *Origanum vulgare* L. (commonly known as oregano) is a perennial plant of *Lamiaceae* family. Due to the rich phytochemical composition of the volatile oil (mainly thymol and carvacrol) it has been demonstrated to have a significant ability to modify and reduce the synthesis of different cytokines [1,2]. The current study is designed in order to evaluate the immunomodulatory potential of OEO (oregano essential oil) hydrogel type formulations (OEO-PM) by investigating different cytokine production (IL-1a, IL-12, TNF- α and IFN- γ), using PBMC cells obtained from subjects with acrochordons. The blood samples were collected from 6 adult volunteer subjects and were used for Ficoll-Paque media density gradient isolation of PBMCs; the supernatants of the immune cells treated with OEO-PM in different concentrations were collected at distinct time points: 24h and 72h. The Quantikine® Human Immunoassay (R&D Systems) was used for assessment of cytokine secretion of the cells. The immune-modulating effects of OEO formulations were variable. From one side it was observed that, the lowest concentration of OEO (100 $\mu\text{g/mL}$) formulation 2- OEO-PM, increased the TNF- α production with an absorbance of 0.2377 $\text{pg}/\mu\text{L}$. Although, in case of the same formulation the highest concentration of OEO (150 $\mu\text{g/mL}$) blocked the production of this cytokine. Significant increase of IFN- γ was achieved for formulation 2- OEO-PM at the lowest concentration (100 $\mu\text{g/mL}$). The same observation was noticed for IL-12, therefore, 150 $\mu\text{g/mL}$ of OEO formulation 2 increased the cytokine secretion. OEO in the lowest tested concentration (100 $\mu\text{g/mL}$) presented immunomodulatory activity on PBMCs by upregulating TNF- α , IFN- γ and IL-12 subunits. However, OEO did not seem to increase production of IL-1 in the set experimental conditions

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9. Green biosynthesis of iron oxide magnetic nanoparticles and their biomedical applications in targeted anticancer drug delivery system

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Plant-based medical practice it is an increasingly used technique in preventative and therapeutic approaches. It is well known that plants naturally contain various active compounds which has several health benefits when administered to patients. On the other hand, nanotechnology gained popularity due to the benefits and potential which it can provide to humans. Nowadays, nanotechnology pay a vital role in the world, becoming progressively influential in various fields of applications, including food industry and biomedical field. Combining the plant-based medical practice with nanotechnology it can be achieved a new field for medications develop, their administration or targeting of a tissue/organ with this medications obtained from natural sources with a plethora of benefits for various patients diseases.

One of the goals of this study is represented by lung cancer, being one of the deadliest cancers worldwide, with more than 30% of cancer-related deaths [1]. The second important goal refers to another type of cancer, ovarian cancer, which is the most lethal gynecological malignancy with an increased incidences worldwide [2]. In order to contribute to the therapeutic management of this diseases, we aim to develop magnetic nanoparticles by green biosynthesis, as support for antitumor active principles. The green byosynthesis involve starting from a natural extract containing biological compounds which may act as both reducing and capping agents, thereby stabilizing the nanoparticles during the synthesis process [3].

The plant extract taken into account is an ethanolic extract based on flowers of *Magnolia liliiflora* Desr, from Magnoliaceae family. In the first stage, it was determined the

poliphenolic composition of the ethanolic extract – 79.82 μg GAE/g extract and the antioxidant activity, expressed as EC_{50} value, yielding an $\text{EC}_{50} = 2.92 \mu\text{g/mL}$. The FT-IR analysis demonstrated that the dried flowers ethanolic extract contains benzenoids, phenylpropanoids, monoterpenoids, monoterpenes and sesquiterpenoids.

In conclusion, taken into account the significant physico-chemical profile, the *M. liliiflora* ethanolic extract can be considered a promising candidate for develop magnetic nanoparticles, used further as support for antitumoral compounds, in targeted drug delivery system.

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10. Effects of *Rosmarinus officinalis* ethanolic extract in HET-CAM and tumor CAM assay

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Rosmarinus officinalis (RO), known as rosemary is a widely cultivated and used aromatic plant, being rich in essential oils, polyphenols and terpenic compounds, is recommended as a traditional remedy in hepatobilliar, cardiovascular and inflammatory conditions. In the past years, RO was highly investigated for effects in various pathological conditions, such as dislipidemia, stress and anxiety, skin diseases, cancer (1,2).

In this study we analysed an ethanolic extract from rosemary leaves cultivated in Banat region, Romania. Polyphenolic content was evaluated through Folin Ciocâlțeu method, and antioxidant potential was assessed by the DPPH test. We also performed an *in vivo* anti-irritation assessment through the HET-CAM (chorioallantoic membrane) protocol and a tumor CAM assay using A375 melanoma cells was also performed.

RO extract showed a high polyphenolic content in corerelation with a strong antioxidative effect compared to standard antioxidant compounds. The *in vivo* investigation indicated that RO ethanolic extract was well tolerated and showed anti-irritation effects on mucosal tissues, while when administered onto the melanoma developing cells in the CAM assay, an important limitative effect on blood vessel development was observed.

RO leaves represents a promising natural product for skin related conditions having important antioxidative potential, a good biocompatibility and anti-irritative effects on mucosal tissues, while limiting the progression of melanoma related angiogenesis.

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11. Fennel – new insights in its applications for human health

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Fennel (*Foeniculum vulgare ssp. vulgare*) is a tall perennial plant, native to the Mediterranean area. All plant parts have a strong sweet aromatic smell, which is correlated to the numerous secretory ducts that go from the roots to the fruits of the plant. Fennel fruits contain up to 6% volatiles, with main constituents being anethole, estragol and fenchone. Non-volatile compounds are phytosterols, flavonoids and coumarins. Several *in vitro* and *in vivo* studies could point out antimicrobial, carminative, antispasmodic, and anti-inflammatory properties. Recently, the favorable effects of this plant were shown extend beyond the traditionally known digestive and respiratory disorders: fennel also has hypoglycemic, hypolipidemic, estrogen-like and memory enhancing properties [1]. New information on the mechanisms of action has become available that explain the health benefits of fennel: the plant increases RNA expression of tight junction proteins in enterocytes, protecting the organism from antigens that may leak into the general circulation. It exerts anti-inflammatory effects through inhibition of nuclear factor kappa B (NF- κ B) and interleukin-1 β [2]. Fennel also displays anti-cancer and anti-metastatic properties in breast cancer [3]. Further research regarding the identification of the most active fractions of fennel seed and aerial parts as cytoprotective and chemopreventive agents will help to improve our use of this plant in human health and disease.

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12. An Integrative Approach to Aerial Hazard of Coal-Contaminated Soils

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The effects of coal-related air pollution have been extensively studied in laboratory vertebrates, particularly rats and mice, but its effect on land snails, and terrestrial invertebrates broadly, is currently not known and seldomly studied. Land snails are pertinent species for monitoring trace metal and PAH accumulation in soils and plants, and also a promising bioindicator for air pollution. Various biologic effects, including enzymatic inhibition, loss of DNA integrity, changes in lysosomal stability and metallothionein levels have been described [1], but not subtle changes in gene expression. Changes at transcriptional level (messenger RNA - mRNA) and translational level (protein synthesis) are associated with toxicological responses to exposure. Although widely employed in occupational toxicology, such biomarkers have rarely been applied in (eco)toxicogenomics, particularly with land snails [2]. Among the known snail proteins, tropomyosin is of crucial importance in respiration – tropomyosin plays a central role in skeletal muscle contraction. Evidence showed that tropomyosin level (proteome) in aquatic mollusks (bivalves) reflects the pollutant-related oxidative stress, but there is little knowledge on the changes at transcriptional level. Transcriptomic biomarkers can be sensitive enough to detect changes in molecular mechanisms and signaling pathways even at low doses of exposure. Therefore, such changes deserve to be investigated for assessing their potential use as biomarkers of air pollution [3]. This approach will provide more environmentally-relevant assay by using land snail as a testing model and tropomyosin gene expression as biomarker. The assay through assessing the chemical fingerprint of coal-related air pollution with an innovative statistical model will significantly contribute to the development in health risk assessment methodology.

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13. Importance of Inorganic Element Determination of Romanian *Populus nigra* L. Buds Extract

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During the formulation of a phytopharmaceutical product some important aspects have to be considered: the raw material from which active principles are extracted (evaluation of the content of toxic elements, especially in the case of plants that are used for phytotherapy) and evaluation of the finished product to define active principles, ensuring that it is not contaminated with toxic metals either from the handling process or from the extractive process.

Poplar bud extract (Pg) was subjected to microwave-assisted digestion for the extraction of inorganic elements in an acidic environment. Using an atomic absorption spectrophotometer with graphite furnace, the concentration of 11 inorganic elements was determined: trace elements (Mn, Cu, Mg, Fe, and Zn) and potentially toxic elements (As, Cd, Pb, Al, Co, and Cr). The inorganic elements concentrations were below the limit of detection for As, Pb, and Co, and cadmium concentration was 0.019 µg /g, all this fulfills regulations stipulated by WHO guidelines for assessing the quality of herbal medicines with reference to the contaminants such as As, Cd, and Pb.

The concentration of the other elements is comparable to those reported in the literature: Mn = 0.59 µg /g, Cr = 0.79 µg/g, Ni = 3.28 µg/g, Cu = 6.66 µg/g, Fe = 39.00 µg/g, Zn = 14.84 µg/g. Aluminium concentration was 2109.87 µg /g and considering that some *in vitro* methods suggest that Al from a tea infusion is potentially available for absorption at only 4.8% and only 0.37% is orally bioavailable, established by *in vivo* experiments, we can consider exposure to Al not to constitute a risk because is less than the tolerable weekly intake of 1 mg/kg body weight/week.

In conclusion, based on experimental outcomes, Pg ethanolic extract had a low contribution to trace elements in dietary intake, but the most valuable conclusion is regarding its safety: Pg extract does not produce any harmful effect of metal toxicity during its therapeutic application.

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14. Innovative extraction of flavonoids from native plants using magnetic nanoparticles

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Natural products extracted from plants are recognized sources of new drugs. The optimization of the extraction parameters is a complex process to ensure a selectivity of the substances used, considering that in the plant matrix usually coexist a series of substances with minimal differences in structure. Our research targets plants with an ethnomedical tradition in Romania, that are known to contain flavonoids: *Juniperus communis* and *Cotinus coggygia*. Pseudo-fruits of the former, and wood of the latter are subjected to an innovative extraction procedure with the help of magnetic nanoparticles [1]. The technique is a solid-phase extraction that requires less solvent consumption. Advantages in yield, cost, ecotoxicity and time are evaluated, with the validation of the most advantageous procedure. The extracts are tested for bioactivity, using *in vitro* tests that are relevant for skin application (toxicity on normal HaCat cells and human melanoma, anti-inflammatory action on murine macrophages, antibacterial action, antioxidant effect).

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15. Sweet wormwood phytochemical analysis and bioactive effects on CAM assay

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Artemisia annua L., known as Sweet wormwood is associated with antimalaria effects due to its artemisinin content (1). More recently, other active phytochemicals and biological activities were reported for Sweet wormwood extracts, such as anti-inflammatory, anticancer, hepatoprotective, antioxidant, antidiabetic effects (2,3).

Our purpose was to analyse a sample of commercial plant material regarding the phytochemical profile of an ethanolic extract and to assess the potential bioactive effects on blood vessels.

Ultrasound assisted extraction in 80% ethanol, followed by solvent removal using a rotary evaporator were used to obtain the dry extract. Polyphenolic content was evaluated using the Folin Ciocalteu method and the antioxidant potential was assessed by the DPPH assay. The effect upon blood vessel level was evaluated using the HET-CAM test for the vascular irritability and by using the chorioallantoic membrane (CAM) assay to seize the impact on the angiogenic process.

The Sweet wormwood extract had a high content in polyphenols in correlation with a significant antioxidant activity. No signs of irritation were registered in the *in vivo* HET-CAM assay, with potential anti-irritative effects, suggesting good tolerability upon mucosal tissues. While when investigating the potential angiogenic modulation of *Artemisia annua* extract, an angiogenic stimulation was observed. Sweet wormwood ethanolic extract with a high polyphenolic content and strong antioxidant potential, with good tolerability, could represent an alternative for angiogenic related pathologies.

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16. Identification of bioactive compounds of *Galium* species

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Nowadays, a field of great interest and perspective is that of natural compounds that have demonstrated important therapeutic effects. Existing technological methods should be exploited and improved to increase the therapeutic utility of plants, as the main renewable sources of active phytochemicals. Understanding how herbal medicines are obtained and standardized can help medical staff advice on choosing an effective treatment at an affordable price. *Galium* species are plants that belong to the *Rubiaceae* family, with proven utility in traditional medicine, especially for the diuretic and choleric effect. Most species of *Galium* have been studied for their content in flavonoids, polyphenols, anthraquinones and iridoids. Tamas et al. performed a comparative analysis of two species of *Galium* in the Romanian flora (*Galium verum* L. and *Galium mollugo* L.), in terms of flavonoids in the composition. Following the TLC analysis, it was obtained that the main flavonoids present are rutosides and hyperosides, the latter being found in smaller quantities in the species *Galium mollugo* L. [1]. In addition, the group conducted by Mocan investigated the chemical composition of four species of *Galium* in terms of content in polyphenolcarboxylic acids, sterols and methoxylated flavones. Following HPLC-MS and HPLC-MS / MS analyzes, caffeic and chlorogenic acids but also β -sitosterol and campesterol were identified in all studied species, and the only methoxylated flavone identified was hispidulin using the LC-MS / MS method [2]. Given the limited data, new and more detailed studies on several classes of phytochemicals are needed for a broader characterization of these plant species, followed by the analysis of their biological activity.

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17. Obtaining and evaluating the bioactivity of some products for external use derived from the leaves and seed oil of the coffee plant (*Coffea arabica*)

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The genus *Coffea* (Rubiaceae family), comprises 124 species, among which *C. arabica*, *C. canephora* and *C. liberica* are cultivated for their seeds. Coffee seeds have been extensively studied, whereas studies related to the phytochemicals and bioactivities of coffee leaves are scarce.

Coffee leaves have a long history for use in the ethnomedicine of countries where coffee plants grow. Recently, attention has been drawn to their health benefits because of abundant bioactive components: alkaloids, flavonoids, terpenes, tannins, xanthines, phenolic acids, phytosterols, and carotenoids. These metabolites contribute to antioxidant, anti-inflammatory, anti-bacterial, and anti-fungal activities [1]. Diterpenes including cafestol, kahweol, and 16-O-methylcafestol, generally found in the lipid fraction of coffee bean, are also detected in the coffee leaves.

Cold pressed oil obtained from green coffee seeds is rich in triglycerides (75%), steroids (5%) and terpenes (19%). It also contains tocopherols and phenolic compounds. This oil has a strong antioxidant character, due to the presence of chlorogenic acid and tocopherol[2]. The use of vegetable oils has promising results in the treatment of skin wounds, as they have an effective impact on the stages of wound healing through their antimicrobial, anti-inflammatory and anti-oxidative activities and by promoting cell proliferation, increasing collagen synthesis, stimulating skin reconstruction and repairing lipid barrier function of the skin.

Our study explores the potential of less explored products originating from *C. arabica*: leaves and seed oil. It enabled the obtainment of coffee oil by Soxhlet extraction, using ethyl acetate as extraction solvent. Various leaf extracts (crude ethanol extract, its partition between petroleum ether, ethyl acetate, n-butanol, and water) were obtained and evaluated regarding their antioxidative and anti-inflammatory effect. The evaluation of fatty oils from seeds, and coffee leaf extracts as bioactive products with topical application will be followed, in terms of their potential in dermato-cosmetology.

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18. Physicochemical screening and biological evaluation of *Aesculus hippocastanum* extracts with potential therapeutic applications in dermatocosmetology

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Aesculus hippocastanum L., commonly known as horse chestnut, is a member of the Sapindaceae family (in past known as Hippocastanaceae family). Over the past few decades, different parts of the *Aesculus hippocastanum* L. were used for the treatment of many diseases like inflammatory skin diseases, skin injuries and venous insufficiency [1]. Moreover, *A. hippocastanum* extract has been shown to exhibit antitumor activities [2]. Nowadays, the extracts are used as an adjunct in the treatment of chronic venous insufficiency, phlebitis, varicose veins and also used topically for clearing skin conditions [3].

The primary active pharmaceutical constituent found in horse chestnut extract, especially in seeds is aescin, which is actually a racemic mixture of triterpene saponins present in two forms: α -escin and β -escin. According to the literature, β -escin appears to be the active component from racemic mixture. *Aesculus hippocastanum* also include flavonoids, like quercetin, kaempferol, rutin, epicatechin and its dimer proanthocyanidin A2, coumarin (fraxin) and tannins. Most of the saponins and flavonoids are found in the seeds, but have also been found in the endosperm and leaves. The horse chestnut flavonoids, like rutin and quercetin has been defined in literature as having radical scavenging, antibacterial, anti-haemorrhagic and antiviral activities.

To this end, the current study aimed: i) design the physico-chemical screening of different extracts (aqueous and hydro-alcoholic) obtained from *A. hippocastanum* leaves and endosperm, ii) the investigation of the *in vitro* effects of both extracts on human melanoma cells and human keratinocytes and iii) the impact of both extracts on physiological skin parameters on SKH-1 hair-less mice, by non-invasive method.

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19. Pharmacological activities of *Galium* species

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Since ancient times, medicinal and aromatic plants have been commonly used as medicines, cosmetics and food. For the vast majority of the population, plants species continue to play an important role in treating various pathologies. Due to their extensive composition in phytochemicals, medicinal plants are the basis for the discovery of new therapeutic remedies, especially in combating and limiting cancer, which are of great interest today. Thus, a number of plant species are used as an alternative therapy in the prevention and treatment of cancer, with fewer toxic reactions than traditional therapy [1]. This category also includes the species of *Galium*, perennial herbaceous plants belonging to the *Rubiaceae* family, which have been studied for their antitumor effect on the oral cavity [2]. Several classes of biocompounds of *Galium* species have been isolated, among which phenolic compounds, triterpenes, iridoids and anthraquinones have been identified in larger quantities. These plant species over the years have proven several pharmacological activities such as antibacterial and antifungal effect, anticancer and antioxidant activity, effects produced on central nervous system but also the action on gastrointestinal and renal system. Chloroform extracts of *Galium* spp. confirmed the antimicrobial action on gram-positive microorganisms but also an inhibitory effect on *Candida* spp. Due to the well-known diuretic effect, *Galium verum* tea is used in urinary tract infections and inflammations, in addition the herbal product can be used in the treatment of gastric and liver disorders, showing spasmolytic and choleric-cholagogue action. Regarding the effect on the CNS, *Galium* spp. have traditionally been used to treat epilepsy and nervousness, it being observed that mainly the asperuloside in the composition is responsible for the sedative effect [3]. Despite the traditional use of *Galium* species, there are still limited studies on pharmacological activity and involvement in the treatment of diseases. Further research are needed to know in detail the chemical composition and to understand the mechanisms of action underlying the therapeutic effects, especially in combating tumor pathologies.

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20. PRELIMINARY INVESTIGATION OF CHIA (*SALVIA HISPANICA*) AERIAL PARTS

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The identification of nutrient-rich food sources with multiple health-promoting properties is a current trend worldwide. Chia (*Salvia hispanica*), a Lamiaceae species, is native to southern Mexico and northern Guatemala. Once a staple food of ancient Precolumbian civilizations, chia seeds have gained global recognition in human nutrition. While the protein, lipid and fiber contents of seeds have been analyzed by various investigators, aerial parts of the plant could also offer a source of bioactive compounds [1]. In fact, these plant parts become available in large amounts in agriculture, after the harvest of seeds. Its belonging to the *Salvia* genus, which is known to include valuable medicinal plants used for their leaves, is a further incentive for the study of chia aerial parts. Although investigations are sparse until now, identified compounds include phenolic acids (caffeic acid, ferulic acid, rosmarinic acid), flavonoids (vitexin, luteolin-O-glucuronide) [1,2] and sesquiterpenes [3]. Determined properties include antioxidative (identified by ORAC and DPPH methods) [2] and antibacterial effects [3].

As a first step in our research, we investigated relevant histological structures of leaves and stems. In the epidermis of both organs are present two types of secretory hairs: peltate and capitate. Peltate glands have a stalk constituted of one cell and a large head constituted of four secretory cells covered by a common cuticle. The secretion consists in red-coloured volatile compounds. In capitate hairs, the stalk and the secretory head consist of one cell, each; the secretion of these glands is colourless. With the aid of Folin-Ciocalteu reagent, we could highlight areas in the cortex of the stem that contain reducing polyphenols. These findings guide further research on the content and bioactivity of volatile oils and phenolic compounds.

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21. Plants Extracts as Active Ingredients in Topical Formulations with Photoprotective Properties

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Chronic exposure to solar or artificial ultraviolet (UV) radiation has been associated with the development of various skin disorders such as premature aging, inflammation, barrier impairment, and cancer. UVA photons penetrate deep into the epidermal and dermal cutaneous layers, affecting most of the skin cellular components (*i.e.*, keratinocytes, fibroblasts, and melanocytes) by generating a massive production of reactive oxygen and nitrogen species (ROS and RNS). UVB photons, on the other hand, induce a direct DNA damage despite their superficial skin penetration. Hence, a conscious protection against UVA- and UVB-induced phototoxicity is necessary.

The traditional strategy of photoprotection is the addition of chemical sunscreens or sun blockers in topical formulations. However, a novel approach is the use of plant extracts or plant-derived compounds as active ingredients which might prevent or reduce the skin penetration of UV radiation, thus diminishing local oxidative stress, DNA damage and inflammation. Beside the UV protective properties, plant extracts and phytochemicals (*i.e.*, phenolic acids, flavonoids, terpenoids) possess additional pharmacological activities (*e.g.*, antioxidant, and anti-inflammatory) gaining significant attention for their potential use in topical formulations.

Many herbal species have been researched as UV blocking agents. For instance, green tea (*Camellia sinensis* L.) is studied due to its richness in catechins, among which (-)-epigallocatechin-3-gallate has been classified as the most effective compound against cutaneous UVA damage, carcinogenesis and inflammation. *Punica granatum* L. fruits contain active anthocyanins and tannins exerting antioxidant, healing, anti-inflammatory, UVA and UVB protective properties. *Thymus vulgaris* L. or thyme is abundant in terpenes such as thymol, carvacrol and borneol, possessing a wide range of biological effects (*i.e.*, antioxidant, antimicrobial, spasmolytic, antitussive). Recent *in vitro* and *in vivo* studies highlight the efficacy of *T. vulgaris* extracts in counteracting the deleterious effects of UVA and UVB radiations. Other important medicinal plants for skin photoprotection include *Aloe vera* sp., *Hippophae rhamnoides*, and *Theobroma cacao*.

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22. The determination of anti-cancer and antioxidant activity of *Melissa officinalis* L.

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Melissa officinalis L. (Lemon balm) is a perennial herbaceous plant, that belongs to the Lamiaceae family, exhibiting a plethora of pharmacological activities such as antioxidant, antiviral, anti-cancer, anti-bacterial, sedative, and anxiolytic effects [1]. The main active compounds of *Melissa officinalis* are volatile oils (geranial, citronellal, geraniol), triterpenes (ursolic and oleanolic acids), and phenols (derivates of caffeic acid: naringin, hesperidin)[2].

This study aimed to quantify the antioxidant activity of *Melissa officinalis*, and test its anti-cancer activity on MCF7 (breast cancer) cell line.

A hydroalcoholic extract was prepared using ethylic alcohol as solvent and water (50:50). The extract was characterized using high-pressure liquid chromatography (HPLC) to determine its composition. Subsequently, the antioxidant activity of the extract was determined using the DPPH (2,2-diphenyl-1-picryl-hydrazylhydrate) photometric assay. The MCF7 cells were cultured in DMEM supplemented with 10% FCS and 1% penicillin/streptomycin. The in vitro cytotoxicity was tested using the MTT assay. The cells in the logarithmic growth phase were seeded onto 96-well plates at a density of 3×10^4 . The optical density was measured using an ELISA reader at 570 nm. The experiments were performed in triplicates.

The DPPH photometric assay demonstrated a remarkable antioxidant activity. The HPLC analysis confirmed that the predominant active compound of *Melissa officinalis* extract is geranial. Moreover, the MTT cytotoxicity assay revealed a significant inhibitory effect on MCF7 cell lines.

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23. Potential cytotoxic activity of an ethanolic extract of *Salvia officinalis*

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Cancer is considered one of the principal causes of death in the world and it is characterized by the uncontrolled cell division of malignant cells. The development of new treatments with high selectivity against malignant cells and reduced side effects represents one main objective of the pharmaceutical field. A highly investigated approach is the use of medicinal plants as potential treatment or as a source for new therapeutic agents [1].

Salvia officinalis is one of the most widespread representatives of the Lamiaceae family with various uses in the pharmaceutical, cosmetic and food industries. It plays an important role in traditional medicine all across the world, due to the biological activities it possesses such as antibacterial, anticancer, hemostatic and spasmolytic which determined different scientific groups to further investigate the composition and properties of this medicinal plant [2].

In our study was tested the cytotoxic activity against the A431 cell line and was evaluated the antioxidant activity of an ethanolic extract 50% v/v of *Salvia officinalis* (SOe). The leaves collected in July were pulverized and mixed with the solvent at room temperature for 3 h, and then the mixture was filtered obtaining the SOe. The HPLC analysis revealed that the main constituent presented in the SOe is the rosmarinic acid, a polyphenol frequently identified in the species of the Lamiaceae family. The antioxidant activity was measured using the DPPH assay and the cytotoxicity was evaluated using the MTT assay. The preliminary results showed the presence of the antioxidant activity and a reduction of the viability of the A431 cell line in the presence of the SOe.

The obtained extract will be further evaluated in vitro against other types of cancer cell lines.

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24. Evaluation of *Boswellia Serrata* hydro-alcoholic extracts

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The *Boswellia* family of trees is much more numerous, but only 4 species produce resin, and of these, *Boswellia serrata* resin is used most often for therapeutic purposes. Since ancient time incense was used in religious rituals and also in traditional medicine.

Over time, numerous studies have been carried out that have reported that *Boswellia serrata* (BS) and the extracted active compounds can be used successfully in the fight against cancer [1,2].

In this study we prepared two hydro-alcoholic extract of BS. Both extracts were prepared with water and ethanol in different ratios, BS-1 – water:ethanol 50:50 (v/v) and BS – 2 water:ethanol 40:60 (v:v). The extracts were characterized by HPLC technique and DPPH assay.

The studied extracts revealed a dose-dependent antioxidant activity and boswellic acids as majoritary constituents; these results are similar to those found in the literature.

Furthermore, the extracts proved a reduction of the cell viability when tested on MCF-7 and MDA-MB-231 cell lines.

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25. Oleanolic acid derivatives as pharmacological importance in the treatment of cancer

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Oleanolic acid (OA) (3 β -hydroxyolean-12-en-28-oic acid) belongs to the class of pentacyclic triterpenes with a very wide therapeutic spectrum due to biological actions such as anti-inflammatory, neutoprotective, hepatoprotective and antitumor. An important source of potential new therapeutic agents is the class of oleanolic acid derivatives. The main structural changes of this phytoconstituent take place in the positions CH₃-OH, C₁₂=C₁₃ and C₂₈-COOH. Numerous oleanolic acid derivatives, such as 2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oic acid, possess more intense therapeutic actions than the parent compound. A study carried out in order to improve the pharmacokinetic properties of oleanolic acid focused on the reaction between OA and 1,3-cyclopropanyl phosphate ester thus obtaining prodrugs with bioavailability and prolonged half-life. In terms of antitumor activity, OA has been shown to be effective in in vitro and in vivo studies. Its derivatives, such as oleanolic acid methyl ester, have shown improved cytotoxic properties on the cervical cancer cell line - HeLa. Also, by formulating OA in amino-appended β -cyclodextrins there was an improvement in the solubility of the derivative and an increase in antitumor activity in several tumor cell lines. An important number of oleanolic acid derivatives are currently in clinical trials to demonstrate therapeutic efficacy. One such derivative is bardoxolone methyl (CDDO-Me). It was studied in 47 human subjects in phase 1 of the clinical trial for the treatment of solid tumors and lymphoma. The derivative was well tolerated by patients and showed antitumor effects. In addition, CDDO-Me was evaluated in Phase 2 of the study for the treatment of chronic renal disease associated with type 2 diabetes. renal pathology. Currently, the compound is in the third phase of the clinical trial to determine the efficacy in connective tissue pathology associated with pulmonary arterial hypertension. In conclusion, OA derivatives have the potential to provide new alternative therapies in a wide variety of pathologies.

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26. Supernatural: a new approach to natural compounds to target mitochondria in antitumor therapy

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Although the main function of the mitochondria is to produce energy, it is also involved in other processes such as the production of reactive oxygen species, the regulation of cell signaling, cell death and cellular adaptation to the environment. For this reason, mitochondria play an important role in the tumor process, and the compounds that target this organ are considered the new generation of antitumor agents. Recently, special attention has been paid to the action of natural compounds on mitochondria, since they are part of the daily diet and represent the foundation of traditional therapy. Many of these compounds act at the mitochondrial level by inhibiting mitochondrial enzymes or by altering mitochondrial signals. Quercetin is a naturally occurring compound known to have the ability to accumulate in this cell organ. The main effects of quercetin are inhibition of ATP synthesis, alteration of succinate oxidase and NADH oxidase enzymes, and inhibition of OXPHOS. Another example of a compound of natural origin is resveratrol. It improves mitochondrial function by increasing the expression of genes involved in oxidative phosphorylation. In addition, resveratrol has beneficial antioxidant activity in antitumor therapy, by decreasing the production of ROS at the mitochondrial level and by modulating the expression of mitochondrial proteins and enzymes involved in the production of ROS. Regarding curcumin, another compound of natural origin, it has been observed that it causes a decrease in ATP synthesis due to its ability to act as a protonophoric uncoupler. In several cell lines such as hepatoma cell lines or retinal epithelial cells, it has been found that curcumin exerts an antioxidant and cytoprotective effect through both direct and indirect mechanism which consists in increasing the expression of genes involved in encoding antioxidant proteins. In conclusion, natural compounds exert multiple effects in the mitochondria, so these compounds can be used both as chemopreventers and as chemotherapeutics in the treatment of cancer.

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27. Medicinal plants and their bioactive compounds related to dental diseases

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Oral and dental hygiene is the basis of a healthy life, being the main factor in preventing oral diseases. Poor oral hygiene and inadequate nutrition are the basis of the most common diseases of teeth and gums (tooth decay, plaque, periodontitis, etc.). Herbal products are a cheap and safe alternative to prevent dental disease. Since ancient times, medicinal plants have been used to treat various diseases, from the simplest to the most complex. The active compounds of plants (secondary metabolites) show a diversity of pharmacological actions and since a century ago they have been the basis for the development of drugs. In the field of dentistry, more recently, the term phytostomatology is adopted, which reflects the use of compounds of natural origin in the prevention and treatment of diseases of the oral cavity. Certain plants have been used as natural toothbrushes and the compounds derived from them are still founded in the composition of certain toothpastes, and many other plant-derived products have been used as different parts of dental materials (e.g. frequent use of eugenol in dental offices). Among other beneficial effects exerted by medicinal plants and the compounds obtained from them are antibacterial effects, antifungal effects, anti-inflammatory effects, antioxidant potential, etc. Thus, the use of these types of natural products in dental practice is a basic adjuvant therapy in dental treatments.

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28. A pharmacology-based overview on medicinal plants antiviral activity

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A role of utmost importance in the health of the global population is represented by biodiversity, which contributes in a significant way to human life and development. Over 80% of the world's population uses products based on medicinal plants, either as a way of prevention or as a way of treating certain pathologies. Since ancient times, humans have relied on the healing powers of natural resources, and the importance of their pharmacological effects was confirmed with the advent of the modern world when a number of herbal medicines were transposed into clinical use. The most relevant examples are digoxin, ergotamine, quinine, salicylate derivatives. The identification, isolation, and evaluation of active principles from plant resources involves a series of stages and many specialists in different fields (botany, biochemistry, chemistry, pharmacy, medicine) and remains a branch of real interest for the medical field, given the needs of new and new pharmacological targets.

In the last two years, the world has been deeply affected by the pandemic generated by the new coronavirus, for which there is still no specific treatment. Investigations regarding the pharmacological effects of natural resources against coronaviruses have highlighted a number of plants with promising potential, including: *Agastache rugosa*, *Mollucoris radiataum*, *Astragalus membranaceus*, *Ecklonia cava*, *Glycyrrhizae uralensis*, *Lindera aggregata*, *Pyrrosia lingua*, *Tinospora cord* etc. On the other hand, several phytocompounds have proven their antiviral potential, and the most common are allicin, quercetin, hesperedin, curcumin, kaempferol, with high chances of. true chiopreventive or even curative agents against COVID-19.

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29. Study on the binding affinity and other structural parameters of polyurethane nanostructures used as a carrier for antibiotics

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The drug delivery domain is developing at an astonishing speed. A huge number of organic and inorganic, natural and synthetic compounds are synthesized to increase the bioavailability of different biological active substances. On the other hand, the targeted and the controlled release are important objectives of the pharmaceutical industry [1].

Polyurethanes are often used in different industries as foams, adhesives and coatings, but many medical applications (catethers and tubes, artificial skin, cardiac pace-maker, coatings of breast implants, intra-aortic and gastric balloons) were developed in the last decades. The first polyurethane drug delivery systems were developed at the beginning of this century and the particles size has decreased from micro- to nano-scale around 15 years ago. Misuse of antibiotics is one of the main causes of the mortality associated with infection associated to the multidrug-resistant bacteria [2, 3].

The present study aims to evaluate different parameters that affect the encapsulation of polyurethanes nanoparticles, using different computational procedures, in order to improve the transmembrane transfer and the drug release of different antibiotics.

Different 2D structures of polyurethane macromolecular chains based on three different diisocyanates (hexamethylene-diisocyanate, HMDI, lysine-diisocyanate, LDI and isophorone-diisocyanate, IPDI) were modeled in ChemBioDraw, while molecular structures of the three active agents (Lincomycin, Ampicillin and Cefazolin) were imported from PubChem database. Virtual tools as HyperChem 8.0, Open Babel 2.4.0 and PyRx 0.9 were used to calculate structural parameters, to convert files and to analyze the binding affinity.

No significant difference was found between the logP, refractivity and polarizability values of the macromolecular nanostructures. The results of the binding affinity indicate a very good compatibility between LDI-based polyurethane and Ampicillin and between HMDI-based polyurethane and Cefazolin. Other studies are needed to investigate the in vitro and in vivo utility of these results.

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30. Computational evaluation of structural parameters of a polyurethane carrier used in the transmembrane transfer of bevacizumab

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Prematurity retinopathy (PR) is known as a proliferative vascular disease of the retina that occurs through altered vasculogenesis and who has a multitude of factors as its source. The disease affects low birth weight preterm infants. There is growing support for highlighting the role of genetic factors in the development of PR, a serious visual morbidity that results from premature birth. The incidence PR is inversely proportional to gestational age and birth weight. The disease may have mild forms or may progress to retinal detachment and eventually lead to blindness [1, 2].

Bevacizumab is the active agent of Avastin, a drug that works by blocking a substance called vascular endothelial growth factor (VEGF). By blocking or inhibiting VEGF, it helps inhibit the growth of the blood vessels that cancer needs to grow. DK Wallace et al [3] have reported an investigation of Bevacizumab used in 61 premature infants with type 1 PR; they have obtained very good results after low-dose bevacizumab treatment for PR.

The aim of this research was to investigate different parameters that affect the encapsulation of bevacizumab inside polyurethanes nanoparticles, using modern computational techniques.

Polyurethane particles were 2D modeled in ChemBioDraw Ultra 14 Suite and they were converted using Open Babel 2.4.0; HyperChem 8.0 and PyRx 0.9 with AutoDock Vina were used to calculate structural parameters and to analyze the encapsulation efficacy as binding affinity. Root-mean-square deviation (RMSD) of atomic positions as RMSD/ub (upper bound) and RMSD/lb (lower bound) were also calculated.

It was found that macromolecular chains based on aliphatic diisocyanates and etheric polyols such as polyethylene-glycol with average mol wt between 200 and 2,000 are much more suitable for bevacizumab encapsulation than polyurethane chains based on aromatic compounds and esters such as polycaprolactone. A comparative investigation between these computational results and the physical and chemical properties of synthesized products are necessary to continue this research.

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31. **In silico evaluation of cross-linking and chain-extending agents in polyurethane drug delivery systems**

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In the field of polyurethanes (PU), new trends are being brought by the medical sector, where more and more researchers are looking for suitable solutions for various prostheses, permeable membranes, medical instruments, and fixing enzymes. The aerospace industry requires a suitable shuttle shell to withstand the conditions of movement in outer space. Even studies on the stabilization of finished polyurethane products, somewhat already established, or those for finding new types of adhesives, protective solutions (PU coatings) are among the current concerns [1].

The synthesis of PU macromolecular chains is based on a polyaddition reaction between two main components: (i) a hydroxilic mixture of polyesters and/or polyethers and diols, diamines with low molecular weight used as chain extenders and (ii) an organic component based on a diisocyanate. Many other auxiliary reagents as solvents (water and acetone), catalysts (tertiary amines and heavy metal complexes), cross-linkers (compounds with functionality $f \geq 3$ as trimethylol-propane) are also used in PU synthesis [2, 3].

In this study, we aim to evaluate the influence of cross-linking and chain extending agents on the encapsulation efficacy, using modern computational techniques.

There were modelled the following PU macromolecular chains: PU_1 (linear structure based on isophorone diisocyanate, IPDI, and polyethylene glycol, PEG, without any cross-linking and chain extending agent), PU_2 (linear structure based on IPDI and PEG with 1,4-butanediol as chain extender) and PU_3 (branched structure based on IPDI and PEG with triethanolamine as cross linker); bevacizumab was used as the entrapped active agent. The structural parameters were calculated in HyperChem after molecules' optimization and the binding affinity and the root-mean-square deviation (RMSD) of atomic positions were evaluated in PyRx with AutoDock Vina.

The best value of the binding affinity was found in the case of PU_1 structure, while the best values of RMSD were discovered in the case of bevacizumab entrapped inside the PU_2 structure. A comparative investigation between these computational results and the physical and chemical properties of synthesized products are necessary to continue this research.

In silico methods are widely used due to their good prediction and reduced resources (time and money). Molecular docking is a computational method that predict the preferred orientation of an active molecule to a transporter molecule; knowing the preferred orientations as well as other parameters that influence the association of these molecules is very important and relatively easy to evaluate nowadays.

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32. Classical medicines, natural plants and synergistic actions for the benefit of human health

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Natural plants are inexhaustible resources of compounds with significant biological activity that can also exert various synergistic effects. These effects involve the concomitant action of different molecules in order to obtain a significantly greater potentiated effect compared to the separate effects of the molecules. At the same time, the aspects related to advantageous costs can be mentioned, taking into account the natural production of bioactive compounds. Several synergistic effects are mentioned in the literature that occur at the interaction between medicinal plants and classical drugs or medicinal plants and other biochemical compounds. Identifying these types of actions and exploiting them is of major importance because they represent a beneficial alternative to conventional treatments that generate toxic side effects and are identified in various pathologies. Treating tumor diseases is one of the biggest challenges and the beneficial synergistic interactions of natural bioactive compound-drug, plant-drug or plant-drug derivative must be carefully investigated to achieve the best effects, in order to increase life expectancy and avoid side effects, pronounced which is most often manifested after chemotherapy treatment. Some of the compounds that have attracted attention are salicylates, known as plant hormones that play various pharmacological roles (anti-inflammatory, antidiabetic, neuroprotective, etc.) most likely due to their defense function against habitual stress and pathogens in plants. Aspirin is the best-known salicylate derivative which despite its frequent use in recent decades still captures attention in terms of new and new beneficial biological effects. Along these lines, a number of other salicylate derivatives are currently being investigated for their beneficial biological effects in various diseases. Among them can be mentioned mesasalazine, amorfrutin, ginkgolic acid, cannabinolic acid, grifolic acid.

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33. Formulations based on natural compounds with increased efficacy and safety in skin pathologies

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Skin pathologies are among the most common pathologies encountered globally, representing up to 22% of the problems facing humanity and ranking fourth in the top of the most common diseases. In addition to the impact exerted by these diseases on the well-being of the individual, globally, skin pathologies have a major influence on socio-economic status [1]. To date, over 3,000 skin pathologies are known to vary in severity and symptoms, from simple benign manifestations on the skin to chronic inflammatory diseases and malignant neoplasms associated with high mortality [2].

In the literature, the main causes of skin pathologies are summarized as: i) skin aging which is a physiological process capable of inducing multiple skin health problems such as dermatosis and skin cancer; ii) oxidative stress that causes alterations in the functioning of epidermal cells, materialized by various manifestations in the skin, including cancer and iii) ultraviolet (UV) radiation considered one of the main causes of severe skin diseases.

Given the major implications of skin pathologies, both in terms of global health and in terms of socio-economic status, recent studies have focused on finding new, more effective and lower-cost therapeutic alternatives for the treatment of these conditions. Particular attention was paid to the plant kingdom, which is an infinite source of active substances, with a toxicological profile suitable for clinical use.

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34. Pharmacotoxicological evaluation of the antitumor effect of *Helleborus purpurascens*

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Although oncological research and technology is constantly evolving, the neoplastic process is not yet fully understood and antitumor therapy is not fully effective. Conventional therapy includes chemotherapy, radiation therapy and surgery, and its main disadvantage is the non-selective mode of action and the occurrence of toxic reactions at the systemic level [1]. Recent research in the field of natural compounds has turned its attention to *Helleborus* species [2]. They have been used since ancient times in the traditional therapy of various psychiatric and cardiovascular pathologies. One of these species, the species of *Helleborus purpurascens*, which grows spontaneously in the Romanian flora, has a content rich in phytoconstituents [3]. To determine the antitumor potential of a hydroalcoholic extract of *H. purpurascens*, four tumor cell lines were selected: squamous carcinoma - A431, murine melanoma - B16A5, and breast cancer - MCF-7 and MDA-MB-231 and two cell lines healthy: human keratinocyte cell lines - HaCaT and murine epidermal cells - JB6 at which five concentrations of extract were tested (50, 100, 250, 500 and 1000 µg/mL). In addition, in order to provide a more complex picture of the antitumor effect, the composition of polyphenols and the potential antioxidant effect were determined. The obtained results showed that the hydroalcoholic extract possesses a concentration-dependent cytotoxic activity, the most affected cell line being that of breast cancer - MCF-7. Furthermore, the hydroalcoholic extract has a high content of polyphenols, especially Epicatechin, Rosmarinic acid, Quercetin and Kaempferol. Polyphenols are known in the literature for their antioxidant activity, which is why *H. purpurascens* extract in a concentration of 100 µg/mL showed an antioxidant activity of approximately 78% compared to ascorbic acid with an antioxidant activity of 100%. These results open a new path in the research of natural compounds in antitumor therapy, *H. purpurascens* being a suitable candidate for alternative antineoplastic therapy.

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