

Bioavailability of ursolic/oleanolic acid, with therapeutic potential in chronic diseases and cancer

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Abstract

This study focused on describing the bioavailability of ursolic/oleanolic acids (UA/OA) and the methods to increase it, so that these 2 bioactive compounds can have therapeutic and preventive effects in chronic diseases and cancer. Ursolic/oleanolic acids are natural compounds that have been known since the 19th century. They are very widespread and offer special benefits for human health – especially that their high absorbability makes them suitable for use in therapeutic and preventive treatment. One of the important aspects of their bioavailability is related to their interaction with other bioactive compounds or drugs. In chronic diseases and cancer, UA/OA may affect the absorption of other nutrients and interact with bioactive compounds. By increasing the bioavailability of UA/OA with various technical processes, especially using nanocarriers and nanoparticles, these compounds can affect collagen production, contributing to maintaining skin elasticity and preventing the appearance of wrinkles. Today, UA/OA are frequently used to treat many conditions, ranging from chronic to metabolic.

Key words: cancer, chronic diseases, bioavailability, ursolic acid, oleanolic acid

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Introduction

Bioavailability is defined as the percentage (fraction) of an orally administered, unchanged dose of a drug that has reached the bloodstream (systemic circulation) or, more simply: bioavailability, is the fraction of an orally administered drug that reaches the systemic circulation.

Wagner¹ defined bioavailability as a drug-specific, orally administered parameter that defines both the amount of active substance released from the drug and absorbed into the bloodstream (systemic circulation) and the rate at which the active substance is released and absorbed.

The World Health Organization (WHO) defines bioavailability as the amount of absorbable (potential) active substance, while the U.S. Food and Drug Administration (FDA)^{2,3} as the amount of active substance that is released, absorbed and reaches the internal organ, the site of action, and manifests its therapeutic effect. The American Pharmaceutical Association (APA)⁴ describes bioavailability as the amount of active substance absorbed unchanged. Therefore, bioavailability is seen as both the amount of active substance released and absorbed, and the rate at which the active substance is released and absorbed, getting to the site of action, thus manifesting its therapeutic effect. This parameter is a key step in ensuring the biological efficacy of bioactive food compounds or oral medicines. Food bioactive compounds, whether from plant or animal sources, must be bioavailable to exert beneficial effects on human health.

Numerous plant compounds provide multiple benefits for human health, among which ursolic/oleanolic acids (UA/OA) play an important role. One of the essential aspects of UA/OA is their bioavailability, i.e., the ability to be efficiently absorbed, used and eliminated by the body. Despite its pentacyclic structure, the UA/OA molecule can be embedded in lipid nanoparticles to ensure its transport and digestion in the small intestine, metabolism in the liver, entry into the systemic circuit, and interaction with other substances.

Ursolic and oleanolic acids are primarily absorbed in the small intestine and can subsequently circulate throughout the body, reaching all tissues and organs. This

is due to the entry of these compounds into the systemic and enterohepatic circulation. The enterohepatic communication pathway is essential for the UA/OA to reach different organs, and exert beneficial effects in various diseases. Low oral bioavailability, demonstrated in some clinical studies, is a major reason why new drugs researched and proposed for approval fail to reach the market.

In this article, we reviewed the practical ways of incorporating UA/OA into inorganic/organic structures and nanoparticles to increase their absorption (bioavailability). Natural plant compounds are an important source of raw materials for obtaining drugs and food supplements with antitumor effect, with a selective mechanism of action and minimal side effects. Ursolic acid and its isomer, OA, are 2 natural compounds with multiple health benefits. The chemical structure of UA/OA is pentacyclic triterpene, with the following formula: $C_{30}H_{48}O_3$ (Fig. 1).⁵

Plants rich in UA

Ursolic acid is found in the peel of many fruits, especially apples, but also in herbs such as rosemary, lavender, thyme, sage, marigolds, etc. Oleanolic acid is found in large quantities in rosemary, lavender, sage, and olive. Table 1^{6–10} shows that:

- The best represented plant family in terms of the UA/OA presence is Lamiaceae-Labiatae (66%);
- The highest amounts of UA are found in marigold flowers, rosemary, sage, and lavender (aerial parts);
- The highest amounts of OA are found in olives (leaves and fruits) and *Silphium trifoliatum* leaves (rich in UA and OA; Fig. 2).¹¹

Discussion

The presence of UA/OA in fruits and plants offers the potential for a wide range of therapeutic effects due to a unique quality of these compounds, namely their bioavailability. This parameter of UA/OA has a significant impact on the use of this compounds in therapeutic and preventive purposes.

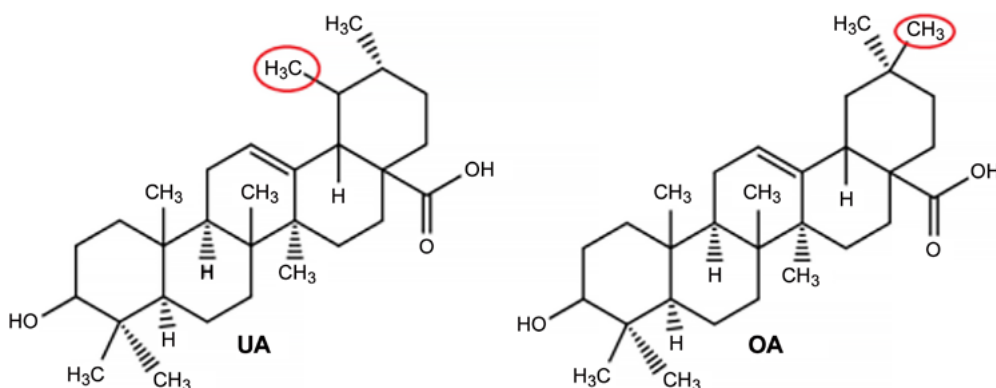


Fig. 1. Chemical structure of ursolic/oleanolic acid, isomers differentiated by the position of the methyl group⁵

Table 1. Natural sources for UA and OA [mg/g dw]¹

Plan species	Family	Plant part	OA [mg/g dw]	UA [mg/g dw]	Reference
Marigold, <i>calendula officinalis</i>	Compositae	flowers	–	20.5	⁶
Whorled Rosinweeds, <i>Silphium trifoliatum</i>	Asteraceae	leaves	22.0	15.5	⁶
Lavender, <i>lavandula angustifolia</i>	Lamiaceae, Labiatae	aerial parts	4.5	15.9	⁷
Lemon balm, <i>mellisa officinalis</i>	Lamiaceae, Labiatae	aerial parts	1.6	6.7	⁷
Basil, <i>ocimum basilicum</i>	Lamiaceae, Labiatae	aerial parts	–	3.0	⁷
Marjoram, <i>origanum majorana</i>	Lamiaceae, Labiatae	aerial parts	1.9	6.6	⁷
Oregano, <i>origanum vulgare</i>	Lamiaceae, Labiatae	aerial parts	–	2.8	⁷
Sage, <i>salvia officinalis</i>	Lamiaceae, Labiatae	aerial parts	6.7	18	⁷
Thyme, <i>thymus vulgaris</i>	Lamiaceae, Labiatae	aerial parts	3.7	9.4	⁷
Mountain savory, winter savory, <i>satureja montana</i>	Lamiaceae, Labiatae	aerial parts	1.4	4.9	⁷
Black elderberry, <i>sambucus nigra</i>	Adoxaceae	leaves bark	1.2 0.8	5.8 3.2	⁷
Olive, <i>olea europaea</i>	Oleaceae	leaves fruits bark	31.0 21.0 9.8	3.8	⁷
Apple, <i>malus domestica</i>	Rosaceae	the peel of the fruit	–	9.4	⁸
Deulkkae, Korean perilla, japanese basil, <i>Perilla frutescens</i>	Lamiaceae, Labiatae	aerial parts	2.33	3.59	⁹
Rosemary, <i>rosmarinus officinalis</i>	Lamiaceae, Labiatae	aerial parts	7.98	16.06	¹⁰

UA – ursolic acid; OA – oleanolic acid; DW – dry weight.

**Fig. 2.** *Silphium trifoliatum* (whorled rosinweed)⁷

Oral bioavailability (F%) is the fraction of a medicine that reaches the systemic circulation.⁸ Bioavailability of orally administered drugs is one of the most important properties in drug design and development. High oral bioavailability consistently reduces the amount of drug administered to achieve the desired pharmacologic effect, and

poor oral bioavailability can result in decreased efficacy and unpredictable response to drug administration.^{12,13}

In the context of dietary supplements, herbs and other nutrients, where the route of administration is typically oral, bioavailability refers to the amount or percentage of the ingested dose that is absorbed.¹⁴ A significant amount of the active ingredient is broken down during digestion when herbal supplements are taken orally. The acidic environment in the stomach, digestive enzymes and gut microbes break down nutrients. As a result, only a small fraction of the ingested nutrients become available for absorption and used by cells.¹⁵

Bioavailability studies have shown that UA/OA are absorbed primarily in the small intestine. Once in the systemic circuit, these biocompounds can circulate and reach various tissues of the human body, including the liver, skin and muscles. The highly bioavailable form in which UA/OA is administered must be the form that makes them easy for the body to use. The molecular details of how UA/OA are absorbed in the body can be clarified by conducting several studies regarding their oral administration. A practical possibility would be the absorption of UA/OA directly from the ethanolic extract on natural carbonic adsorbents (herbal medicinal charcoal) or their adsorption into the molecular lattice of natural biopolymers (such as lignans in flaxseed meal) using the molecular imprinting method.^{16–18} Natural polymers have a much higher adsorption capacity and specificity in ethanol than in water at pH 7.0. Another practical way to increase the bioavailability of UA/OA

is to incorporate them into a nanocarrier lipid fraction (liposomes), which facilitates the transport and digestion of these compounds in the small intestine and their metabolism in the liver, since digestion in the stomach degrades these compounds due to the acidic environment of the stomach, digestive enzymes and intestinal microbes. In this case, only a part of the total compounds that we ingest becomes available for their metabolism in the intestine and the liver, and thus for absorption and use at the cellular level. Liposomes make the UA/OA easy to use by the organism. Another practical way is to get some UA/OA inclusion complexes with hydrophilic semisynthetic cyclodextrins, which represent a possibility to increase the aqueous solubility and to optimize the pharmacokinetic properties of the guest molecule.¹⁹ Another theoretical and practical possibility is the derivatization of UA/OA by a condensation reaction (at the COOH group, C₂₈) with a primary amino group present in the structure of 3-R-4-amino-mercapto-1,2,4-triazoles and the use of gold nanoparticles as transporters, for the compounds thus produced.²⁰ Finally, triazole derivatives of triterpenic acids (UA/OA) bioconjugated with gold particles are obtained, with a cytotoxic effect on malignant melanoma cell lines. Another practical possibility by which a maximum bioactivity of UA/OA can be obtained, with the minimum amount of triterpenes used, is the use of inorganic nanostructures (complex nanostructures, composites, silicon oxide, titanium oxide, etc.) for the incorporation (adsorption) of UA/OA. The inorganic nanostructures have a large surface area, inhibit bacterial growth, are stable, have low toxicity, and are capable of activating many molecules.^{21–24} As indicated above,²⁰ in addition to bioavailability, research has also focused on how UA/OA act in the body. In this regard, studies have found that UA/OA have anti-inflammatory, antioxidant and anti-cancer properties. They can help lower blood cholesterol and fat levels by influencing lipid metabolism. These multiple effects make UA/OA potential allies in the prevention and treatment of cancer, cardiovascular disease and chronic inflammation, in cosmetic applications (these compounds can influence collagen production, helping maintain skin elasticity and prevent the appearance of wrinkles), and sometimes as ingredients in the food industry.^{25–29} The bioavailability of UA/OA is a crucial aspect in understanding and exploiting their benefits and their ability to be efficiently absorbed, circulate in the body and interact with other substances. This demonstrates remarkable potential for improving human health. Laboratory studies have shown that UA/OA may inhibit the growth of cancer cells in several types of cancer, including stomach, colon, pancreatic, and liver cancer.^{30,31} Ursolic/oleanolic acids inhibit the viability and proliferation of cancer cells, prevent their migration and metastasis, and induce their apoptosis. Both in vitro and in vivo studies indicate that UA/OA are promising anti-cancer agents that may prevent

carcinogenesis at every step. Furthermore, cancers at all stages are susceptible to the UA/OA activity. The anti-tumorigenic effect of UA/OA on gastric, colon, pancreatic, and liver cancers, as well as the mechanisms underlying this process, have already been presented.³⁰ Furthermore, other authors have showed the antitumor effects of UA/OA in vitro with gastric cancer cell line BGC-823.³¹

Ursolic/oleanolic acids induce apoptosis, inhibit cancer cell proliferation and prevent tumor growth and metastasis. Nanoformulations with UA/OA and their bioavailability have a very good inhibitory effect preventing tumor growth and metastasis.³² Zou et al.³² reviewed the great potential of UA as a drug candidate in the field of cancer therapy in terms of suppressing tumor initiation, progression and metastasis.

Due to their cytotoxicity against cancer cell cultures, the group of triterpenoid derivatives of UA/OA is considered a promising anticancer drug. In addition, due to their various pharmacological activities, including antiangiogenic, anti-inflammatory and antioxidant effect and their ability to improve cell differentiation, they are more than just an anticancer drug. The group of triterpenoid derivatives of UA/OA is indicated and suitable for future modern anticancer strategies. Furthermore, they are considered essential parts of human nutrition due to their chemopreventive potential to combat the development of cancer.³³ Ursolic acid is a promising biomolecule with anti-inflammatory and analgesic activity, in applications with anti-arthritis potential, as presented in the study by Ahmad et al.³⁴ In this study, formulations and evaluations of nanostructured lipid carriers with *Ocimum sanctum* L. (holy basil) were described, for a transdermal application, improved in UA, in anti-arthritis treatment.

The *Ocimum sanctum* leaf extract was prepared by the extraction method with supercritical CO₂. Various surfactants (Tween 80), solid lipids (glyceryl monostearate) and liquid lipids (Capryol-90) have been used to prepare nanostructures loaded with *Ocimum sanctum* (Fig. 3; visual representation of the technological flow).^{35,36} The resulting nanoparticles facilitate the transport of *Ocimum sanctum* through tissues via passive or active targeting. Passive targeting involves diffusion into transdermal tissue, while active targeting involves conjugation of ligands (mannitol) to nanoparticles for greater specificity and absorption at the site of inflammation. The results demonstrated the efficiency of treatment with lipid nanostructures compared to the standard formulation with diclofenac topical gel, in antiarthritic applications.

Conclusions

The bioavailability of UA/OA can be shaped by their interactions with other substances or bioactive compounds, such as certain receptors or proteins in the body, which can modify or amplify the effects of UA/OA. For instance,

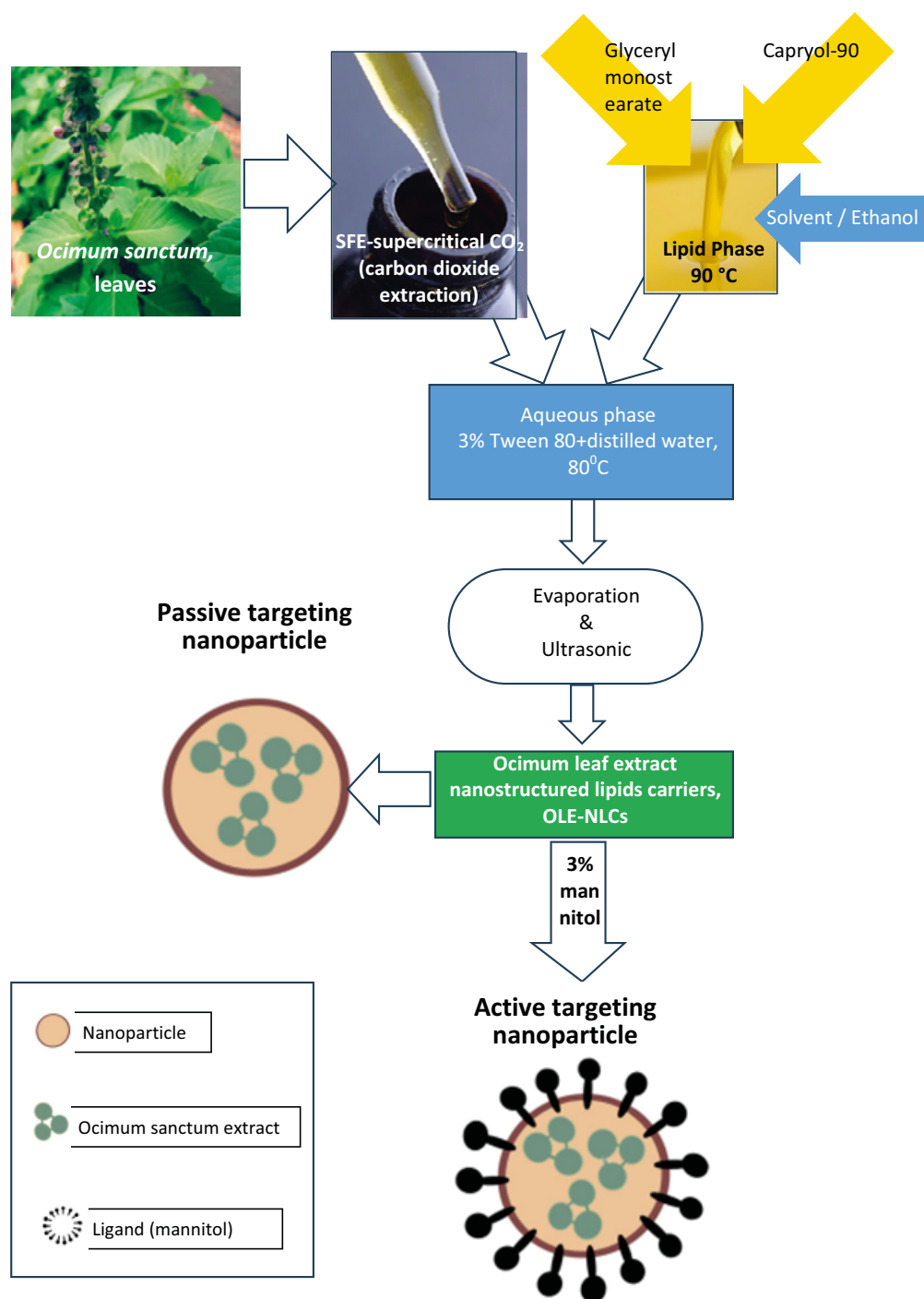


Fig. 3. Obtaining lipid nanostructures loaded with *Ocimum sanctum* leaf extract^{35,36}

interactions with plant flavones can create synergies that enhance human health benefits by increasing the antioxidant, anti-inflammatory and anticancer activity of these plant compounds. The availability of these acids in the body creates promising perspectives in the fields of human health. It is essential to continue research to fully understand their potential and to develop practical applications in medicine. Establishing the optimal dosage of UA/OA is essential for their use in long-term treatment programs. Additional studies may provide guidance on appropriate dosing and can evaluate side effects and potential interactions of UA/OA with other substances and metabolites.

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References

1. Wagner JG. *Biopharmaceutics and Relevant Pharmacokinetics*. Washington, D.C, USA: Drug Intelligence Publications; 1971. ISBN:978-0-914768-18-0.
2. U.S. Food and Drug Administration (FDA). Guidance for Industry: Immediate Release Solid Oral Dosage Forms, Scale-Up and Post-Approval Changes: Chemistry, Manufacturing and Controls, In Vitro Dissolution Testing and in Vivo Bioequivalence Documentation. Rockville, USA: U.S. Food and Drug Administration (FDA); 1995. <https://www.fda.gov/media/70949/download>.

3. U.S. Food and Drug Administration (FDA). Guidance for Industry: Dissolution Testing of Immediate Release Solid Oral Dosage Forms. Rockville, USA: U.S. Food and Drug Administration (FDA); 1997. <https://www.fda.gov/media/70936/download>.
4. United States Pharmacopoeial Convention. *The United States Pharmacopoeia*. 30th ed. Rockville, USA: US Pharmacopoeial Convention Inc. 2007.
5. Gudoityte E, Arandarcikaite O, Mazeikiene I, Bendokas V, Liobikas J. Ursolic and oleanolic acids: Plant metabolites with neuroprotective potential. *Int J Mol Sci*. 2021;22(9):4599. doi:10.3390/ijms22094599
6. Kowalski R. Studies of selected plant raw materials as alternative sources of triterpenes of oleanolic and ursolic acid types. *J Agric Food Chem*. 2007;55(3):656–662. doi:10.1021/jf0625858
7. Jäger S, Trojan H, Kopp T, Laszczyk MN, Scheffler A. Pentacyclic triterpene distribution in various plants: Rich sources for a new group of multi-potent plant extracts. *Molecules*. 2009;14(6):2016–2031. doi:10.3390/molecules14062016
8. Ludeña-Huaman MA, Ramos-Inquiltupa DA. Determination of the content of ursolic and oleanolic acid in the cuticular wax of fruits of different species of Rosaceae. *Rev Colomb Quim*. 2019;48(2):15–20. doi:10.15446/rev.colomb.quim.v48n2.77046
9. Staicu V. Separation and purification of plant extracts by removal of chlorophyll, xanthophylls and pigments using mineral adsorbents in liquid chromatography (CLS). *Curr Trends Eng Sci*. 2023;3(6):1046. doi:10.54026/CTES/1046
10. Staicu V. Extracte vegetale si valorificarea lor. Obținerea compusilor bioactivi din deseuri vegetale si plante medicinale cu ajutorul ultrasunetelor si microundelor, Facultatea de inginerie chimica si biotehnologii [doctoral thesis]. Bucharest, Romania: National University of Science and Technology; 2023.
11. Kowalska G, Baj T, Kowalski R, Hanif MA. Characteristics of selected *Silphium* species as alternative plants for cultivation and industry with particular emphasis on research conducted in Poland: A review. *Sustainability*. 2022;14(9):5092. doi:10.3390/su14095092
12. Hinderliter P, Saghir SA. Pharmacokinetics. In: Wexler P, ed. *Encyclopedia of Toxicology*. 3rd ed. London, UK: Academic Press; 2014:352. ISBN:978-0-12-386455-0.
13. Pării S, Nicolae E, Ungureanu A, Pării E, Valica V. Current aspects in the bioavailability of drugs [in Romanian]. *Revista Farmaceutica a Moldovei*. 2016;1–4:[no pages given].
14. Duan JZ. Pharmacokinetics of oral absorption. In: Shargel L, Yu ABC, eds. *Applied Biopharmaceutics and Pharmacokinetics*. 7th ed. New York, USA: McGraw-Hill Education; 2016:177–204. ISBN:978-0-07-182964-9.
15. Lee MK. Liposomes for enhanced bioavailability of water-insoluble drugs: In vivo evidence and recent approaches. *Pharmaceutics*. 2020;12(3):264. doi:10.3390/pharmaceutics12030264
16. Martín-Esteban A. Molecularly imprinted polymers: New molecular recognition materials for selective solid-phase extraction of organic compounds. *Fresenius J Anal Chem*. 2001;370(7):795–802. doi:10.1007/s002160100854
17. Sánchez-Barragán I, Costa-Fernández JM, Pereiro R, et al. Molecularly imprinted polymers based on iodinated monomers for selective room-temperature phosphorescence optosensing of fluoranthene in water. *Anal Chem*. 2005;77(21):7005–7011. doi:10.1021/ac050400a
18. Kim SH, Jun CD, Suk K, et al. Gallic acid inhibits histamine release and pro-inflammatory cytokine production in mast cells. *Toxicol Sci*. 2006;91(1):123–131. doi:10.1093/toxsci/kfj063
19. Soica C, Oprean C, Borcan F, et al. The synergistic biologic activity of oleanolic and ursolic acids in complex with hydroxypropyl- γ -cyclodextrin. *Molecules*. 2014;19(4):4924–4940. doi:10.3390/molecules19044924
20. Mioc M, Soica C. HeteroTerA: Proiect: Sinteza si evaluarea de noi bioconjugati de nanoparticule de aur-triazol-triterpene, utilizate ca agenti activi in melanomul malign. Contract PD, 2020. Proiect PN III-P1-1.1-PD-2019-1078. Timișoara, Romania: Victor Babeș University of Medicine and Pharmacy; 2020. http://old.umft.ro.heterotera_931. Accessed August 15, 2024.
21. Petrișor G, Motelica L, Trușcă RD, et al. The antimicrobial potency of mesoporous silica nanoparticles loaded with *Melissa officinalis* extract. *Pharmaceutics*. 2024;16(4):525. doi:10.3390/pharmaceutics16040525
22. Low SS, Lim CN, Yew M, et al. Recent ultrasound advancements for the manipulation of nanobiomaterials and nanoformulations for drug delivery. *Ultrason Sonochem*. 2021;80:105805. doi:10.1016/j.ultrasonch.2021.105805
23. Low SS, Yew M, Lim CN, et al. Sonoproduction of nanobiomaterials: A critical review. *Ultrason Sonochem*. 2022;82:105887. doi:10.1016/j.ultrasonch.2021.105887
24. Ealia AM, Saravanakumar MP. A review on the classification, characterisation, synthesis of nanoparticles and their application. *IOP Conf Ser Mater Sci Eng*. 2017;263:032019. doi:10.1088/1757-899X/263/3/032019
25. Stielow M, Witczyńska A, Kubryń N, Fijałkowski Ł, Nowaczyk J, Nowaczyk A. The bioavailability of drugs: The current state of knowledge. *Molecules*. 2023;28(24):8038. doi:10.3390/molecules28248038
26. Maisto M, Piccolo V, Novellino E, et al. Optimization of ursolic acid extraction in oil from Annurca apple to obtain oleolytes with potential cosmeceutical application. *Antioxidants (Basel)*. 2023;12(2):224. doi:10.3390/antiox12020224
27. Rein MJ, Renouf M, Cruz-Hernandez C, Actis-Goretta L, Thakkar SK, Da Silva Pinto M. Bioavailability of bioactive food compounds: A challenging journey to bioefficacy. *Br J Clin Pharmacol*. 2013;75(3):588–602. doi:10.1111/j.1365-2125.2012.04425.x
28. Wang L, Yin Q, Liu C, Tang Y, Sun C, Zhuang J. Nanoformulations of ursolic acid: A modern natural anticancer molecule. *Front Pharmacol*. 2021;12:706121. doi:10.3389/fphar.2021.706121
29. Ayeleso T, Matumba M, Mukwevho E. Oleanolic acid and its derivatives: Biological activities and therapeutic potential in chronic diseases. *Molecules*. 2017;22(11):1915. doi:10.3390/molecules22111915
30. Pięć M, Paduch R. Ursolic and oleanolic acids as potential anticancer agents acting in the gastrointestinal tract. *Mini Rev Org Chem*. 2018;16(1):78–91. doi:10.2174/1570193X15666180612090816
31. Xiao S, Wang W, Liu Y. Research progress on extraction and separation of active components from loquat leaves. *Separations*. 2023;10(2):126. doi:10.3390/separations10020126
32. Zou J, Lin J, Li C, et al. Ursolic acid in cancer treatment and metastatic chemoprevention: From synthesized derivatives to nanoformulations in preclinical studies. *Curr Cancer Drug Targets*. 2019;19(4):245–256. doi:10.2174/1568009618666181016145940
33. Laszczyk M. Pentacyclic triterpenes of the lupane, oleanane and ursane group as tools in cancer therapy. *Planta Med*. 2009;75(15):1549–1560. doi:10.1055/s-0029-1186102
34. Ahmad A, Abuzinadah MF, Alkreathy HM, Banaganapalli B, Mujeeb M. Ursolic acid rich *Ocimum sanctum* L leaf extract loaded nanostructured lipid carriers ameliorate adjuvant induced arthritis in rats by inhibition of COX-1, COX-2, TNF- α and IL-1: Pharmacological and docking studies. *PLoS One*. 2018;13(3):e0193451. doi:10.1371/journal.pone.0193451
35. Almatroodi SA, Alsahli MA, Almatroodi A, Rahmani AH. *Ocimum sanctum*: Role in diseases management through modulating various biological activity. *Pharmacogn J*. 2020;12(5):1198–1205. doi:10.5530/pj.2020.12.168
36. Chen Q, Tan Qian Lin K, Yow Li-Wen NS, Heng S, Hui C, Chon Mun Ping A. Nanotechnology: A better diagnosis and treatment strategy for brain tumour? *J Young Invest*. 2024;25(3):33–47. <https://www.jyi.org/2022-march/2022/3/1/nanotechnology-a-better-diagnosis-and-treatment-strategy-for-brain-tumour>. Accessed August 15, 2024.