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FROM WASTE TO HEALTH: AN INTEGRATIVE BIOINFORMATICS APPROACH TO THE THERAPEUTIC POTENTIAL OF BURGUND GRAPE POMACE EXTRACTS OBTAINED BY MICROWAVE-ASSISTED EXTRACTION

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Abstract
This study explores a sustainable strategy for recovering and assessing the bioactivity of resveratrol from Burgund grape pomace. Wet and dried pomace were milled and subjected to microwave-assisted extraction (MAE) with 99.9% ethanol (1:10 w/v, 20 min). Wet pomace yielded a slightly higher total polyphenol content (6.25 mg GAE/g) than dried samples (6.13 mg GAE/g). UHPLC analysis confirmed resveratrol levels of 0.047–0.055 µg/mL in wet pomace, exceeding those in dried samples. Antioxidant activity (DPPH assay) correlated strongly with polyphenol content. In silico profiling indicated compliance with Lipinski's and Veber's rules, high intestinal absorption (~91%), moderate permeability, CYP3A4-mediated metabolism, and a favorable safety profile. These findings demonstrate the efficiency of MAE and underline the therapeutic potential of resveratrol, supporting grape pomace as a reproducible, ethical, and eco-responsible resource.

Keywords: bioactivity, bioinformatics approach, Burgund grape pomace, resveratrol.

1. INTRODUCTION

In recent years, there has been increasing interest in natural compounds with applications in the pharmaceutical, food, and agricultural sectors (Sasidharan et al., 2011). Plants and algae are recognized as major sources of bioactive substances. Plant extracts and isolated secondary metabolites are increasingly investigated for their potential to improve healthcare outcomes while reducing adverse effects and complications associated with synthetic treatments.

Additionally, growing attention is being given to the valorization of plant wastes and by-products, which often contain substantial amounts of secondary metabolites. Studies show that, in many cases, the polyphenol content in these wastes is at least twice that found in the edible pulp of fruits

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or vegetables (Diamanti et al., 2017; Fernandez et al., 2018; Doria et al., 2021). Polyphenols, as plant secondary bioactive metabolites, exhibit versatile properties, including long-term cardiovascular protection, chemoprotective effects, antioxidant activity, and anti-inflammatory potential (Tangney and Rasmussen, 2013; Cheng et al., 2017; Siracusa et al., 2017; Srinivasan et al., 2018).

Grape pomace, the solid residue from winemaking, has gained considerable attention due to its high content of bioactive compounds (Abreu et al., 2024). Among these, resveratrol, a polyphenolic stilbene with antioxidant, anti-inflammatory, and cardioprotective properties, is notable for its experimentally demonstrated pharmacological effects (Baur and Sinclair, 2006; Salehi et al., 2018).

Conventional polyphenol extraction methods from grape pomace are often limited by low yields and thermal degradation of sensitive compounds. Microwave-assisted extraction (MAE) has emerged as an efficient and eco-friendly alternative, capable of maximizing polyphenol recovery, including resveratrol, while maintaining molecular bioactivity (Wang, 2012; Accomasso et al., 2024).

Building on these considerations, the present study adopts a stepwise approach to a phytotherapeutic strategy focused on the valorization of Burgund grape pomace, emphasizing resveratrol extraction and the assessment of its therapeutic potential. The novelty of the study lies in the integration and synergy of advanced experimental methods with computational pharmacology and bioinformatics tools, within a framework that promotes the principles of the circular economy.

2. MATERIALS AND METHODS

Reagents and chemicals

The 99,9% ethyl alcohol, 2,2-diphenyl-1-picrylhydrazyl (DPPH), Folin-Ciocalteu reagent, distilled water, Na_2CO_3 powder, gallic acid, were purchased from AMEX Healthcare GmbH.

Primary Processing of Plant Material

The plant material, represented by Burgund grape pomace, was obtained from INCDBH Ștefănești – Argeș. A portion of this by-product was used in its native, high-moisture form for the extraction procedure, while the remainder underwent a primary preprocessing step. This included drying the pomace in an oven at 40°C to prevent degradation of the bioactive compounds of interest, followed by storage in paper bags, protected from moisture and sunlight exposure. The secondary step involved milling the plant material, both in its wet and dried forms, using a laboratory mill under the following parameters: pulse milling for 5 minutes at 3000 revolutions per minute (RPM) and continuous milling for 60 seconds at 10,000 RPM.

Obtaining Plant Extracts by Microwave-Assisted Extraction (MAE)

For the microwave-assisted extraction of secondary metabolites, particularly resveratrol, ethyl alcohol (99.9% purity) was used as the solvent, with a plant-to-solvent ratio of 1:10. The mixtures of solvent and powder were irradiated for 20 minutes at powers of 110 W and 220 W, respectively. Microwave-assisted extraction was performed using the NEOS-GR equipment (Milestone).

The resulting experimental variants (Table 1) were then centrifuged twice (total time 10 minutes) at 6000 RPM. The supernatants were subsequently filtered under vacuum through Pall Flex Membrane Filters (QRY:100; MM: 47) using a Rocker filtration system (model VF6). Until analysis of total polyphenol content, antioxidant activity, and UHPLC profiling, the samples were stored in glass vials at –18°C in a refrigerated system.

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Table 1. Burgund Grape Pomace Extracts

Sample	Powder Type	Extraction Method	Plant:Solvent Ratio	Extraction Parameters
BMH_0.5	Wet pomace	MAE	1:10	110 W, 20 minutes
BMH_1	Wet pomace	MAE	1:10	220 W, 20 minutes
BMD_0.5	Dried pomace	MAE	1:10	110 W, 20 minutes
BMD_1	Dried pomace	MAE	1:10	220 W, 20 minutes

Characterization of Burgund Grape Pomace Extracts

Quantitative determination of polyphenolic structure compounds in the obtained extracts was carried out by the Folin-Ciocalteu spectrophotometric method (Manolescu et al., 2022). Total polyphenol content (TPC) analysis was performed on the Ocean Optics HR2000+ UV-VIS spectrophotometer at 765 nm wavelength. TPC values, expressed in mg gallic acid equivalent/g plant were obtained according to the formula (Phuyal et al., 2020): TPC= (CMxDF)/1000, Where C is the concentration measured from the calibration curve, M is the dry plant mass and DF is the dilution factor.

UHPLC Analysis of Grape Pomace Extracts for Resveratrol Content

Identification and quantification of resveratrol were performed using a Waters Arc System equipped with a Waters 2998 PDA detector and a Waters QDa mass detector.

Determination of Antioxidant Activity of Extracts by the DPPH Method

The antioxidant capacity of the extracts was assessed through the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. The procedure followed the method described by Shimamura et al. (2014), with minor modifications. The DPPH radical inhibition (%IP) was determined as described by Adebiyi et al. (2017), using the formula $\%IP=\{(A0-A1)/A0\}\times100$, where A_0 is the control absorbance and A_1 is the sample absorbance.

In Silico Evaluation of the Bioactivity and Pharmacokinetic Properties (Druglikeness and ADMETox) of Resveratrol Obtained from Burgund Grape Pomace Extract

To assess whether resveratrol (Figure 1) obtained from grape pomace can be considered a compound with pharmacological potential, Lipinski's Rule of Five was applied, a widely used criterion for evaluating the drug-likeness of candidate molecules. Complementarily, Veber's Rule was also applied to provide additional information on the compound's oral bioavailability. The analysis was based on the SDF structure of resveratrol retrieved from the PubChem database, and molecular property calculations were performed using Molinspiration software.

Subsequently, the pharmacokinetic profile of resveratrol isolated from Burgund grape pomace was evaluated using the pkCSM platform, employing the canonical SMILES representation from PubChem. This analysis enabled detailed predictions of ADMET parameters - absorption, distribution, metabolism, excretion, and toxicity - thus providing an integrative perspective on the molecule's pharmacological potential.

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Figure 1. 3D structure of resveratrol generated in Chem3D Pro 12.0

3. RESULTS AND DISCUSSIONS

For both dried and wet pomace, increasing the plant-to-solvent ratio resulted in higher phenolic content. Higher values (≈6.1–6.2 mg GAE/g plant) were obtained at a ratio of 1 g/10 mL. Comparing samples BMD_0.5 and BMH_0.5 (both at 0.5 g/10 mL), dried pomace showed a slightly higher phenolic content (3.77 vs. 3.54 mg GAE/g plant) (Table 2).

Table 2. Total Polyphenol Content, Antioxidant Activity, and UHPLC Analysis

Sample	TPC (mg GAE/g plant)	Antioxidant Activity (%)	Resveratrol µg/L
BMD 0.5	3.77	15.33	0.034
BMD 1	6.13	28.80	0.034
BMH 0.5	3.54	14.20	0.047
BMH 1	6.26	25.74	0.055

However, comparing samples BMD_1 and BMH_1 (both at 1 g/10 mL), wet pomace exhibited a slightly higher phenolic content (6.25 vs. 6.13 mg GAE/g plant). This suggests that drying can help preserve phenols but may also lead to partial losses due to thermal oxidation if not properly controlled. Wet pomace, despite its water content, retains phenols in their native state, and rapid microwave extraction can be effective before enzymatic degradation occurs.

To validate the results, they were compared with data from the literature. Garrido et al. (2019) investigated microwave-assisted extraction of polyphenols from Chardonnay grape pomace using 48% ethanol, with a solid-to-liquid ratio of approximately 1.77 g/20 mL (≈1:11), obtaining an equivalent content of ~6.8 mg GAE/g plant, similar to the values obtained in the present study despite the difference in solvent concentration.

Chen et al. (2012) analyzed extraction from grape seeds and reported contents up to 13 mg GAE/g dry material using 32% ethanol. This higher result is explained by the different nature of the plant material, as seeds are richer in polyphenols than the rest of the pomace.

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Ma et al. (2014) used microwave-assisted extraction for red grape pomace and obtained values between 5.8 and 6.9 mg GAE/g plant, using a solid-to-liquid ratio of 1:20 and 50% ethanol. These results are comparable to those of the present study, confirming the efficiency of extraction using concentrated ethanol and a 1:10 solid-to-liquid ratio.
Therefore, it can be concluded that the method applied in this study (microwave-assisted extraction, 99% ethanol, 1:10 ratio) is effective for valorizing grape pomace as a source of phenolic compounds, producing results comparable with those reported in the international literature. Additionally, using wet pomace without a prior drying step proves to be a practical and economically efficient approach.
Furthermore, samples with higher TPC also exhibited increased antioxidant activity, confirming the positive correlation between phenolic content and antioxidant capacity.
Quantitative determination of resveratrol in the grape pomace extracts, performed by high-performance liquid chromatography (UHPLC), revealed significant differences depending on the physical state of the raw material and the plant-to-solvent ratio. Extracts from wet pomace (BMH) showed higher resveratrol concentrations (0.047 µg/mL at 0.5 g/10 mL and 0.055 µg/mL at 1 g/10 mL) compared with those from dried pomace (BMD), which remained relatively constant and lower. These results suggest that pre-drying the pomace may lead to partial degradation of the active compound, possibly through oxidation or thermal losses. Increasing the plant material from 0.5 g to 1 g per 10 mL solvent led to a significant increase in resveratrol concentration only in the wet pomace, indicating higher extraction efficiency under this condition.
The *in silico* analysis, presented in Table 3, shows that resveratrol complies with both Lipinski's Rule of Five and Veber's Rule, suggesting high pharmacological potential. The molecule exhibits an optimal balance between lipophilicity and hydrophilicity (miLogP = 2.99), a low polar surface area (TPSA = 60.68 Å²), and a small molecular weight (MW = 228.25 Da), parameters that favor efficient absorption and distribution in the body. The number of hydrogen bond donors and acceptors, along with the low number of rotatable bonds, indicates adequate solubility and structural flexibility for stable interactions with target proteins. The molecular volume and absence of drug-likeness violations confirm compatibility with optimal pharmacokinetic properties, suggesting a promising profile for further preclinical studies.

Table 3. Lipinski's and Veber's Rules for Resveratrol, Polyphenol Extracted from Burgund Grape Pomace

Parameter	Value
miLogP	2.99
TPSA	60.68
natoms	17
MW	228.25
nON	3
nOHNH	3
nviolations	0
nrotb	2
Volume	206.92

The results obtained from the *in silico* predictions (Table 4) highlight that resveratrol exhibits a complex, multi-target pharmacological profile, confirming its pleiotropic nature as described in the literature (Baur and Sinclair, 2006; Berman et al., 2017).

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Table 4. Target Prediction Results for Resveratrol – SwissTarget Prediction

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Monoamine oxidase A	MAOA	P21397	CHEMBL1951	Oxidoreductase	1.0	4 / 6
Carbonic anhydrase II	CA2	P00918	CHEMBL205	Lyase	1.0	51 / 9
Estrogen receptor alpha	ESR1	P03372	CHEMBL206	Nuclear receptor	1.0	272 / 28
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase	1.0	9 / 24
Norepinephrine transporter	SLC6A2	P23975	CHEMBL222	Electrochemical transporter	1.0	2 / 3
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase	1.0	3 / 10
Carbonic anhydrase VII	CA7	P43166	CHEMBL2326	Lyase	1.0	14 / 9
Beta amyloid A4 protein	APP	P05067	CHEMBL2487	Membrane receptor	1.0	7 / 3
Carbonic anhydrase I	CA1	P00915	CHEMBL261	Lyase	1.0	48 / 9
Carbonic anhydrase III	CA3	P07451	CHEMBL2885	Lyase	1.0	3 / 3
Carbonic anhydrase VI	CA6	P23280	CHEMBL3025	Lyase	1.0	5 / 6
PI3-kinase p110-beta subunit	PIK3CB	P42338	CHEMBL3145	Enzyme	1.0	2 / 1
Carbonic anhydrase XII	CA12	O43570	CHEMBL3242	Lyase	1.0	27 / 9
Cytochrome P450 1A2	CYP1A2	P05177	CHEMBL3356	Cytochrome P450	1.0	2 / 4
Cytochrome P450 2C9	CYP2C9	P11712	CHEMBL3397	Cytochrome P450	1.0	2 / 1
Cytochrome P450 3A4	CYP3A4	P08684	CHEMBL340	Cytochrome P450	1.0	2 / 1
Carbonic anhydrase XIV	CA14	Q9ULX7	CHEMBL3510	Lyase	1.0	13 / 9
Carbonic anhydrase IX	CA9	Q16790	CHEMBL3594	Lyase	1.0	34 / 9
Cytochrome P450 2C19	CYP2C19	P33261	CHEMBL3622	Cytochrome P450	1.0	2 / 1
Carbonic anhydrase IV	CA4	P22748	CHEMBL3729	Lyase	1.0	8 / 3
Carbonic anhydrase VIII	CA8	Q8N1Q1	CHEMBL3912	Lyase	1.0	3 / 3
Quinone reductase 2	NQO2	P16083	CHEMBL3959	Enzyme	1.0	1 / 1
Carbonic anhydrase VB	CA5B	Q9Y2D0	CHEMBL3969	Lyase	1.0	5 / 5
PI3-kinase p110-alpha subunit	PIK3CA	P42336	CHEMBL4005	Enzyme	1.0	11 / 1
Carbonic anhydrase alpha	CA5A	P35218	CHEMBL4789	Lyase	1.0	5 / 6

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The molecule showed affinity for enzymes involved in oxidative stress and inflammation, such as MAOA, COX-1/2, and NQO2, suggesting potential neuroprotective, antidepressant, and anti-inflammatory effects, consistent with previously reported experimental observations (Liu et al., 2018).

Resveratrol was also found to interact with multiple isoforms of carbonic anhydrase (CA I–XIV), supporting the hypothesis of potential anticancer activity, in agreement with recent studies indicating the role of CA IX and CA XII inhibition in tumor progression (Supuran, 2011). Interaction with the estrogen receptor α (ESR1) confirms previously described phytoestrogenic activity (Bowers et al., 2000), with implications for breast cancer and osteoporosis. The predicted binding to amyloid precursor protein (APP) suggests a potential role in Alzheimer's disease prevention, consistent with experimental results reported in neurodegenerative models (Porquet et al., 2013).

Additionally, resveratrol exhibited interactions with multiple cytochrome P450 isoforms (CYP1A2, CYP2C9, CYP3A4), indicating possible effects on xenobiotic metabolism and drug interactions, in line with data reported by Chan et al. (2018). Its involvement in the PI3K/Akt/mTOR signaling pathways reinforces its role in regulating cell proliferation, inflammation, and aging processes (Utpal et al., 2025).

Overall, the *in silico* predictions align with literature observations, supporting the notion that resveratrol possesses broad therapeutic potential, including management of cancer, neurodegenerative diseases, chronic inflammation, and hormonal disorders. These data justify further experimental research to validate the predicted biological activities.

The in silico prediction of the pharmacokinetic profile of resveratrol (Table 5) indicates that resveratrol recovered from Burgund grape pomace exhibits highly efficient intestinal absorption (~91%), although its low water solubility may slightly limit bioavailability. Intestinal membrane permeability is moderate, suggesting effective passage into the bloodstream.

Table 5. ADMET Results for Resveratrol, Extracted from Burgund Grape Pomace

Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.178	Numeric (log mol/L)
Absorption	Caco2 permeability	1.17	Numeric (log Papp in 10-6 cm/s)
Absorption	Intestinal absorption (human)	90.935	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.737	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	0.296	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.166	Numeric (Fu)
Distribution	BBB	-0.048	Numeric (log BB)

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	permeability		
Distribution	CNS permeability	-2.067	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.076	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	Yes	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.331	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	No	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.529	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.533	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	*T.Pyriformis* toxicity	0.746	Numeric (log ug/L)
Toxicity	Minnow toxicity	1.522	Numeric (log mM)

Regarding distribution, the relatively low volume of distribution indicates that resveratrol is concentrated mainly in the blood and certain tissues, while the fraction unbound in plasma is low, which may influence its biological activity and elimination.

Resveratrol is primarily metabolized by CYP3A4, not by CYP2D6, and it inhibits CYP1A2 and CYP2C19, which may lead to interactions with other drugs metabolized by these isoenzymes. However, it does not inhibit CYP2D6 or CYP3A4, reducing the risk of additional interference.

Excretion is relatively slow, contributing to a longer duration of action. Regarding toxicity, resveratrol does not exhibit significant hepatotoxic or cardiotoxic effects, does not induce skin sensitization, and has moderate oral toxicity. However, the AMES test indicates potential

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mutagenicity, and the maximum tolerated dose is relatively low, which should be considered for long-term administration or high-dose treatments.

4. CONCLUSIONS

This study presents an innovative framework for valorizing Burgund grape pomace as a sustainable source of resveratrol, reinforcing the principles of the circular economy and green biotechnology. In contrast to existing literature, no prior research has specifically addressed the use of this grape variety for resveratrol extraction, highlighting the originality and scientific contribution of the study. The systematic application of microwave-assisted extraction (MAE) demonstrated high efficiency with minimal environmental impact, while the integration of precise quantification via UHPLC with advanced bioinformatic analyses (drug-likeness, Lipinski's and Veber's rules, ADMETox profiling) provided synergistic validation of the results, enhancing both robustness and translational relevance.

This dual approach allows for early assessment of pharmacological potential, reducing reliance on animal testing and adhering to the ethical principles of the 3Rs. Moreover, the obtained results open promising avenues for further research, including optimization of extraction techniques, exploration of other grape pomace varieties, and in-depth investigation of the therapeutic applications of resveratrol across multiple domains.

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6. REFERENCES

Abreu, T., Sousa, P., Gonçalves, J., Hontman, N., Teixeira, J., Câmara, J. S., & Perestrelo, R. (2024). Grape Pomace as a Renewable Natural Biosource of Value-Added Compounds with Potential Food Industrial Applications. *Beverages, 10(2)*, 45.

Accomasso, G., Turku, F., Sapino, S., Chirio, D., Peira, E., Gallarate, M. (2024). Resveratrol: Extraction Techniques, Bioactivity, and Therapeutic Potential in Ocular Diseases. *Scientia Pharmaceutica, 92(4)*, 59.

Adebiyi, O.E., Olayemi, F.O., Ning-Hua, T., Guang-Zhi, Z. (2017). In vitro antioxidant activity, total phenolic and flavonoid contents of ethanol extract of stem and leaf of Grewia carpinifolia. *Beni-Seuf Univ J Appl.*, *6*, 10-14.

Baur, J.A., Sinclair, D.A. (2006). Therapeutic potential of resveratrol: the *in vivo* evidence. *Nature reviews. Drug discovery*, *5(6)*, 493–506.

Berman, A.Y., Motechin, R.A., Wiesenfeld, M.Y., Holz, M.K. (2017). The therapeutic potential of resveratrol: a review of clinical trials. *NPJ precision oncology, 1,* 35.

Bowers, J.L., Tyulmenkov, V.V., Jernigan, S.C., Klinge, C.M. (2000). Resveratrol acts as a mixed agonist/antagonist for estrogen receptors alpha and beta. *Endocrinology, 141(10)*, 3657–3667.

Chen, B., Zhang, Y., & Zuo, Y. (2012). Optimization of microwave-assisted extraction of phenolic antioxidants from grape seeds. *Journal of Food Science, 77(2)*, C253–C261.

Cheng, Y.C., Sheen, J.M., Hu, W.L., Hung, Y.C. (2017). Polyphenols and Oxidative Stress in Atherosclerosis-Related Ischemic Heart Disease and Stroke. *Oxid Med Cell Longev*, *2017*, 8526438.

Diamanti, A.C., Igoumenidis, P.E., Mourtzinos, I., Yannakopoulou, K., Karathanos, V.T. (2017). Green extraction of polyphenols from whole pomegranate fruit using cyclodextrins. *Food Chem*, *214*, 61–6.

Doria, E., Boncompagni, E., Marra, A., Dossena, M., Verri, M., Buonocore, D. (2021). Polyphenols Extraction From Vegetable Wastes Using a Green and Sustainable Method. *Front. Sustain. Food Syst. 5*, 690399.

Fernandez, M.D.L.A., Espino, M., Gomez, F.J.V., Silva, M.F. (2018). Novel approaches mediated by tailor-made green solvents for the extraction of phenolic compounds from agro-food industrial by-products. *Food Chem*, *239*, 671–8.

Garrido, L., Barrales, F. M., & Gómez, M. (2019). Microwave-assisted extraction of phenolic compounds from Chardonnay grape marc. *Food Chemistry, 275*, 127–135.

*Corresponding author, E-mail address: georgiana.cirstea93@upb.ro

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Liu, Y., Tong, L., Luo, Y., Li, X., Chen, G., & Wang, Y. (2018). Resveratrol inhibits the proliferation and induces the apoptosis in ovarian cancer cells via inhibiting glycolysis and targeting AMPK/mTOR signaling pathway. *Journal of cellular biochemistry*, *119*(7), 6162–6172.

Ma, H., Wang, B., Liu, D., & Tian, M. (2014). Microwave-assisted extraction of polyphenols from red grape marc. *Food and Bioproducts Processing, 92(4),* 375–381.

Manolescu, D., Uță, G., Șuțan, A., Ducu, C., Din, A., Moga, S., Avram, S. (2023). Biogenic synthesis of noble metal nanoparticles using *Melissa officinalis* L. and *Salvia officinalis* L. extracts and evaluation of their biosafety potential. *Caryologia, 75(3)*, 65–83.

Pedroza, M.A., Amendola, D., Maggi, L., Zalacain, A., De Faveri, D.M., Spigno, G. 92015). Microwave-Assisted Extraction of Phenolic Compounds from Dried Waste Grape Skins" *International Journal of Food Engineering*, *11(3)*, 359-370.

Phuyal, N., Jha P.K., Raturi, P.P., Rajbhandary, S. (2020). Total phenolic, flavonoid contents, and antioxidant activities of fruit, seed, and bark extracts of Zanthoxylum armatum DC. *Sci World J*, *16*, 1-7.

Porquet, D., Casadesús, G., Bayod, S., Vicente, A., Canudas, A. M., Vilaplana, J., Pelegrí, C., Sanfeliu, C., Camins, A., Pallàs, M., & del Valle, J. (2013). Dietary resveratrol prevents Alzheimer's markers and increases life span in SAMP8. *Age (Dordrecht, Netherlands)*, *35(5),* 1851–1865.

Salehi, B., Mishra, A.P., Nigam, M., Sener, B., Kilic, M., Sharifi-Rad, M., Fokou, P.V.T., Martins, N., Sharifi-Rad, J. (2018). Resveratrol: A Double-Edged Sword in Health Benefits. *Biomedicines*, *6(3)*, 91.

Sasidharan, S., Chen, Y., Saravanan, D., Sundram, K.M., Latha, Y.L. (2011). Extraction, isolation and characterization of bioactive compounds from plants' extracts. *African Journal of Traditional Complementary and Alternative Medicines 8* (1), 1–10.

Shimamura, T., Sumikura. Y., Yamazaki, T., Tada. A., Kashiwagi, T., Ishikawa, H., Matsui, T., Sugimoto, N., Akiyama, H., Ukeda, H. (2014). Applicability of the DPPH assay for evaluating the antioxidant capacity of food additives − inter-laboratory evaluation study. *Anal Sci., 30*, 717-721.

Siracusa, R., Impellizzeri, D., Cordaro, M., Crupi, R., Esposito, E., Petrosino, S., & Cuzzocrea, S. (2017). Anti-Inflammatory and Neuroprotective Effects of Co-UltraPEALut in a Mouse Model of Vascular Dementia. *Front. Neurol. 8*, 233.

Srinivasan, P., Vijayakumar, S., Kothandaraman, S., and Palani, M. (2018). Anti-diabetic Activity of Quercetin Extracted from Phyllanthus Emblica L. Fruit: *In Silico* and *In Vivo* Approaches. *J. Pharm. Anal. 8*, 109–118.

Supuran, C.T. (2011). Carbonic anhydrase inhibitors and activators for novel therapeutic applications. *Future medicinal chemistry, 3(9),* 1165–1180.

Tangney, C.C., Rasmussen, H.E. (2013). Polyphenols, inflammation, and cardiovascular disease. *Curr Atheroscler Rep., 15(5)*, 324.

Utpal, B.K., Mokhfi, F.Z., Zehravi, M., Sweilam, S.H., Gupta, J.K., Kareemulla, S., C,R.D., Rao, A.A., Kumar, V.V., Krosuri, P., Prasad, D., Khan, S. L., Roy, S.C., Rab, S.O., Alshehri, M.A., Emran, T.B. (2025). Resveratrol: A Natural Compound Targeting the PI3K/Akt/mTOR Pathway in Neurological Diseases. *Molecular neurobiology*, *62(5),* 5579–5608.

Wang, B. (2012). Orthogonal test design for optimisation of extraction of trans-resveratrol from Pinot Noir-grape pomace. *Natural product research, 26(9)*, 821–829.

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