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Biological Potential of Grape Skin Extracts: A Comparative Study of Grape Varieties from the Šumadija Region

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Abstract: The growing demand for environmentally friendly nutritional and medicinal products has stimulated the research of natural bioactive compounds, especially those obtained from agricultural waste such as grape skins. This study provides an overview of previous findings on the antioxidant and anti-inflammatory activity of grape skin extracts from four grape varieties - Marcellin, Shiraz, Cabernet Franc and Petit Verdot - originating from the Šumadija region. The extracts were obtained using ultrasonic extraction with green solvents: water, ethanol and ethyl acetate. Total phenolic content (TPC) was measured by the Folin-Chocolate method, while antioxidant activity was assessed using the DPPH and ABTS assays. Anti-inflammatory activity was assessed by the lipoxygenase (LOX) inhibition assay. Ethyl acetate extracts showed the highest antioxidant potential. It is noteworthy that GSE5 (Shiraz-ethyl acetate extract) and GSE2 (Marselane-ethyl acetate extract) showed the most significant activity. GSE5 had IC_{50} values of 24.5 μg/ml (DPPH) and 5.3 μg/ml (ABTS), while GSE2 showed strong reducing power (0.1823 at 700 nm compared to 0.1249 for ascorbic acid). In the LOX assay, GSE5 and GSE2 achieved IC_{50} values of 15.2 μg/ml and 25.3 μg/ml, respectively. These findings highlight the potential of grape skin extracts as natural agents for managing oxidative stress and inflammation, with applications in the food and pharmaceutical industries.

Keywords: Grape-skin extracts, Ultrasound extraction, Antioxidative activities, Anti-inflammatory potential

1. Introduction

Grape skins, although often overlooked, play an extremely important role as they are rich in numerous bioactive compounds with strong antioxidant, anti-inflammatory and protective properties. Their use represents an important step towards reducing waste in the food and wine industry, while contributing to the creation of additional value from material that would otherwise be discarded. Such an approach fits perfectly into the

concept of the circular economy, as it allows the use of by-products towards sustainable and environmentally responsible production [1].

Thanks to their high content of polyphenols and other beneficial compounds, grape skins can be used in numerous areas – as functional components in food, dietary supplements, active ingredients in cosmetics, and even as raw materials in the production of pharmaceutical products. This multifunctionality makes them an extremely valuable resource in the development of innovative and sustainable products.

This review presents previously published research results on the antioxidant and anti-inflammatory activities of skin extracts from Marselan, Syrah, Petit Verdot and Cabernet Franc varieties [2,3]. The results obtained serve as a basis for the development of formulations incorporating these extracts for use both in the food industry and in the treatment of various skin conditions.

3. Methodlogy

3.1 Preparation of samples

Grape skin samples from Marseillan, Shiraz, Cabernet Franc, and Petit Verdot—obtained as by-products from local wineries in the Šumadija region—were washed, dried, and extracted using ultrasound-assisted extraction. Each sample (20 g dried skins) was treated with 200 mL of ethyl acetate, absolute ethanol, or 50% ethanol.

3.2. Determination of total phenolic content, In Vitro Antioxidant Potential Assessment and LOX inhibition activity of grape skin extracts

The total phenolic content (TPC) of grape skin extracts was measured using the Folin–Ciocalteu method with minor modifications [4]. Results were expressed as mg gallic acid equivalents per gram of dry extract (mg GAE/g GSE) and reported as mean ± SD from triplicate measurements.

Antioxidant potential of the extracts was evaluated using three *in vitro* assays: DPPH, ABTS, and FRAP, known for their reliability in assessing antioxidant capacity of compounds and extracts [4]. Anti-inflammatory activity was determined via a LOX inhibition assay by measuring the effect of extracts on lipoxygenase activity. Reactions included the extract, LOX enzyme, sodium linoleate, and Tris buffer, with absorbance measured at 234 nm. NDGA served as a positive control, and IC_{50} values were calculated from triplicate measurements [4].

2. Results and Discussion

The isolation of compounds with therapeutic potential from plant sources, such as grape skins, is highly dependent on the extraction method. Ultrasound-assisted extraction (UAE) stands out as a very effective technique for obtaining these compounds.

In this study, grape skin extracts from the varieties Marcellin (**GSE1** – absolute ethanol, **GSE2** – ethyl acetate, **GSE3** – 50% ethanol), Shiraz (**GSE4** – absolute ethanol, **GSE5** – ethyl acetate, **GSE6** – 50% ethanol), Cabernet Franc (**CF1** – ethyl acetate, **CF2** – absolute ethanol, **CF3** – 50% ethanol) and Petit Verdot (**PV1** – ethyl acetate, **PV2** – absolute ethanol, **PV3** – 50% ethanol) were investigated. The yield of the obtained extracts

varied from 5.1% to 11.5%, depending on the polarity of the solvent and the grape variety (Table 1).

Total phenolic content (TPC) was determined by the Folin-Chocolteu method and expressed in milligrams of gallic acid per gram of extract (mg GAE/g). The values ranged from 2.6 to 11.6 mg GAE/g, with ethyl acetate extracts consistently showing higher TPC values than ethanol extracts, indicating a significant influence of solvent polarity on the efficiency of phenolic compound extraction.

The antioxidant activity of the extracts was examined by the DPPH, ABTS and reducing power assays. A clear trend in efficiency was observed depending on the solvent and indicating that ethyl acetate is the most effective in extracting antioxidants.

The highest free radical scavenging ability was shown by **CF1** with IC_{50} values of 16.7 μg/mL (DPPH) and 11.3 μg/mL (ABTS). It was followed immediately by **GSE5**, with values of 24.5 μg/mL (DPPH) and 5.3 μg/mL (ABTS), confirming their high antioxidant potential.

The reducing power test showed that **GSE5** (0.2068) and **GSE2** (0.1823) had higher absorbance at 700 nm compared to ascorbic acid (0.1249).

In the lipoxygenase (LOX) inhibition assay, **GSE5** and **GSE2** achieved the best results with IC_{50} values of 15.2 μg/mL and 25.3 μg/mL, while the other extracts showed significantly weaker activity (87.3–500 μg/mL). Although slightly weaker than NDGA (5.2 μg/mL), these results indicate that **GSE5** and **GSE2** combine potent antioxidant and anti-inflammatory activity, making them highly promising for use in the treatment of conditions associated with oxidative stress and inflammation.

Table 1. Antioxidant, anti-inflammatory activity, and total phenolic content of investigated grape skin extracts and standards

Grape variety	Extract	Yield (%)	DPPH	ABTS	FRAP	TPC	LOX
			IC_{50} (mg/mL)		A_{700nm} (5 mg/mL)	mg GAE/g GSE	IC_{50} (mg/mL)
Cabernet Franc	CF1	9.6	16.7 ± 0.7	11.3 ± 0.6	0.1045 ± 0.0035	7.9 ± 0.6	87.3 ± 0.1
	CF2	6.3	98.0 ± 1.6	66.6 ± 1.8	0.0601 ± 0.0071	2.2 ± 0.3	>500
	CF3	10.2	76.5 ± 1.1	63.9 ± 2.0	0.0677 ± 0.0006	2.7 ± 0.9	>500
Petit Verdot	PV1	8.7	57.6 ± 0.9	43.7 ± 1.7	0.0700 ± 0.0061	2.9 ± 0.7	369.5 ± 0.7
	PV2	7.8	77.4 ± 1.3	55.1 ± 1.3	0.0457 ± 0.0044	2.7 ± 0.4	>500
	PV3	11.5	76.7 ± 0.6	45.4 ± 2.4	0.0685 ± 0.0145	2.8 ± 0.2	>500
Marselan	GSE1	7.8	39.7 ± 0.9	13.9 ± 0.6	0.1022 ± 0.0036	6.4 ± 0.1	150.5 ± 0.4
	GSE2	5.1	37.6 ± 1.5	12.5 ± 0.4	0.1823 ± 0.0035	7.4 ± 0.3	25.3 ± 0.4
	GSE3	8.9	46.8 ± 1.7	16.7 ± 0.8	0.0835 ± 0.0042	6.4 ± 0.7	181.9 ± 0.5
Shiraz	GSE4	9.2	48.9 ± 0.3	21.2 ± 0.3	0.0372 ± 0.0027	2.8 ± 0.4	329.8 ± 0.1
	GSE5	6.1	24.5 ± 0.4	5.3 ± 0.2	0.2068 ± 0.0008	11.6 ± 0.1	15.2 ± 0.1
	GSE6	10.4	43.1 ± 0.6	16.8 ± 0.7	0.0767 ± 0.0016	2.6 ± 0.6	180.3 ± 0.4
Standards	Trolox	/	/	1.3 ± 0.1	/	/	/
	Ascorbic acid	/	18.1 ± 0.1	31.1 ± 0.1	0.1249 ± 0.0022	/	/
	NDGA	/	0.5 ± 0.1	/	/	/	5.2 ± 0.1
	Quercetin	/	0.6 ± 0.1	/	/	/	13.1 ± 0.4

4. Conclusions

The results of this study show that ultrasonic extraction, in combination with the choice of an appropriate solvent, significantly affects the yield and biological activity of grape skin extracts. Ethyl acetate proved to be the most effective solvent in the extraction of phenolic compounds with high antioxidant and anti-inflammatory properties. The most significant activity was shown by the etil acetate extracts **GSE5** (Shiraz) and **GSE2** (Marselan), with a pronounced ability to neutralize free radicals, high reducing power and effective inhibition of LOX enzymes. Their dual functionality indicates the potential for application in the prevention and therapy of conditions associated with oxidative stress and inflammation, which places them among the promising natural sources of bioactive compounds for further pharmacological development.

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