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Chemometric Optimization of Biologically Active Compounds Extraction from Grape Marc: Composition and Antimicrobial Activity

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Abstract: The article focuses on the optimization of the extraction process of biologically active compounds (BAC) from grape marc—a by-product of the wine industry. The influence of temperature, specifically 30 °C, 45 °C and 65 °C, and ethanol concentration in solutions, specifically 0–96% (*v*/*v*) on the extraction yield of polyphenols, flavonoids, tannins and anthocyanins, were investigated. The composition of individual polyphenols, anthocyanins and organic acids, antioxidant activity (DPPH and ABTS) and CIELab chromatic characteristics of the grape marc extracts (GME), were characterized. The microbiostatic and microbicidal effects in direct contact of GME with pathogenic microorganisms, *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, were determined in vitro. The influence of extraction parameters on the total polyphenol content (TPC), total flavonoid content (TFC), tannin content (TC), total anthocyanin content (TAC) and their interdependencies were studied using information analysis. A mathematical model was developed on cubic spline functions. The analysis of individual compounds showed the presence of a wide range of flavonoids (procyanidin B2, procyanidin B1, hyperoside and quercetin), flavones (catechin), hydroxybenzoic acid derivatives (gallic, protocatechuic, *p*-hydroxybenzoic acids, *m*-hydroxybenzoic acid, syringic acid), hydroxycinic acid derivatives and ferulic acid methyl ester. The malvidol-3-glucoside was the main anthocyanin identified in the extract. A high amount of tartaric acid was also found. GME showed significant antimicrobial activity against Gram-positive bacteria and lower activity against Gram-negative bacteria.

Keywords: grape marc; extraction parameters; biologically active compounds; mathematical models; antimicrobial activity; pathogenic microorganisms

1. Introduction

Alcoholic and non-alcoholic beverage production generates waste and by-products that can be recovered. This would not only minimize their disposal costs and environmental hazards, but also add value to the development of new products. Traditional methods of using waste as fertilizer or animal feed use only a small part of the waste and are often not very effective [1]. Efforts must also be made to isolate and structurally elucidate new bioactive compounds. This will lead to achievements in the recovery of bioactive molecules, important for the development of innovative products, but it will also contribute to reducing environmental pollution [2]. A significant amount of residues is generated by the processing of grapes, among them, grape marc [3]. These residues are generally undervalued and used in animal feed (with low nutritional value), turned into fertilizer and even dumped in the environment, generating other problems, i.e., increased soil acidity, phytotoxicity, methane gas production, etc. [4]. Grape marc can become a product with potential economic profitability because it is a source of BAC (phenolic compounds, fatty acids, pectins, etc.) that can be used in the manufacture of food, cosmetics, dyes, supplements [5–8].

Numerous studies have shown the beneficial effects of polyphenols in grapes or wine on human health [9,10]. The general compositions of some grape marc have also been described [11,12]. Grape marc contains components that inhibit the proliferation of Caco-2 and HT-29 cancer cells by triggering apoptosis, has strong free radical scavengers and may provide some level of protection against certain cancers [13]. The profiles of phenolic compounds, recovered from waste from various wineries, were dominated by gallic acid, catechin and epicatechin. In addition, hydroxytyrosol, tyrosol, cyanidin glycosides and various phenolic acids, such as caffeic, procathechinic, syringic, vanillic, *o*-coumaric, *p*-coumaric acid, have also been identified [14]. A significant content of polyphenols (199.31 ± 7.21 mg gallic acid equivalents (GAE)/g), high antioxidant activity (cupric reducing antioxidant capacity test (CUPRAC)- 1036.98 mg trolox equivalents (TE)/g), enzyme inhibition (α-tyrosinase:151.30 ± 1.20 mg kojic acid equivalents (KAE)/g), is attested. The anti-inflammatory activity, as well as the antimicrobial activity of grape skin decoction, is higher than that reported for wine [15,16]. The extracts remarkably inhibit glucosyltransferases B and C (70–85% inhibition). Glycolytic decrease in pH can be attributed to partial inhibition of F-type adenosine triphosphate (F-ATP) activity (inhibition 30–65% at 125 μg/mL).

The biological activity of fermented marc is either as effective or significantly better than grape extracts [17]. Many phenolic compounds show significant antibacterial activity [18]. This is of particular interest for the development of natural alternatives to synthetic food preservatives and cosmetic applications [19,20]. Phenolic grape extracts, especially from different types of grape marc, are very effective against the specific virulence traits of *Streptococcus mutans*, despite major differences in their phenolic content. The mechanisms of antibacterial action of phenolic compounds are not yet fully deciphered, but it is known that these compounds involve many sites of action at the cellular level [21]. Several authors have explained this activity by the change of the permeability of cell membranes, the modification of the various intracellular functions induced by hydrogen binding of phenolic compounds to enzymes or by the changing of the rigidity of the cell wall, which leads to loss of integrity [22,23]. Polyphenols can induce irreversible damage to the cytoplasmic membrane, coagulation of cell contents and inhibition of intracellular enzymes. Tannins induce damage to the cell membrane, while phenolic acids can disrupt membrane integrity, causing leakage of essential intracellular constituents [24,25]. Flavonoids can bind to the cell walls of bacteria, promoting the formation of complexes, inhibit energy metabolism, DNA and RNA synthesis, intracellular changes in pH and interference with ATP [26,27].

Given the chemical composition of the grapes—and grape marc is obviously influenced by environmental factors and grape varieties [28–31]—extraction techniques should be optimized according to the composition of the pomace and directions for subsequent use of the extracts.

Several techniques are used to recover polyphenols from wine by-products, such as conventional solvent extraction, also called solid–liquid extraction (SLE), which is the most applied technique from an industrial point of view [32]. Several solvents have been studied for the extraction of polyphenols, but the preferred systems for food, pharmaceutical or cosmetic applications are those based on water and ethanol [33]. New unconventional techniques have emerged that can reduce extraction time, process temperature and solvent consumption, thus contributing to higher extraction efficiency and lower energy consumption. Some of the most relevant technologies are: ultrasonic-assisted extraction (UAE) [6,34], microwave-assisted extraction (MAE) [35,36], supercritical fluid extraction (SFE) [37], liquid pressure extraction (PLE) [38], ohmic heating (OH) [39], pulsed electric fields (PEF) [40,41] and enzyme-assisted extraction (EAE) [42]. Some enzymes, such as cellulases, hemicellulases, pectinases or amylases, can break down or weaken cell walls, releasing cytoplasmic contents (e.g., phenolic compounds) into the extraction solvent and thus improving extraction recovery. EAE can also be combined with other extraction techniques, such as EAU, MAE, PLE or SFE [43].

The optimization of the extraction parameters is easy to obtain in reproducible conditions, but the non-uniformity of by-products requires the presence of flexible solutions, easily adaptable to the composition of the extraction matrix. Response surface methodology (RSM) and artificial neural network (ANN) were used to model and optimize the extraction of polyphenolic compounds [44,45]. Statistical indicators have demonstrated the superiority of ANN. The comparison of different models of prediction of total polyphenols was performed by three mathematical equations: Spiro, Peleg and logarithmic, and two data extraction techniques: multivariate adaptive regression splines (MARS) and artificial neural network (ANN). The obtained results show that the data-mining techniques (MARS and ANNs) allow the creation of fast models and simple application, with a very good acceptability (coefficients of determination over 0.99) [45].

The aim of this article was to optimize the process of extracting bioactive compounds from red grape pomace according to temperature and solvent concentration, to model the interdependencies between extraction parameters by chemometric approach and to characterize the composition of extracts, antioxidant capacity and antimicrobial activity for subsequent use of these extracts in the food industry.

To optimize the extraction process, the polynomial spline functions were applied, which allows a division of the entire space of each independent variable into different sub-regions. Subsequently, truncated spline functions on two sides were defined as basic functions for describing the relationships between dependent and prediction variables in each distinct interval of the prediction variable. This model allows the adaptation of the extraction process to the fluctuating conditions of the composition of the grape marc solid fraction. For the solid–liquid extraction, the classic model was applied, applicable in the conditions of small grape processing enterprises, without additional expenses in terms of sophisticated equipment.

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