Glycerol

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Glycerol (1,2,3-propanetriol) is a viscous odorless and colorless liquid, with a syrupy sweet flavor that may derive from both renewable and fossil sources

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1. Glycerol-Properties, Sources and Uses

Commodities traded under the name “glycerin” refer to commercial glycerol solutions and “crude glycerol” is a product containing 70–80% pure glycerol. This product may be concentrated to afford 95.5–99% pure glycerol [1]. The pure anhydrous glycerol has a density of 1.261 g mL^{-1}, a melting point of 18.2 °C and a boiling point of 290 °C, where it decomposes. Glycerol is a common constituent of foods, pharmaceuticals and cosmetics, with practically no toxicity and environmentally benign. It possesses three hydroxyl groups, which make it water-soluble and endow it with hygroscopicity. Glycerol molecules may associate with each other with an extended network of hydrogen bonds, lending it with unusually high boiling point and viscosity.

Glycerol is one of the main constituents of triacylglycerols (triglycerides) occurring in living tissues and the major sources of glycerol are activities pertaining to transformation of animal fats and vegetable oils. Amongst them, the biodiesel industry plays a prominent role, since crude glycerol is generated in large amounts as a by-product of biodiesel production [2][3]. Traditionally, biodiesel manufacturing process involves transesterification reaction between triacylglycerols (e.g., vegetable oil) and methanol, catalyzed by KOH. In this process, treatment of 100 kg of oil affords 10.5 kg glycerol, and further purification requires refining steps to remove water and impurities, such as salt, methanol, and free fatty acids [2]. Glycerol refinement results in obtaining various degrees of purity required for applications in foods, pharmaceutical and personal care products, but it significantly increases the production cost.

As crude glycerol availability is tightly associated with the biodiesel production, the increases in the latter over the past 15 years have led to glycerol market saturation [2]. Yet the, food glycerin market is valued at 619.1 million USD in 2020, and it is expected to reach 874.5 million USD by the end of 2026, growing at a compound annual growth rate (CAGR) of 5.0% during 2021–2026 [4], and the global glycerol market size is expected to reach 3.5 billion USD by 2027, expanding at a CAGR of 4.0% [5]. Glycerol is mainly used in foods, pharmaceutical formulations, and cosmetics [2]. In cosmetics, glycerol is a very common ingredient (third after water and fragrance), functioning primarily as a humectant and skin protectant. Its pharmaceutical uses include applications in some over-the-counter drugs, such as ophthalmic and dermal products, and external analgesic. In food products, it is added usually as humectant and sweetener.

Glycerol is considered a renewable feedstock for the production of various chemicals [6][7], and a series of glycerol-derived liquids, such as 1,3-dialkoxy-2-propanols and 1,2,3-trialkoxy-propanes, have been tested as green solvents that could replace some petroleum-based ones [8][9][10]. The use of glycerol and glycerol-derived solvents as alternative media for organic reactions has emerged as a promising new field of research, opening new ways to revalorize glycerol for applications in synthetic organic chemistry, catalysis and biocatalysis [11]. In this concept, a series of glycerol applications, mainly in catalyzed synthesis, have been reviewed [9][10], providing data that are illustrative of the value of glycerol as a handful tool in synthetic organic chemistry. Likewise, the use of several glycerol-based solvents, such as glycerol carbonate, glycerol esters, ethers, and acetals, has been compiled to further bring out the significance of glycerol as a versatile solvent. The production of glycerol carbonate, glycerol acetates and glycerol reforming into hydrogen have also been proposed as very promising routes of crude glycerol purification and valorization [3].

2. Use of Glycerol in Solid-Liquid Extraction of Polyphenolic Phytochemicals

The use of glycerol as an extraction solvent or stabilizing agent has been sporadically documented for pollen extracts [12], grapefruit extracts [13], *Echinacea purpurea* extracts [14], epigallocatechin gallate [15], and *Castanea sativa* leaf extracts [16]. However, its systematic investigation as a solvent for polyphenol extraction was initiated by the study of Apostolakis et al., 2014 [17], who explicitly proposed water/glycerol mixtures as highly efficient media for polyphenol recovery from olive leaves. This report sparked off a series of following examinations, which demonstrated the potential of water/glycerol mixtures to effectively extract polyphenols from several plant materials, including various plant food processing by-products and botanicals.

2.1. Plant Food By-Products

The importance of glycerol as a green and high-performance solvent for the recovery of polyphenols and pigments from vinification solid wastes has been recently acknowledged [18]. However, glycerol has been tested on several plant food processing residues, as witnessed by studies published between 2014 and 2020. An overview of the studies reported so far is given in Table 1.

Table 1. Representative examples of total polyphenol recovery from plant food wastes using aqueous glycerol mixtures.

Plant Material	Glycerol Proportion	Extraction Mode	Conditions	Yield in Total Polyphenols (mg GAE g^{-1})	Reference
Olive leaves	9.3% (*w*/*v*)	Stirred-tank	*T* = 80 °C; *t* = 241 min; $R_{L/S}$ = 60 mL g^{-1}	51.91	[17]
Apple peels	70% (*w*/*v*)	Stirred-tank	*T* = 80 °C; *t* = 160 min; $R_{L/S}$ = 100 mL g^{-1}	16.59	[19]
Onion solid wastes	90% (*w*/*v*)	Ultrasound-assisted	*T* = 50 °C; *t* = 60 min; $R_{L/S}$ = 90 mL g^{-1}	90.07	[20]
Red grape pomace	90% (*w*/*v*)	Ultrasound-assisted	*T* = 45 °C; *t* = 60 min; $R_{L/S}$ = 90 mL g^{-1}	66.70	[21]
Coffee brewing residues	3.6% (*w*/*v*)	Ultrasound-assisted	*T* = 45 °C; *t* = 175 min; $R_{L/S}$ = 50 mL g^{-1}	8.15	[22]
Eggplant peels, potato peels, coffee brewing residues	80% (*w*/*v*)	Stirred-tank	*T* = 80 °C; *t* = 180 min; $R_{L/S}$ = 100 mL g^{-1}		[23]
Red grape pomace	20% (*w*/*v*)	Stirred-tank	*T* = 23 °C; *t* = 180 min, $R_{L/S}$ = 50 mL g^{-1}	5.65	[24]
Potato peels	83% (*w*/*v*)	Ultrasound-assisted	*T* = 23 °C; *t* = 80 min, $R_{L/S}$ = 81 mL g^{-1}	8.71	[25]
Eggplant peels	90% (*w*/*v*)	Ultrasound-assisted	*T* = 50 °C; *t* = 90 min, $R_{L/S}$ = 100 mL g^{-1}	13.51	[26]
Oak acorn husks	60% (*w*/*v*)	Stirred-tank, addition of 13% (*w*/*v*) HP-β-CD [1]	*T* = 80 °C; *t* = 180 min, $R_{L/S}$ = 50 mL g^{-1}	122.19	[27]
Olive leaves	60% (*w*/*v*)	Stirred-tank, addition of 7% (*w*/*v*) HP-β-CD [1]	*T* = 60 °C; *t* = 180 min, $R_{L/S}$ = 50 mL g^{-1}	54.33	[28]
Onion solid wastes	60% (*w*/*v*)	Stirred-tank, addition of 13% (*w*/*v*) HP-β-CD [1]	*T* = 80 °C; *t* = 240 min, $R_{L/S}$ = 50 mL g^{-1}	3.13	[29]

Plant Material	Glycerol Proportion	Extraction Mode	Conditions	Yield in Total Polyphenols (mg GAE g^{-1})	Reference
Rice bran	19.5% (*v*/*v*)	Orbital shaking	*T* = 67 °C; *t* = 90 min, $R_{L/S}$ = 33 mL g^{-1}	7.09	[30]
Rice bran	15.9% (*w*/*v*)	Orbital shaking	*T* = 90 °C; $R_{L/S}$ = 31.6 mL g^{-1}	5.50	[31]
Grapefruit peels	20% (*w*/*v*)	Stirred-tank, HVED [3] pretreatment	*T* = 50 °C; *t* = 60 min	19.3	[32]
Red grape pomace	50% (*w*/*v*)	Homogenizer-assisted	10,000 rpm, t = 30 s, 15,000 rpm, t = 30 s $R_{L/S}$ = 22.4 mL g^{-1}	21.40	[33]
Mangosteen pericarp	99% (*w*/*w*)	Stirred-tank	*T* = 40 °C; *t* = 24 h, $R_{L/S}$ = 10 mL g^{-1}	4.00	[34]
Red grape pomace	32.5% (*w*/*v*)	Pressurized-liquid extraction	*T* = 150 °C; $R_{L/S}$ = 10 mL g^{-1}	Nr [4]	[35]

Notes: [1] 2-Hydroxypropyl β-cyclodextrin; [2] Refers to total anthocyanin pigments (expressed as cyanidin 3-*O*-glucoside equivalents); [3] High-voltage electric discharges; [4] Not reported as sum.

As mentioned earlier in the text, interest was stimulated by the study of Apostolakis et al., [17], who performed an optimization study, employing aqueous glycerol solutions with glycerol concentration varying from 7.5 to 10% (*w*/*v*). The authors demonstrated that at 80 °C, a glycerol aqueous mixture with a concentration of 9.3% outperformed a previously optimized method based on water/ethanol mixtures and carried out at 24 °C, providing almost 10% higher total polyphenol yield. Extraction kinetics was also faster with aqueous glycerol at 80 °C, compared to aqueous ethanol at 24 °C. However, in a study on apple waste peel polyphenol extraction, the rate constant found for the extraction with 70% (*w*/*v*) glycerol was significantly lower than those recorded with 50% (*v*/*v*) ethanol and 50% (*v*/*v*) butanediol, at 80 °C [19]. On the other hand, no important differences were seen for diffusivity (D_e).

A subsequent examination of red grape pomace extraction employing water/glycerol solutions showed that yield in total polyphenols, total flavonoids and total pigments peaked at a glycerol concentration of 20% (*w*/*v*). Incorporation of tartaric acid in this solvent up to 2% (*w*/*v*) disfavored increases in extraction yield and antioxidant activity of the extracts [24]. However, homogenizer-assisted extraction of red grape pomace indicated 50% (*w*/*v*) glycerol concentration as being the optimum for maximizing total polyphenol, total flavonoid and pigment extraction yield [33]. A concomitant maximization was also seen for the antioxidant activity of the extract obtained. Likewise, pressurized liquid extraction of red grape pomace at 150 °C demonstrated 50% glycerol to be the most suitable solvent for flavanol, stilbene and phenolic acid extraction, but flavonol extraction was favored with a 32.5% solution [35].

For other waste material tested, the optimum glycerol concentration displayed significant differences, stressing the importance of the nature of phenolics to be extracted, but also the extraction conditions. Huang et al., [30] reported that rice bran polyphenol extraction required 19% glycerol, at a temperature of 67 °C. A latter investigation on rice bran was in line with this outcome, suggesting an optimum concentration of 16%, at 90 °C [31]. A similar level of 20% (*w*/*v*) was also proposed for the extraction of polyphenols from grapefruit peels, which had been pretreated with high-voltage electric discharges [32].

When tested pure, glycerol was also shown to be more effective than ethanol and water, but less so compared to propylene glycol, in the extraction of mangosteen (*Garcinia mangostana* Linn) pericarp polyphenols [34]. In investigations involving fixed level of glycerol concentration (no optimization), 80% (*w*/*v*) glycerol was demonstrated to perform equally compared to 50% aqueous methanol and 50% aqueous ethanol, in extracting total polyphenols from potato peels, eggplant peels and coffee brewing residues, at 80 °C [23]. Yet, the hydroglycerolic solvent was significantly more efficient in total flavonoid extraction. Nevertheless, for apple waste peels a 70% (*w*/*v*) glycerol solution at 80 °C was found to be of comparable efficiency with 50% (*v*/*v*) ethanol and 50% (*v*/*v*) butanediol [19].

Apart from traditional stirred-tank extraction, ultrasound-assisted extraction (UAE) has also been implemented in combination with hydroglycerolic solvents, providing in some cases outstanding yields in total polyphenols and pigments. The first report on such an attempt was on polyphenol recovery from coffee brewing residues, where incorporation of glycerol at a rather low level (3.6% *w*/*v*) resulted in 7.4% increase in total polyphenol yield [22]. Kinetic investigation also

demonstrated that extraction obeyed a second-order model, being faster with water compared to water/glycerol mixture. However, D_e was higher in water/glycerol than in pure water. Response surface optimization of the UAE of eggplant (*Solanum melongena*) peel polyphenols using water/glycerol solutions indicated that effective extraction would require 90% (*w*/*v*) glycerol, at 50 °C, whereas identical total polyphenol yields were attained with 40% (*v*/*v*) ethanol, at 80 °C [26]. Under these conditions, extraction with both solvents followed second-order kinetics, with the water/ethanol extraction displaying higher extraction rate and D_e. In the same line, Paleologou et al., [25] showed that potato peel extraction with water/glycerol and with water/ethanol solutions was optimal with a glycerol concentration of 83% (*w*/*v*), at 80 °C, and ethanol concentration of 59% (*v*/*v*), at 77 °C, respectively. No statistical difference was found in the total polyphenol yields achieved using either solvent. In this case too, extraction was effectively described by a second-order model. Furthermore, water/ethanol extraction exhibited higher extraction rate and higher D_e.

On the other hand, in a study on UAE of polyphenols from onion solid wastes, a different outcome was reached [20]. Although extraction optimization suggested 90% (*w*/*v*) as being the most appropriate solvent composition, the kinetic assay performed showed that extraction of both total polyphenols and total pigments followed first-order kinetics. In addition, it was evidenced that increasing temperature from 50 to 80 °C was not favorable for total polyphenol extraction, as opposed to total pigment yield, which displayed an increasing trend. Likewise, optimization of UAE of red grape pomace once again proved 90% (*w*/*v*) glycerol to be the highest-performing solvent for total polyphenol and total pigment extraction, which obeyed a first-order kinetic model [21]. For both total polyphenol and total pigment extractions, the rate constant and D_e increased by raising the temperature from 50 to 80 °C. An investigation on UAE of flavonoids from onion solid wastes and red grape pomace using 90% (*w*/*v*) glycerol did confirm that first-order kinetic model could effectively describe the extraction behavior from both plant materials [36].

Combination of water/glycerol solutions with cyclodextrin as co-solvent for the recovery of polyphenolic substances have also been reported. Using oak (*Quercur robur*) acorn husks as plant matrix, polyphenol yield was optimized with 60% (*w*/*v*) glycerol and 13% (*w*/*v*) 2-hydroxypropyl β-cyclodextrin (HP-β-CD), at 80 °C [27]. Identical values for glycerol, HP-β-CD and temperature were also determined for the optimization of pigment (anthocyanin) extraction from onion solid wastes [29]. The extract thus generated was successfully used as a natural yogurt colorant. Finally, optimization of olive leaf polyphenol extraction demonstrated 60% (*w*/*v*) glycerol and 7% (*w*/*v*) HP-β-CD to be the most efficient combination, at 60 °C [28].

2.2. Medicinal and Aromatic Plants (MAPs)

Typical examples of MAP extraction using glycerol or glycerol-based mixtures are given in Table 2 [37][38][39][40][41][42][43][44][45]. The evidence emerged from early studies [46] indicated that mixtures of ethanol/glycerol (1–20%) were more effective for the extraction of phenolics such as carvacrol and rosmarinic acid from *Origanum onites* L.; *Origanum vulgare* spp. *hirtum* and *Origanum vulgare* L. than mixtures of ethanol/propylene glycol. A solvent of water/ethanol (1/1) that contained 30% (*w*/*v*) glycerol was also significantly more efficacious that water/ethanol (1/1) in extracting polyphenols from *Origanum onites* L [43]. Moreover, simple maceration with 95% glycerol was found to be a convenient means of producing polyphenol-enriched extracts from *Thymus vulgaris* and *Origanum vulgare* [45]. Contrary to those, a more recent investigation demonstrated higher efficiency of alkanediols including 1,2-ethanediol, 1,2-propanediol and 1,3-propanediol, compared to glycerol, towards recovery of polyphenols from *Juglans regia* L. [42]. All these solvents were tested as water mixtures, at solvent/water proportion of 8/2 (*w*/*w*).

Table 2. Representative examples of total polyphenol recovery from botanicals using aqueous glycerol mixtures.

Plant Material	Glycerol Proportion	Extraction Mode	Conditions	Yield in Total Polyphenols (mg GAE g^{-1})	Reference
Hypericum perforatum	**10% (*w*/*v*)**	**Stirred-tank**	***T* = 70 °C; *t* = 69 min $R_{L/S}$ = 50 mL g^{-1}**	**89.90**	[37]
***Hypericum triquetrifolium* Turra**	**10% (*w*/*v*)**	**Stirred-tank**	***T* = 70 °C; *t* = 73 min $R_{L/S}$ = 50 mL g^{-1}**	**54.83**	[38]
***Artemisia arborescens* *Artemisia inculta* Delile**	**90% (*w*/*v*)**	**Stirred-tank**	***T* = 80 °C; *t* = 160 min $R_{L/S}$ = 100 mL g^{-1}**	**48.45 59.91**	[39]

Plant Material	Glycerol Proportion	Extraction Mode	Conditions	Yield in Total Polyphenols (mg GAE g^{-1})	Reference
Salvia triloba (fruticosa)	**40–75% (*v*/*v*)**	**Ultrasound-assisted Pressurized-liquid**	**T = 25 °C; t = 88 min $R_{L/S}$ = 40 mL g^{-1} (UAE)**	**nr**	[40]
Glycyrrhiza glabra	**85% (*w*/*w*)**	**Ultrasound-assisted**	**T = 70 °C; t = 20 min $R_{L/S}$ = 50 mL g^{-1}**	**nr**	[41]
Juglans regia	**20% (*w*/*w*)**	**Stirred-tank**	**T = 50 °C; t = 120 min $R_{L/S}$ = 33 mL g^{-1}**	**18.30**	[42]
Origanum onites	**30% (*w*/*v*)**	**Stirred-tank**	**T = 45 °C; t = 75 min $R_{L/S}$ = 30 mL g^{-1}**	**59.11**	[43]
***Salvia fruticosa* Mill.**	**60% (*w*/*v*)**	**Stirred-tank, ultrasonication pretreatment**	**T = 50 °C; t = 150 min $R_{L/S}$ = 25 mL g^{-1}**	**92.00**	[44]
Origanum vulgare* *Thymus vulgaris	**95% (*w*/*w*)**	**Maceration**	**T = 55 °C; t = 10 days $R_{L/S}$ = 19 mL g^{-1}**	**47.85 33.46**	[45]

Regarding hydroglycerolic mixtures, the first report on their use for polyphenol extraction from MAPs was by Karakashov et al., [37], who showed that 10% (*w*/*v*) glycerol was significantly more effective than water for the extraction of *Hypericum perforatum* (St John's wort). In line with results from plant food by-products previously mentioned, extraction kinetics, which obeyed second-order model, was faster with water than with 10% (*w*/*v*) glycerol, at optimum temperature of 70 °C. The authors attributed this finding to the increased viscosity of water/glycerol mixtures compared to pure water. Results drawn from a similar study on *Hypericum triquetrifolium* were alike [38], showing the supremacy of water/glycerol over pure water in achieving higher total polyphenol extraction yields, in spite of the slower extraction rate seen with the water/glycerol solvent.

The optimization of polyphenol extraction from two *Artemisia* species [39] demonstrated that maximum total polyphenol yield could be achieved with 90% (*w*/*v*) glycerol, in absolute accordance with the results reported by Philippi et al., [26], Katsampa et al., [20] and Trasanidou et al., [21]. The implementation of the second-order kinetic model also revealed that both extraction rate constant and D_e increased as a response to increasing temperature, up to 80 °C. The increases in total polyphenol yield as a function of increasing temperature were accompanied by concomitant enhancement of both antiradical activity and ferric-reducing power. Extracts from licorice with an optimum glycerol content of 85% were also shown to possess excellent antiradical and Fe^{2+}- chelating properties, as well as tyrosinase and elastase inhibitory activity and anti-inflammatory activity [41]. The authors supported that, on this evidence, licorice hydroglycerolic extracts might have excellent anti-aging properties, making them promising constituents of specialized cosmeceutical formulations.

In a more recent study, a blend of ultrasonication pretreatment and hydroglycerolic solvent was found to be a convenient means of producing *Salvia fruticosa* (otherwise known as *S. triloba* L.) with high polyphenol concentration and enhanced antioxidant activity [44]. Maximum yield was achieved with 40 min ultrasonication and subsequent batch stirred-tank extraction with 60% (*w*/*v*) aqueous glycerol, at 50 °C. By contrast, aqueous extracts of *S. triloba* L. generated with pressurized liquid extraction were shown to be richer in polyphenols and displayed stronger antioxidant effects compared to extracts produced with various water/glycerol combinations [40].

3. Glycerol-Based Deep Eutectic Solvents (DES) in Polyphenol Extraction

Deep eutectic solvents (DES) are neoteric designer liquids, which over past five years have been a subject of intensive research as very promising solvents. DES are usually composed of two constituents, one hydrogen bond donor and one hydrogen bond acceptor (HBA), which upon heating they form hydrogen bond-based mixtures exhibiting a eutectic point. Numerous of these mixtures are liquid under regular atmospheric conditions and may be used as green, high-performance solvents for the extraction of a variety of bioactive substances, including terpenoids, alkaloids and polyphenols [47][48][49]. Ever since its introduction as a DES constituent [50][51], the interest on glycerol as hydrogen bond

donor (HBD) has been increasingly high. The physical-chemical properties of several glycerol-based DES have been extensively tested [51][52][53][54][55][56], while glycerol-based DES are now being widely used in polyphenol extraction (Table 3[57][58][59][60][61][62][63][64], a fact highlighting their importance and prospects [64][65][66][67].

Table 3. Representative examples of total polyphenol recovery from plant materials using glycerol-based DES.

Plant Material	HBA	Extraction Mode	Conditions	Yield in Total Polyphenols (mg GAE g^{-1})	Reference
Various plant food wastes	Sodium acetate Sodium-potassium tartrate Choline chloride	Ultrasound-assisted	*T* = 80 °C; *t* = 90 min $R_{L/S}$ = 100 mL g^{-1}	1.53–88.03	[57]
Olive leaves	Sodium-potassium tartrate	Ultrasound-assisted	*T* = 73 °C; *t* = 60 min $R_{L/S}$ = 45 mL g^{-1}	26.75	[58]
Satureja thymbra	Trisodium citrate dihydrate	Stirred-tank	*T* = 50 °C; *t* = 200 min $R_{L/S}$ = 45 mL g^{-1}	171.48–186.95	[59]
Origanum dictamnus	Sodium propionate Sodium butyrate	Stirred-tank	*T* = 50 °C; *t* = 200 min $R_{L/S}$ = 45 - 47 mL g^{-1}	64.99–76.79	[61]
Humulus lupulus	Glycine	Ultrasound-assisted pretreatment Stirred-tank	*T* = 80 °C; *t* = 180 min $R_{L/S}$ = 59 mL g^{-1}	118.97	[62]
Onion solid wastes	Sodium propionate	Stirred-tank	*T* = 80 °C; *t* = 150 min $R_{L/S}$ = 100 mL g^{-1}	137.50	[63]
Moringa oleifera	Nicotinamide	Ultrasound-assisted pretreatment Stirred-tank	*T* = 80 °C; *t* = 180 min $R_{L/S}$ = 100 mL g^{-1}	82.87	[64]

3.1. Glycerol as Hydrogen Bond Donor

Albeit glycerol is a common HBD of numerous DES reported in the literature, there is only a few examinations pertaining to the systematic testing of glycerol as HBD, in combination with various HBA, for the development of polyphenol extraction methodologies. Mouratoglou et al. [57] were the first to report synthesis of novel, glycerol-based DES, using sodium acetate and sodium-potassium tartrate as HBAs. The authors demonstrated that aqueous mixtures of these DES may in some instances significantly outperform water and aqueous ethanol in extracting polyphenols from several plant food wastes. A similar outcome was seen for the extraction of olive leaf polyphenols, indicating a glycerol/sodium-potassium tartrate/water DES to be equally effective with aqueous glycerol [58].

Likewise, glycerol-based DES with choline chloride were shown to be particularly effective in extracting specific bioactive substances, such as oleuropein from olive leaves [59]. Glycerol-based DES with choline chloride, sodium acetate and trisodium citrate were shown to be highly effective for polyphenol extraction from *Satureja thymbra*. In that study, it was also reported for the first time the unusual decrease in the extraction rate as a function of temperature [60]. In those examinations, the importance of HBD/HBA molar ratio was also stressed with regard to DES stability, since below a certain HBD/HBA ratio, DES were unstable at ambient temperature, a fact manifested with HBA crystallization. This phenomenon was further confirmed by following studies using glycerol/glycine DES [68]. Testing of several DES for rutin extraction from tartary buckwheat suggested glycerol/choline (1/1) as the highest-performing solvent [69].

Some other investigation highlighted the role of the molar ratio HBD/HBA in the extraction performance of glycerol-based DES. In particular, maximization of polyphenol extraction from *Moringa oleifera* Lam. leaves was shown to occur with glycerol/sodium acetate at a molar ratio of 6 [70], whereas lower or higher molar ratios were not favorable in this regard. Such a behavior was confirmed by several following studies employing DES composed of glycerol/L-alanine [62], glycerol/nicotinamide [64], glycerol/sodium propionate [63] and glycerol/citrates [71]. Finally, another study on glycerol-based

DES with sodium acetate, sodium propionate and sodium butyrate, illustrated that the longer the carbon chain length of the HBA, the higher the amount of water required in the DES/water mixture to attain maximization of polyphenol extraction from *Origanum dictamnus* [61].

3.2. Glycerol vs. Other Hydrogen Bond Donors

An issue of high significance pertaining to polyphenol extraction efficiency was raised by studies on testing glycerol, as well as other HBDs, on a comparative basis. Sodium acetate-based DES demonstrated to be more efficient solvents for the recovery of polyphenols from red grape pomace when combined with L-lactic acid as the HBD, whereas combinations with glycerol were of lower efficiency. Yet, glycerol/sodium acetate (5/1) outperformed L-lactic acid/sodium acetate (5/1) in total flavonoid extraction [72]. In another study, a series of DES based on glycerol and L-lactic acid as HBDs, and sodium citrate salts as HBAs, were synthesized and screened for their efficiency in extracting polyphenols from *Salvia fruticosa* Mill [71].

It was concluded that L-lactic acid was a more efficacious HBD, providing significantly higher total polyphenol yield. The same conclusion was reached when a glycerol/citric acid DES was compared with an ethylene glycol/citric acid DES, at identical HBD/HBA ratio, for the extraction of *Hibiscus sabdariffa* anthocyanins [73]. In opposition to these findings, a series of glycerol/sodium propionate DES were consistently more efficient in polyphenol extraction from onion solid wastes compared to L-lactic acid analogues [63].

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