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Effect of solute polarity on extraction efficiency using deep eutectic solvents

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Supplementary information

1.1 Calibration curves

To determine the partition coefficients of the 4 test solutes between cyclohexane and DESs calibration curves were produced for different amounts of the solute in cyclohexane. **Figure S1** shows the calibration curves of GC-FID area for the 4 test solutes. In all cases, 3 replicate measurements were made and **Figure S1** shows that the standard deviation in most cases was relatively small. The figure also shows that a good correlation was achieved with an R^2 value of 0.99 for each of the solutes.

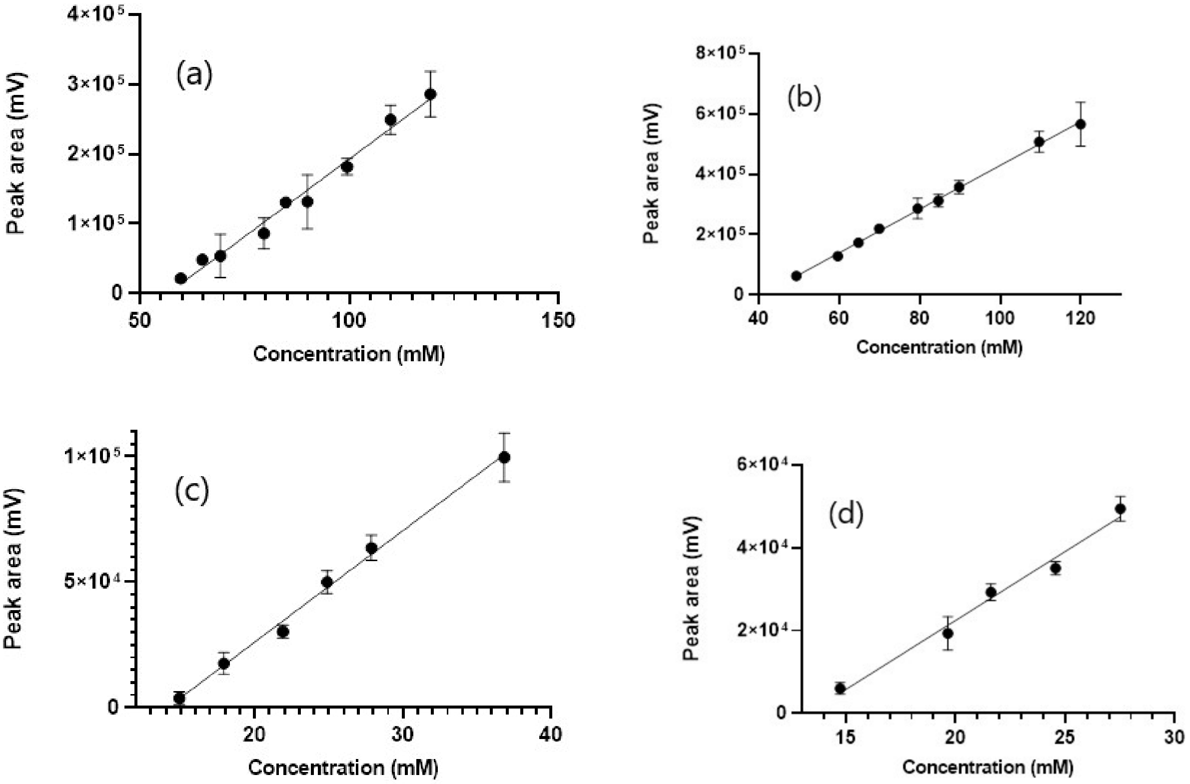

Figure S1: *Standard calibration curves of (a) butanoic acid, (b) 1-pentanol, (c) 2-pentanone and (d) ethyl acetate in cyclohaexane measured by GC-FID.*

Consistent with the GC-FID, the results show that the minimum amount of butanoic acid, 1-pentanol, 2-pentanone and ethyl acetate in cyclohexane that can be transferred to the DESs were around 59, 49, 14 and 14.4 mM respectively.

Additionally, the GC-FID showed that the retention times were found to be 2.22, 2.14 and 2.07 min for benzyl alcohol, phenol and cyclohexanol respectively. **Figure S2** displays the calibration curves of GC-FID area for the 3 test solutes.

As can be seen, the results show that the minimum amount of phenol, benzyl alcohol and cyclohexanol in cyclohexane that can be transferred to the DESs are around 5, 8 and 10 mM respectively.

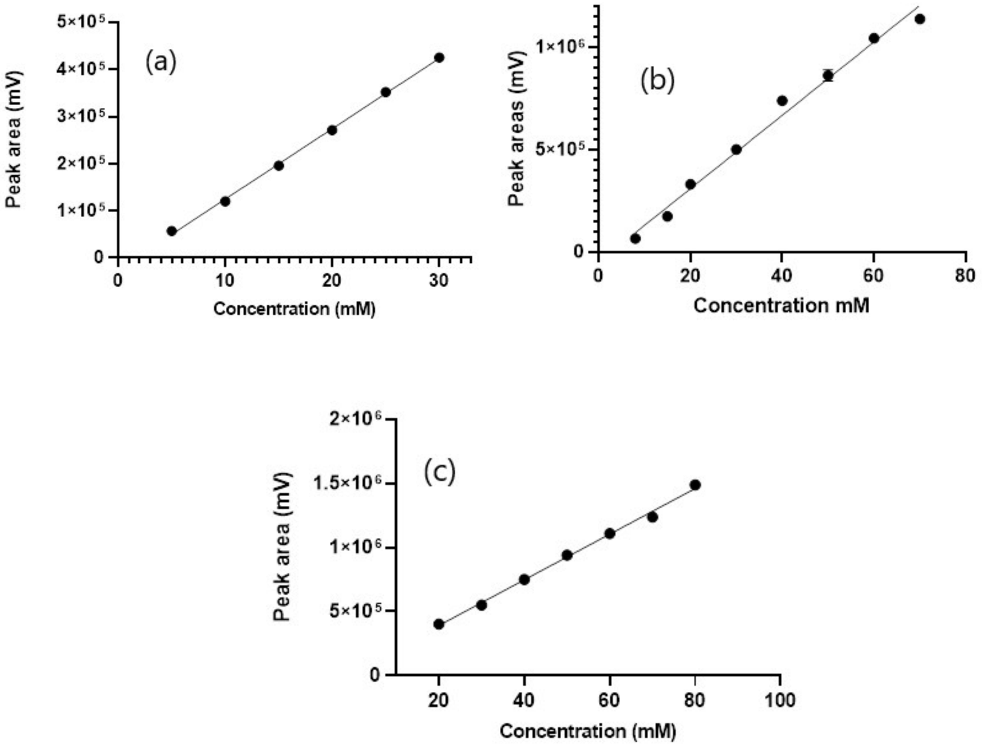

Figure S2: *Standard calibration curves of (a) phenol, (b) benzyl alcohol and (c) cyclohexanol in cyclohaexane measured by GC-FID.*

To determine the partition coefficients of the 5 tested solutes between triolein and DESs calibration curves were produced for different amounts of the solute in triolein. **Figure S3** shows the calibration curves for the extracted antioxidants. In all cases, 3 replicate measurements were made, and **Figure S3** shows that the standard deviation in most cases was relatively small. The figure also shows that a good correlation was achieved with an R^2 value of 0.99 for each of the solutes.

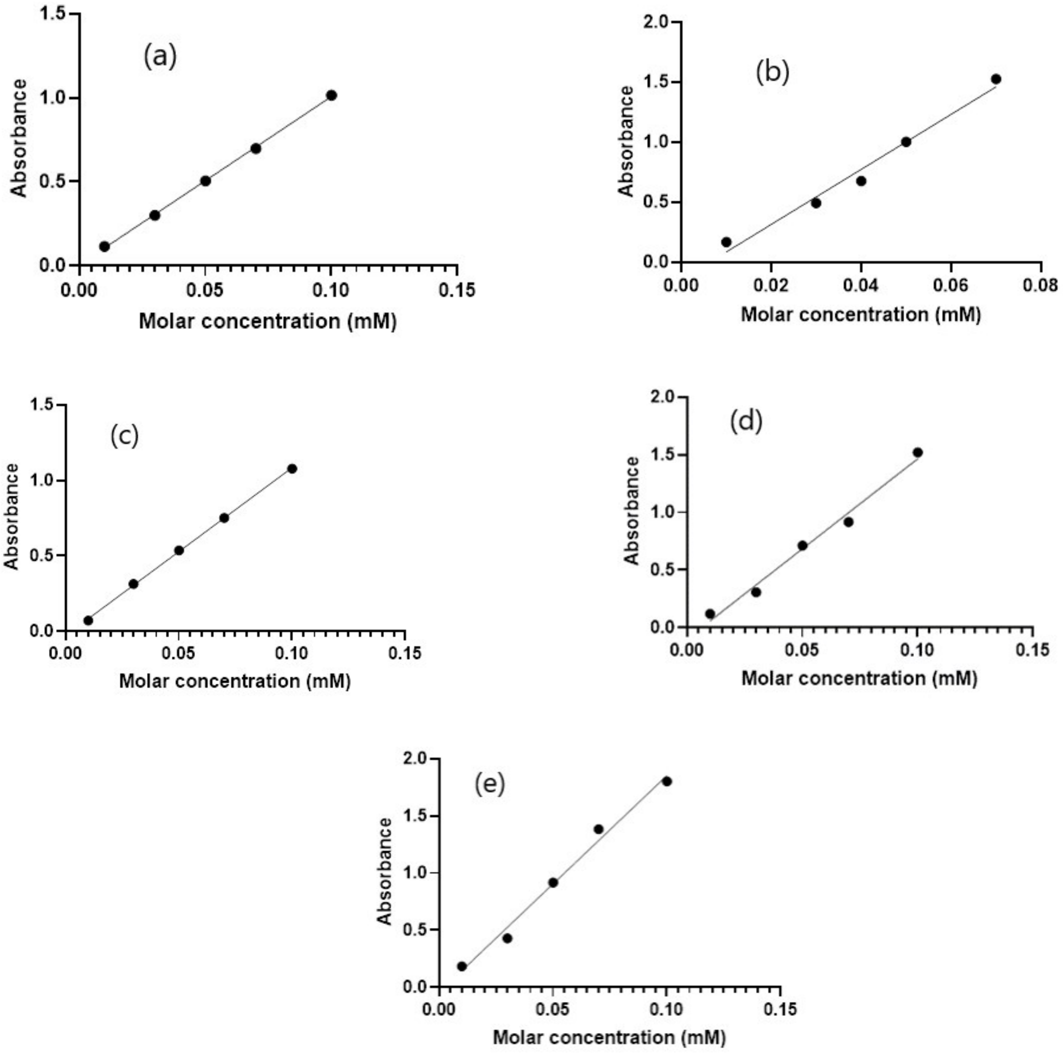

Figure S3: *Standard calibration curves of (a) tyrosol, (b) p-coumaric acid, (c) vanilic acid, (d) ferulic acid and (e) apigenin in triolein measured by UV-Vis spectrophotometry.*

After liquid-liquid extraction was carried out, the partition coefficients and then extraction efficiency were obtained using UV-visible spectroscopy and they are shown in **Table S1**.

Table S1: *Extracted phenolic compounds from triolein to Ethaline at two temperatures.*

Phenolics extracted	MW / g mol^{-1}	*pKa*	Extraction efficiency / %	
			at 25 ^{o}C	at 40 ^{o}C
Tyrosol	138.16	10.2	79 ± 1.34	92 ± 2.55
p-coumaric acid	164.16	4	84 ± 1.70	98 ± 4.13
Vanilic acid	168.15	4.16	87 ± 1.93	95 ± 3.05
Ferulic acid	194.18	4	80 ± 1.43	96 ± 3.35
Apigenin	270.24	6.63	67 ± 3.75	73 ± 6.02

Table S2: *Extraction efficiency of 1-pentanol, ethyl acetate, 2- pentanone, phenol, benzyl alcohol and cyclohexanol from cyclohexane into different DESs.*

DESs	Extraction efficiency / %	
	at 25 ^{o}C	at 40 ^{o}C
	1-pentanol	
Ethaline	55.03 ± 4.23	48.89 ± 3.62
Glyceline	30.50 ± 2.23	27.60 ± 1.81
Oxaline	41.70 ± 3.25	44.53 ± 3.50
Reline	24.05 ± 1.62	21.47 ± 1.56
DESs	***ethyl acetate***	
Ethaline	9.86 ± 1.22	17.49 ± 2.90
Glyceline	8.56 ± 1.27	15.55 ± 1.80
Oxaline	13.90 ± 1.81	18.44 ± 2.30
Reline	9.35 ± 1.37	18.16 ± 2.49
DESs	***2- pentanone***	
Ethaline	2.15 ± 0.24	3.79 ± 0.40
Glyceline	12.97 ± 1.75	17.08 ± 2.30
Oxaline	14.74 ± 2.06	17.24 ± 2.04
Reline	11.40 ± 1.58	18.84 ± 2.90
DESs	***phenol***	
Ethaline	94.11 ± 5.40	93.78 ± 4.88
Glyceline	98.70 ± 4.44	98.71 ± 3.50
DESs	***benzyl alcohol***	
Ethaline	86.62 ± 5.73	85.96 ± 4.36
Glyceline	84.27 ± 6.05	82.61 ± 4.81
DESs	***cyclohexanol***	
Ethaline	81.93 ± 6.66	79.44 ± 7.45
Glyceline	71.56 ± 4.83	67.70 ± 4.22

Process Optimisation

The extraction of natural products from one phase to another is controlled by transport of the species to the interface followed by solvation by the extracting phase. The extent of the equilibrium is controlled by the thermodynamics of solvation and obviously this is affected by the temperature of the system. The time taken for equilibrium to be set up depends on the physical parameters of the extraction process such as stirring rate and liquid viscosity. **Table S3** shows the effect of time, temperature, stirring rate and solute: solvent ratio on the amount of solute extracted. For the purposes of the experiment tyrosol was chosen as a solute as it showed the lowest partition coefficient in **Table 3** and therefore had the potential to increase its extraction efficiency by optimising the parameters. The concentration of tyrosol in triolein was chosen as 0.05 mM L^{-1}. This is similar to that found in extra virgin olive oil. The mass ratio of triolein: DES was initially chosen to be 1:1 (2g). This is clearly not a practical option, but it is one of the variables optimised below.

Table S3 shows that extending the extraction time beyond 120 min does not significantly affect the extraction of tyrosol at 40 °C showing that the system is already at equilibrium. A slight reduction in the tyrosol yield was observed when the extraction time was increased, which could be attributed to the thermal degradation of tyrosol. The obtained results are consistent with the trends reported by multiple research works, whereas the prolonging the extraction time can significantly improve the extraction of phenolic compounds, while extended extraction time in high-pressure or high temperature reactor can negatively influences extraction yields.[1, 2, 3] At 25 °C, there is a slight increase in extraction efficiency with longer times suggesting that the system may not quite be at equilibrium and this may account for some of the deviation from linearity in **Figure 1**.

The data in **Tables 4** and **S3** do, however show that at elevated temperature the system is relatively rapid to reach equilibrium. It also suggests that if the extraction were carried out at > 50 °C the partition coefficient would be about 100 i.e., effectively quantitative extraction.

Table S3 shows that variable volumetric (DESs/ triolein) ratios of 1:1, 1:2 and 1:3 have an impact on the extraction percentage of tyrosol. The value of the percentage extraction of tyrosol decreased as the Ethaline volume ratio to triolein decreased. This is attributed to the decrease in the amount of extractant available. In addition, it is anticipated that the thermodynamic equilibrium of the extraction system is also impacted by modifying the two-phase ratio. When there is a lower volume of Ethaline, equilibrium is reached at a lower concentration than when there is a greater proportion of the extractant i.e. Ethaline.[4]

This section has shown that optimisation of extraction is relatively easy given that the enthalpy for extraction is positive. Moderate extraction times, temperatures and stirring rates are required. From this perspective it appears to be an easy process to achieve. To put this work into perspective it is important to determine the Green Chemistry metrics of the process and compare them to conventional extraction methods.

Table S3: *The extraction of tyrosol from triolein to Ethaline as a function of time, temperature, stirring rate and initial tyrosol concentration.*

Time (min)	**at 25 °C**	**at 40 °C**
120[a]	79%	92%
180[a]	83%	88%
240[a]	87%	91%
DES: triolein		
1:1 [b]	79%	92%
1:2 [b]	61%	70%
1:3 [b]	53%	59%
Stir rate/ rpm		
500[c]	79%	92%
400 [c]	75%	88%
300 [c]	72%	85%
where [a] DES: triolein = 1:1 stir rate = 500 rpm: [b] t = 120 min, stir rate = 500 rpm: [c] t = 120 min, DES: triolein = 1:1		

With conventional natural product extraction, a molecular solvent is usually used which can be evaporated to yield a solid extract. The issue associated with natural product extraction using DESs is that they have very low vapour pressure and so evaporation is not an option to remove the solvent. Recent work by a French company Naturex uses a process called Eutectys™, where the DES is used as a carrier and design of a benign DES means that it remains in the final product. One example of a relatively benign DES is an equimolar mixture of betaine and lactic acid. The company has used this approach to create a range of plant extracts with antioxidant properties. In the approach of the following section, it is assumed that the DES will remain in the final product.

Green Chemistry Metrics

The thermal energy required to warm up the extraction system from the laboratory room temperature (20 °C) can be estimated using the equation:

$$Q = mC_p \Delta T \quad \textbf{(S1)}$$

where Q is the heat energy, m is the mass of the extraction phases, *Cp* is the specific heat capacity of the solvent and *ΔT* is the temperature change. The heat capacity of olive oil is 1.97 kJ/kg K and that of Ethaline is 1.1 kJ/kg K. As the extraction system is composed of two phases (i.e., DES and triolein), the thermal energy of each phase was calculated, and the total thermal energy was calculated by summing the two energies as follow

$$Q_{Total} = Q_{Triolein} + Q_{DES} \quad \textbf{(S2)}$$

In this calculation, the heat loss in the extraction system to the environment was ignored assuming good thermal insulation of the system and energy required to heat the reactor was also ignored. These two terms will be reactor specific and so for comparison sake they will be assumed to be the same for all calculations. Therefore, the energy is only required to heat the extraction phases to the specific temperature (This is clearly an over-simplification, but it is a necessary step at this stage). In addition, the energy required to operate the magnetic stirrer during extraction is needed to calculate the total energy consumption of the system. The power requirement (*P*) of the stirrer used is 10W, which operated for 120 minutes (t=2 hours) to extract a certain mass (m) of triolein and DES (i.e. DES (g) + triolein (g) = 4, 6 or 8g). As a result, the energy consumed to stir the extraction system ($E_{stirring}$) is:

$$E_{stirring} = \frac{P \times t}{m} \quad \textbf{(S3)}$$

Finally, the thermal energy was added to the energy required to stir the solvents to estimate the total energy of the extraction system as shown in **Table S3**. Romero and Brenes stated that cost of energy needed to run an extration process can be determined by multiplying the reaction time consumed by the power consumption by the average cost of the electricity (In the United Kingdom at the time of publication this is approximately 14.5p kWh^{-1}).[40] By applying the same principle, calculations were performed for the other studies to calculate the thermal energies and any other mechanical or kinetic energy consumed as shown in **Table S4**.

Table S4: *Temperature, reaction time and energy consumption and cost for the extraction of tyrosol using different extraction systems.*

Study	Extraction System	T (°C)	t (hr)	extractant Thermal Energy (kJ) $^{(2)}$	Triolein/Olive Oil Thermal Energy (kJ) $^{(2)}$	Total Thermal Energy/ (kWh) $^{(3)}$	Extraction-Assistant Method	Energy (Watt) $^{(4)}$	Mechanical Energy (kWh) $^{(5)}$	Total Energy (kWh) $^{(6)}$	Energy Cost (£kg^{-1}) $^{(7)}$
This study	Ethaline (1:1 ^{1})	25	2	2.8	4.8	4.2×10^{-3}	Stirring	10	0.02	0.02	0.07
Fernández-Bolaños et al.	Glycerol-DES	40	1	308	532	0.23	Shaking	50	0.05	0.28	0.03
	80% Methanol			700		0.34				0.39	0.04
	Water			1176		0.47				0.52	0.05
Tzia et al.	Glycerol DES + HAE	60	0.5	2640	152	0.39	Homogenization speed 12,000rpm	1050	0.525	0.91	0.67
	Water + HAE			4200		0.60				1.13	0.82
	70% Ethanol + HAE			2500		0.37				0.89	0.65
	Glycerol DES +UAE	60	0.5	2640	152	0.39	60 Hz	280	0.14	0.53	0.39
	Water + UAE			4200		0.60				0.74	0.54
	70% Ethanol + UAE			2500		0.37				0.51	0.37
	Glycerol DES + HHPAE	20	0.2	330	19	1.9×10^{-2}	600 MPa	4500	0.9	0.92	0.67
	Water + HHPAE			525		2.9×10^{-2}				0.93	0.68
	70% Ethanol + HHPAE			312.5		1.8×10^{-2}				0.92	0.67

(1): Mass ratio of DES: Triolein (2): Thermal energy = $C_p\ x\ m\ x\ \Delta T$ (3) Total thermal energy = [(extractant thermal energy + substrate thermal energy) x time]/ 36x10^{5} (4) Source: Instrument manufacturer (5) Mechanical energy (KWh) = (Energy x t)/1000 (6) Total Energy = Total thermal energy + Mechanical energy (7) Energy cost (£kg^{-1}) = (Total Energy x 14.6 p)/mass of substrate (kg).

References

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[1] L. Paniwnyk, E. Beaufoy, J. P. Lorimer and T. J. Mason., The extraction of rutin from flower buds of Sophora japonica, *Ultrason. Sonochem.* **8**, 2001, 299–301.

[2] T. Jerman, P. Trebše and B. Mozetič Vodopivec., Ultrasound-assisted solid liquid extraction (USLE) of olive fruit (Olea europaea) phenolic compounds, *Food Chem.* **123**, 2010, 175–182.

[3] B. Aliakbarian, A. A. Casazza and P. Perego., Valorization of olive oil solid waste using high pressure–high temperature reactor, *Food Chem.* **128**, 2011, 704-710.

[4] R. Julio, C. Zambra, G. Merlet, R. Cabezas, G. Correa, G. Salinas, J. González, F. Veliz and R. Lemus-Mondaca., Liquid–liquid extraction of hydroxytyrosol, tyrosol, and oleuropein using ionic liquids, *Sep. Sci. Technol.* **54**, 2019, 2895–2906.