Universidade de Aveiro

Departamento de Química

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# Extraction of Phenolic Compounds with Aqueous Two-Phase Systems

Trabalho realizado por: Ana Filipa Cláudio
Orientação: Prof. João Coutinho e Dra. Mara Freire

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# 1. Introduction



## 1.1. Scopes and Objectives:

❖ Use of aqueous two phase systems (ATPS) composed by ionic liquids (ILs) and typical inorganic salts to develop more benign extraction techniques than those used nowadays;

❖ ILs appear as potential and alternative replacements for VOCs due to their negligible vapor pressures and intrinsic character of “designer solvents”;

❖ PhCs present general attractive properties, such as their antioxidant, anti-inflammatory, anti-microbial and anticarcinogenic capacities, among others.

# 1. Introduction



## 1.2. Aqueous Two-Phase Systems (ATPS)

❖ Consist in two aqueous-rich phases mutually incompatible, containing polymer/polymer, polymer/salt or salt/salt combinations;

❖ Simple method and easiness in scale-up operations;

❖ Used to recover and separate a wide range of biomolecules;

❖ The partitioning of the biomolecule depends on the biomolecule size, surface properties, molecular weight, temperature, pH, type of inorganic salts, type of interactions involved, among others.

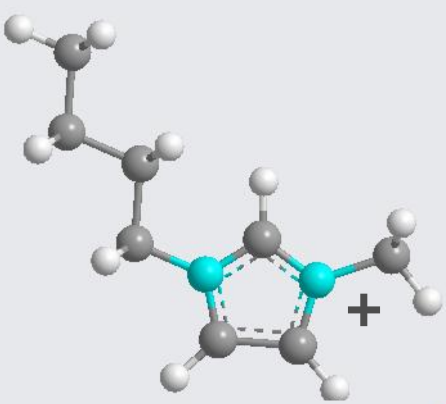
# 1. Introduction

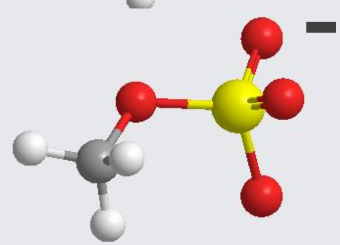


## 1.3. Ionic Liquids (ILs)

**Characteristics**

- Constituted by large and organic cations and organic or inorganic anions;
- Melting point below 100 ºC;
- Negligible flammability and vapour pressure;
- High chemical stability in a wide range of temperature;
- Easiness in recovery and recycling them;
- Most of ILs don´t denature biomolecules;
- “Benign solvents”;
- Tunnable solvents → “Designer solvents”



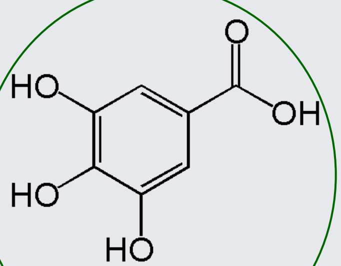

**Applications**

- Catalysis;
- Organic synthesis;
- Chemical reactions;
- Chromatographic separations;
- Extraction of metal ions;
- Separation of biomolecules.

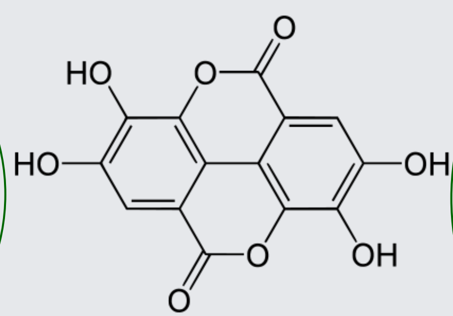
## 1.4. Phenolic Compounds (PhCs)

- Present in wood, fruits, vegetables and residues from the industrial or agricultural activities;

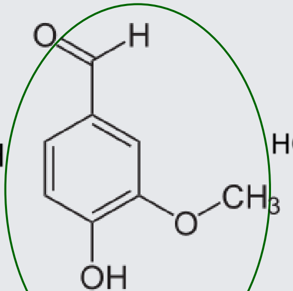
- PhCs have a special properties, such as:
  - High antioxidant capacity;
  - Ability of lowering cholesterol;
  - Depression of hypertension;
  - Protection against cardiovascular disease and human leukemia cells;
  - Toxic to bacteria.



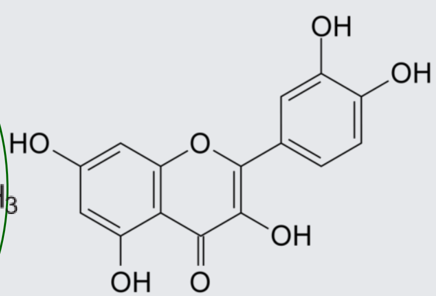
Gallic acid



Ellagic acid



Vanillin

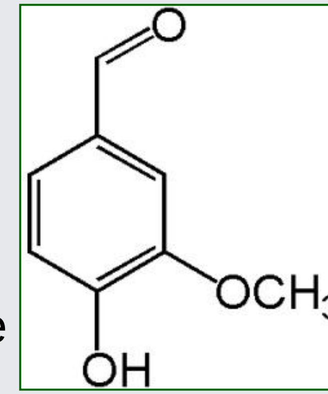


Quercetin

# 2. Extraction of vanillin in ATPS with ILs



## 2.1. Vanillin




pK$_a$= 8.2 at 298 K

Major compound of vanilla

Used in foods, beverages, pharmaceutical products and fragrance industry.

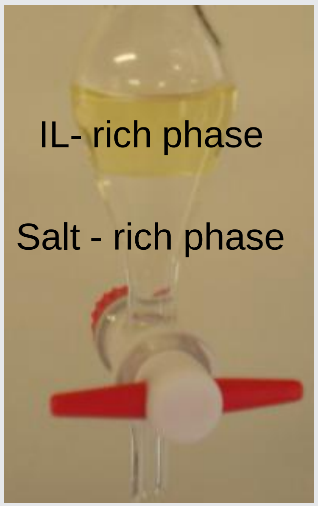
Due to the scarcity of vanillin in natural sources, the synthesis and recovery of this component is very important.

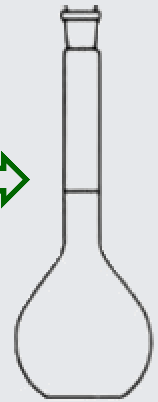



# 2. Extraction of vanillin in ATPS with ILs

## 2.2. Experimental Section

IL
+
$K_3PO_4$
+
vanillin



$$K_{\text{Van}} = \frac{[\text{Van}]_{\text{IL}}}{[\text{Van}]_{K_3PO_4}}$$

# 2.3. Results and discussion

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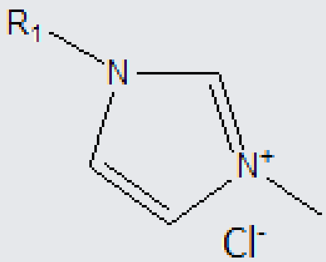
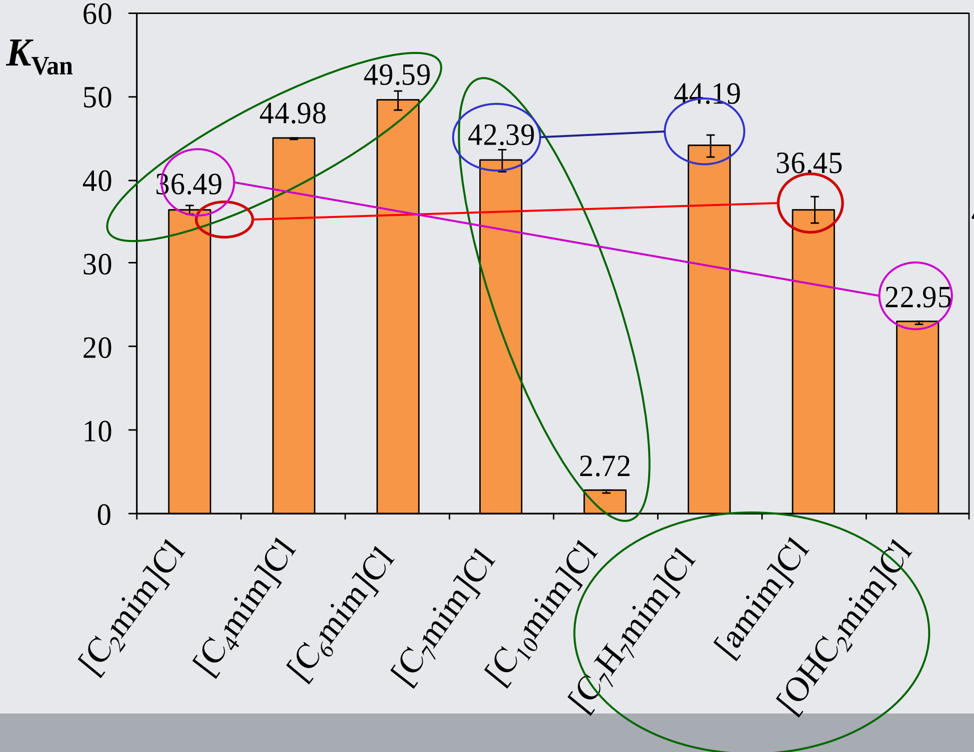
## Effect of IL Cations in Vanillin Partitioning at 298.15 K




↑ Alkyl side chains ⇒ ↓ Surface tension ⇒ ↑ $K_{Van}$

↑↑ Alkyl side chains ⇒ ↑ Dispersive interactions ⇒ ↓ $K_{Van}$




Additional double bounds, aromatic or hydroxyl groups

⇓

↑ Affinity for water ⇒ Do not improve the vanillin extraction

❖ The cation-anion interaction strengths are the major forces driving the partitioning of vanillin.

# 2.3. Results and discussion

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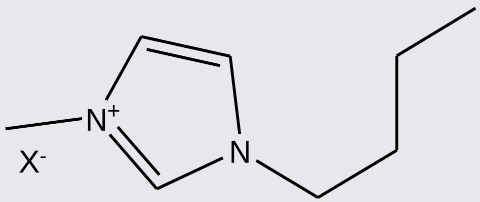
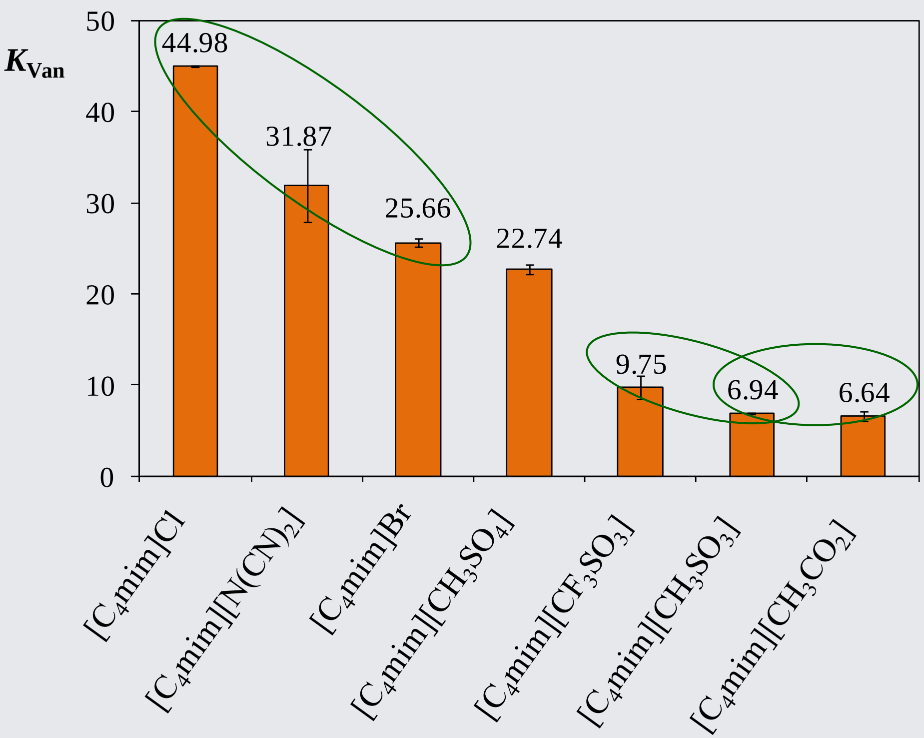
## Effect of IL Anions in Vanillin Partitioning at 298.15 K




- Vanillin partitions preferentially for IL-rich phases composed by $Cl^-$, $Br^-$, or $[N(CN)_2]^-$.

- The fluorination of $[C_4mim][CH_3SO_3]$ to give $[C_4mim][CF_3SO_3]$

$\uparrow$ Hydrophobicity $\Rightarrow$ $\uparrow$ $K_{Van}$

- $[CH_3SO_3]^-$ and $[CH_3CO_2]^-$ are strongly salting-out inducing ions

High charge density ions

$\downarrow$ $K_{Van}$

# 2.3. Results and discussion

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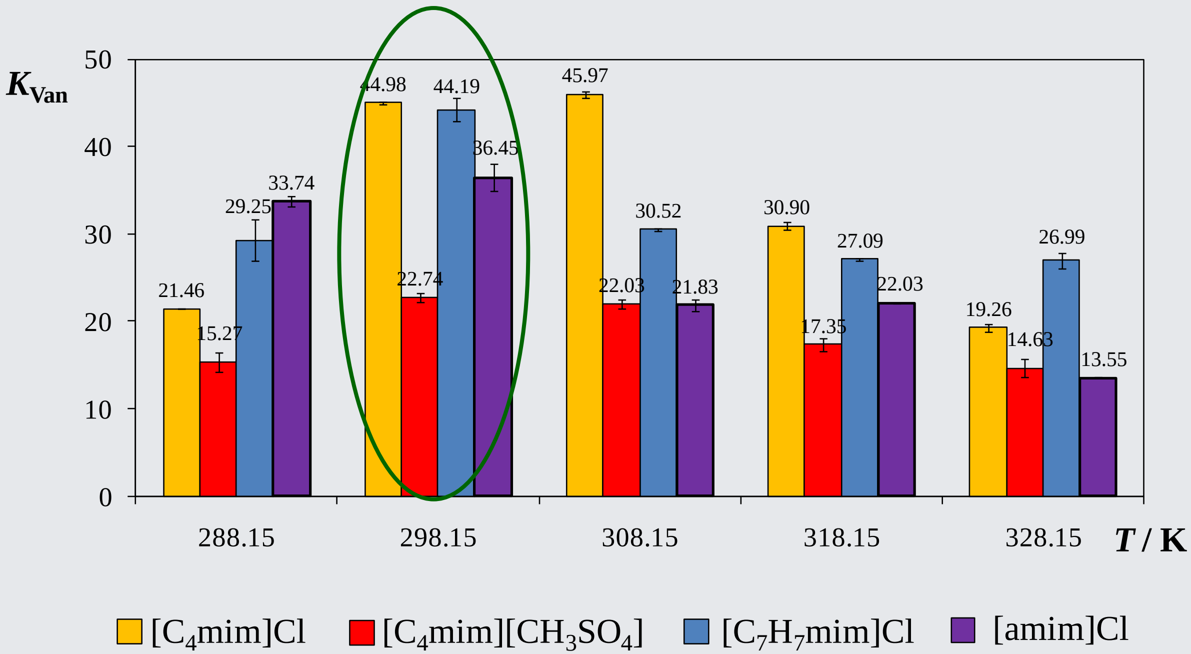
## Effect of Temperature in Vanillin Partitioning




❖ Temperature greatly influences the vanillin partitioning

Maximum values in $K_{Van}$

⇩

Energetic and entropic contributions

# 2.3. Results and discussion

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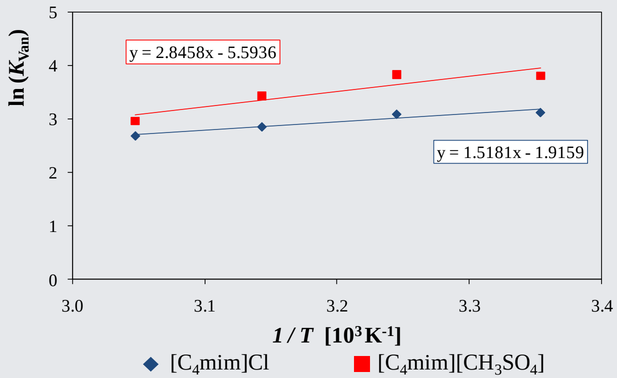
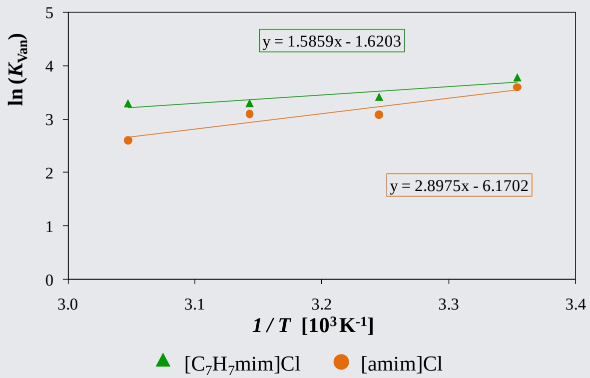
## Termodynamic parameters of transfer - Van´t Hoff approach




❖ ln($K_{van}$) *versus* $T^{-1}$ exhibits linearity

$\Delta_{tr}G_m^0 < 0$ ⇒ Spontaneous process

$$\ln(K_{Van}) = -\frac{\Delta_{tr}H_m^0}{R} \times \frac{1}{T} + \frac{\Delta_{tr}S_m^0}{R}$$

$$\Delta_{tr}G_m^0 = \Delta_{tr}H_m^0 - T\Delta_{tr}S_m^0$$

$$\Delta_{tr}G_m^0 = -RT\ln(K_{Van})$$

$\Delta_{tr}H_m^0 < 0$ ⇒ Exothermic process

⇓

Favourable vanillin-IL interactions

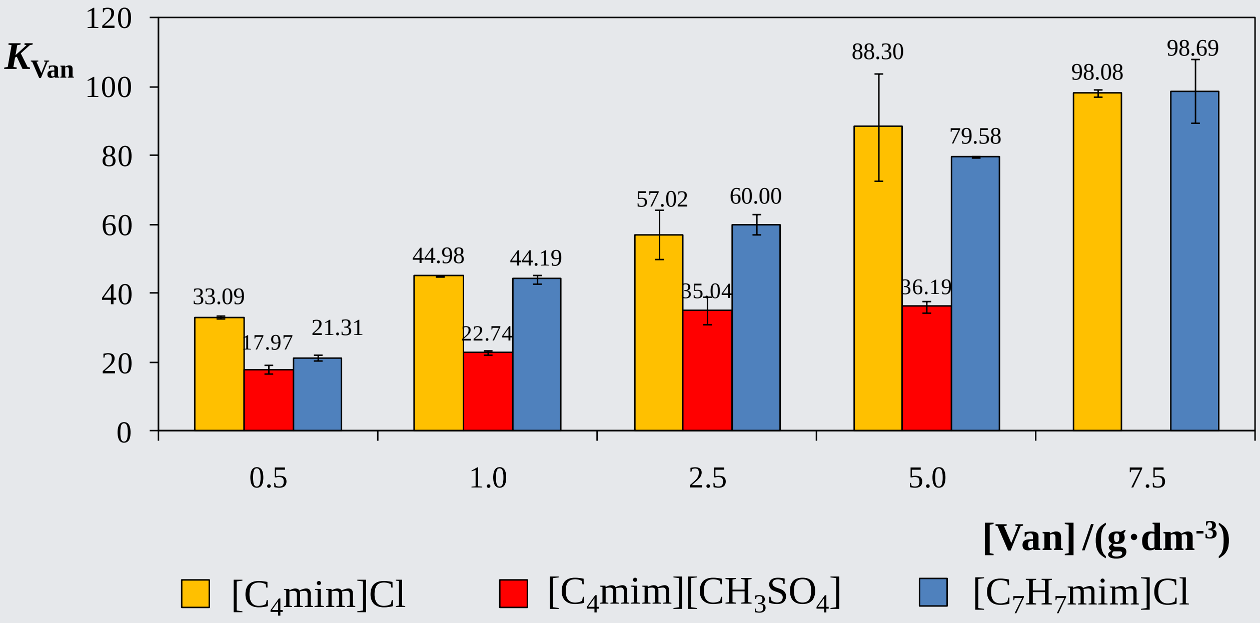
| System | $\Delta_{tr}H_m^0$ / $kJ \cdot mol^{-1}$ | $\Delta_{tr}S_m^0$ / $J \cdot mol^{-1} \cdot K^{-1}$ | $\Delta_{tr}G_m^0$ / $kJ \cdot mol^{-1}$ | $\ln(K_{Van})$ |
|---|---|---|---|---|
| $[C_4mim]Cl + K_3PO_4 + water$ | -23.66 | -46.51 | -9.79 | 3.95 |
| $[C_4mim][CH_3SO_4] + K_3PO_4 + water$ | -12.62 | -15.93 | -7.87 | 3.18 |
| $[C_7H_7mim]Cl + K_3PO_4 + water$ | -13.19 | -13.47 | -9.17 | 3.70 |
| $[amim]Cl + K_3PO_4 + water$ | -24.09 | -51.30 | -8.80 | 3.55 |

$\Delta_{tr}H_m^0$ Depends on anion nature and more complex cations

# 2.3. Results and discussion



## Effect of Concentration in Vanillin Partitioning




↑ [Van] ⇨ ↑ $K_{Van}$

❖ IL cation influences the dependency of the partitioning of vanillin with the solute content.

# 2.3. Results and discussion

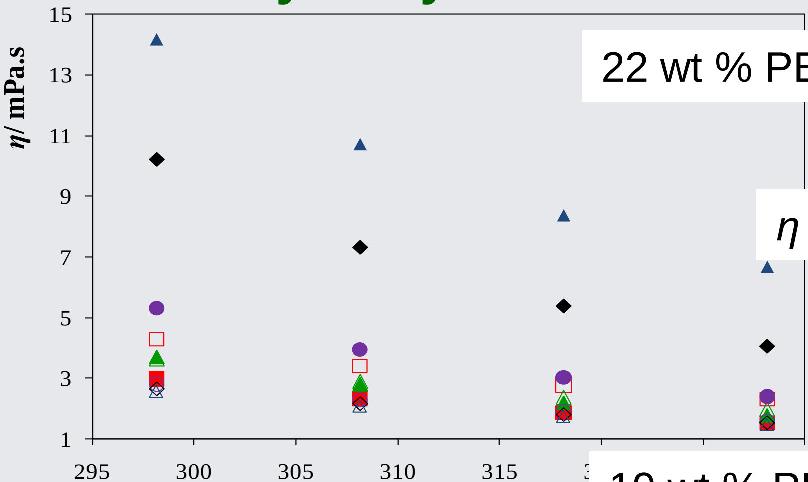


## Viscosity of Systems

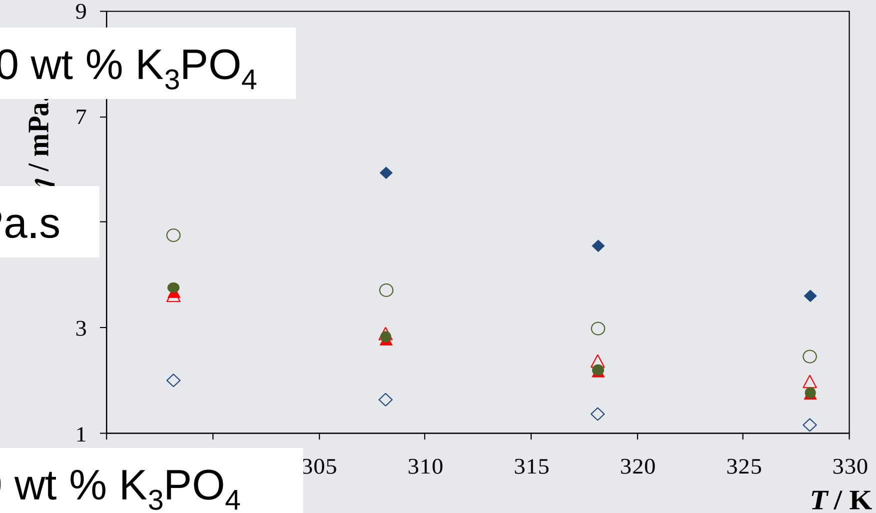
IL-rich phase (full symbols) and $K_3PO_4$-rich phase (open symbols)

22 wt % PEG2000 + 10 wt % $K_3PO_4$

$\eta$ = 18.94 mPa.s



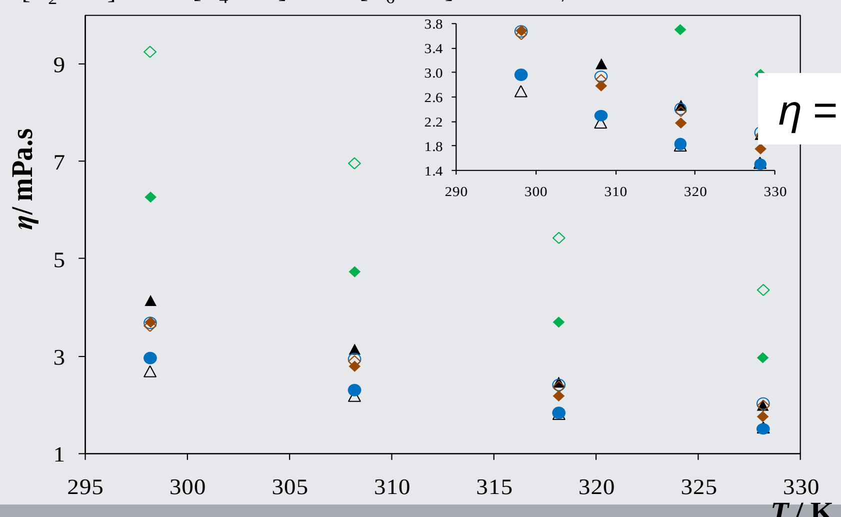

■ [C$_2$mim]Cl ▲ [C$_4$mim]Cl ● [C$_6$mim]Cl ◆ [C$_7$mim]Cl ▲ [C$_{10}$mim]Cl



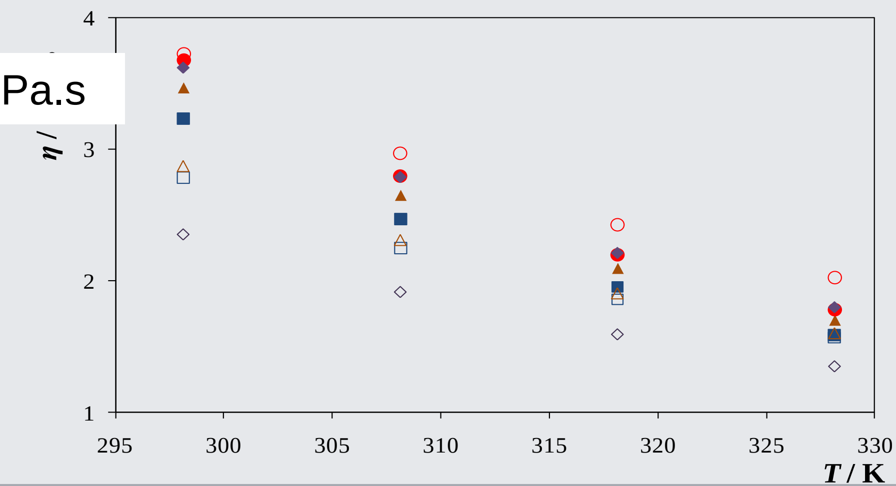

◆ [C$_4$mim][CF$_3$SO$_3$] ▲ [C$_4$mim]Cl ● [C$_4$mim][CH$_3$CO$_2$]

19 wt % PEG4000 + 9 wt % $K_3PO_4$

$\eta$ = 40.06 mPa.s




▲ [C$_7$H$_7$mim]Cl ◆ [OHC$_2$mim]Cl ● [amim]Cl ◆ [C$_4$mim]Cl




■[C$_4$mim]Br ▲[C$_4$mim][CH$_3$SO$_4$] ●[C$_4$mim][CH$_3$SO$_3$] ◆[C$_4$mim][N(CN)$_2$]

# 3. Extraction of gallic acid in ATPS with ILs

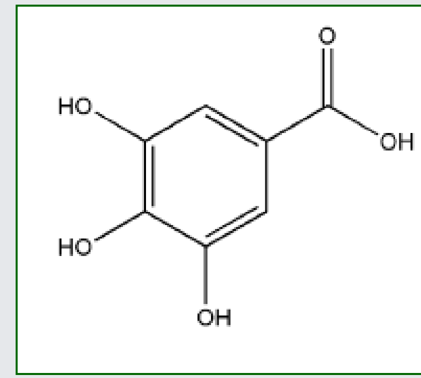


## 3.1. Gallic acid

Characterists: antioxidant, anti-inflammatory, antifungal, anti-tumor, diuretic, depurative, intestinal antiseptic, bacteriostatic, bactericidal and anti-arthritic.

Pharmaceutical, nutraceutical and cosmetic applications

Treatment of gastric tonus problems, anorexia, bloating, gases, urinary diseases gout, skin repairer and as sedative.




$pK_a$= 4.4 at 298 K

Gallic acid is present in fruits (grapes), pomegranate husk, vegetables, green and black teas, oak wood and residual waste.

# 3. Extraction of gallic acid in ATPS with ILs

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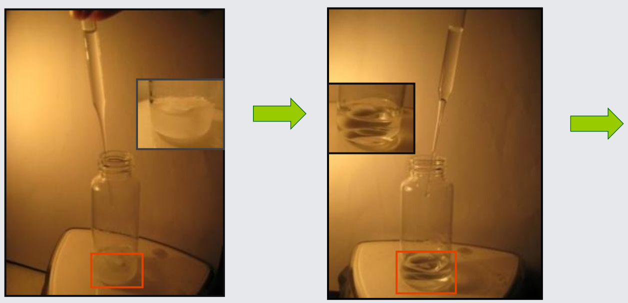
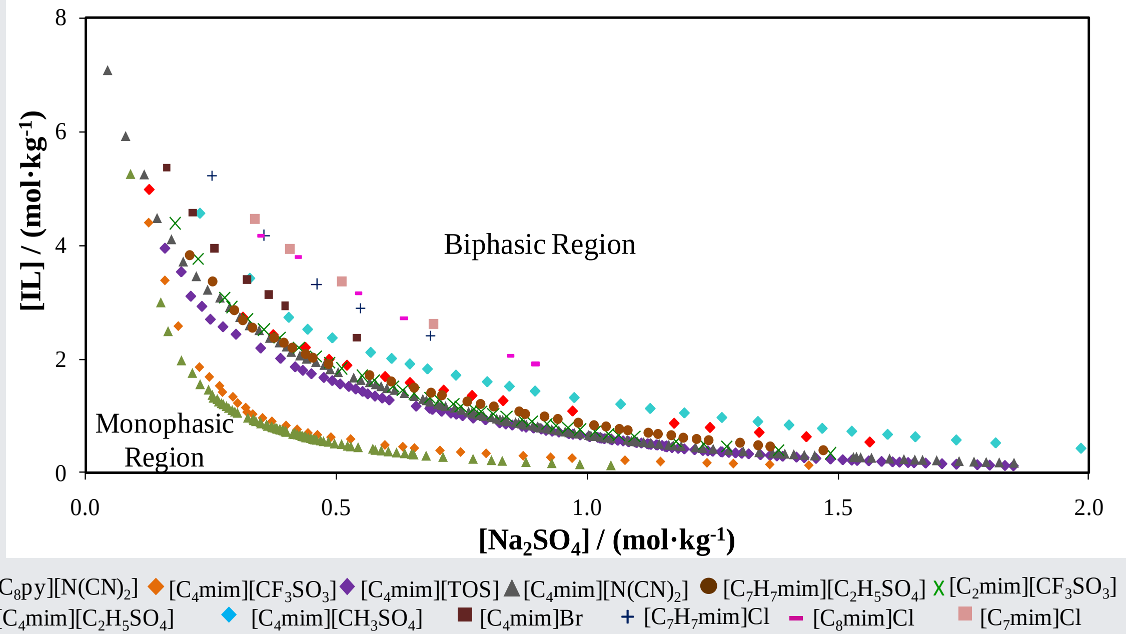
## 3.2 Experimental Section: Phase Diagrams

$Na_2SO_4 + H_2O$

$H_2O$

IL + $H_2O$






Anions or cations with more hydrophobic characteristics have a greater capacity to promote ATPS

ILs containing the anions $[N(CN)_2]^-$ and $[CF_3SO_3]^-$ or larger alkyl side chains at the cation

# 3. Extraction of gallic acid in ATPS with ILs

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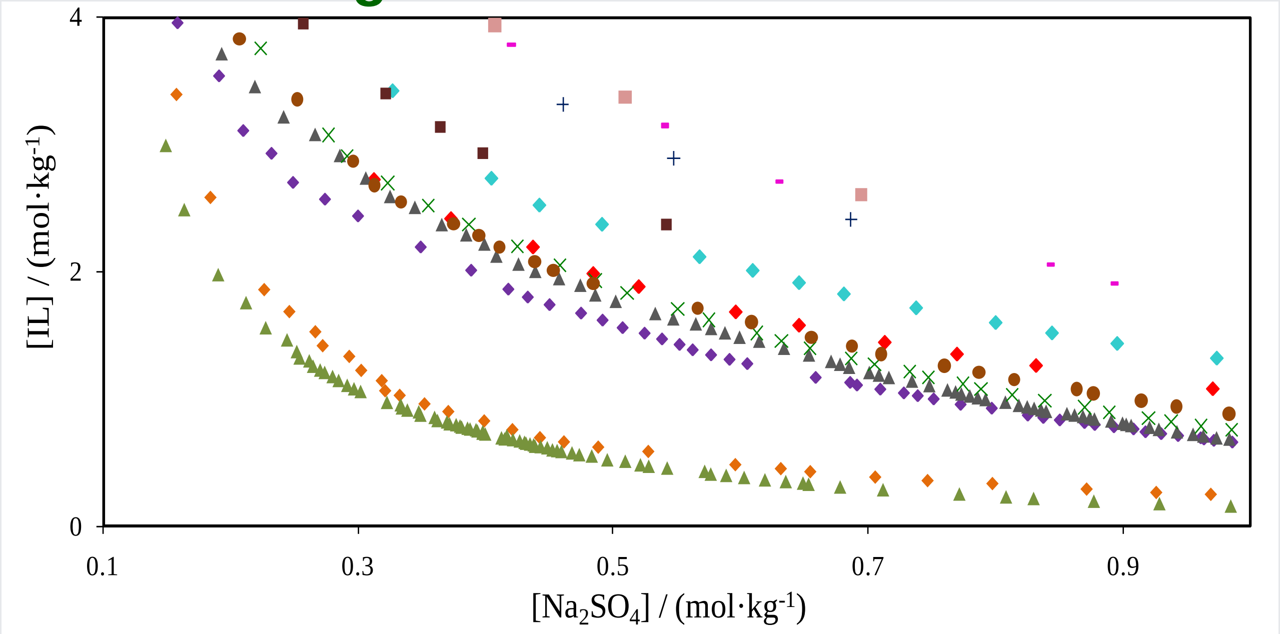
## Phase Diagrams




[C8py][N(CN)2] [C4mim][CF3SO3] [C4mim][TOS] [C4mim][N(CN)2] [C7H7mim][C2H5SO4] [C2mim][CF3SO3]
[C4mim][C2H5SO4] [C4mim][CH3SO4] [C4mim]Br [C7H7mim]Cl [C8mim]Cl [C7mim]Cl

❖ Fixing $[C_4mim]^+$

$[CF_3SO_3]^- > [TOS]^- > [N(CN)_2]^- > [C_2H_5SO_4]^- > [CH_3SO_4]^- > Br^-$

❖ Fixing $[C_7H_7mim]^+$

$[C_2H_5SO_4]^- > Cl^-$

❖↑alkyl chain in anion or cation

↑ability of the IL for ATPS formation

❖ longer alkyl chains

↑ ability of the IL for ATPS formation

❖ Higher capability by ILs to promote ATPS

with stronger salting-in inducing behavior

# 3.3. Results and discussion

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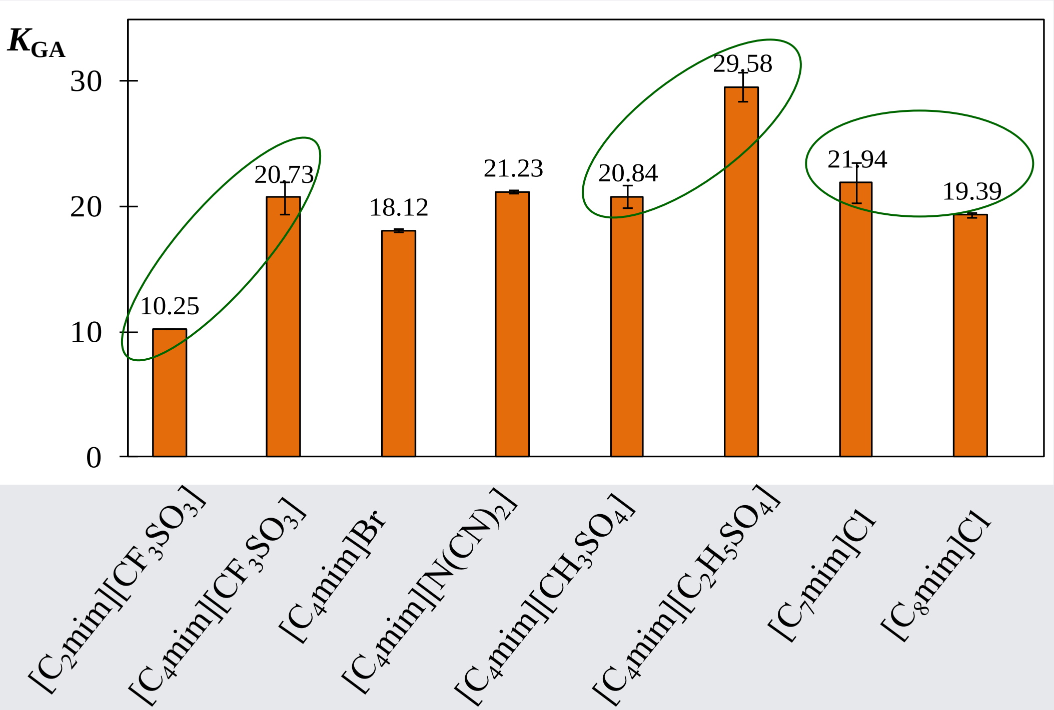
## Effect of IL ions in the acid gallic partitioning

↑ Alkyl chains cation or anion → ↓ Surface tension → ↑ $K_{GA}$

↑↑ Alkyl side chains → ↑ Dispersive interactions → ↓ $K_{GA}$



# 3.3. Results and discussion

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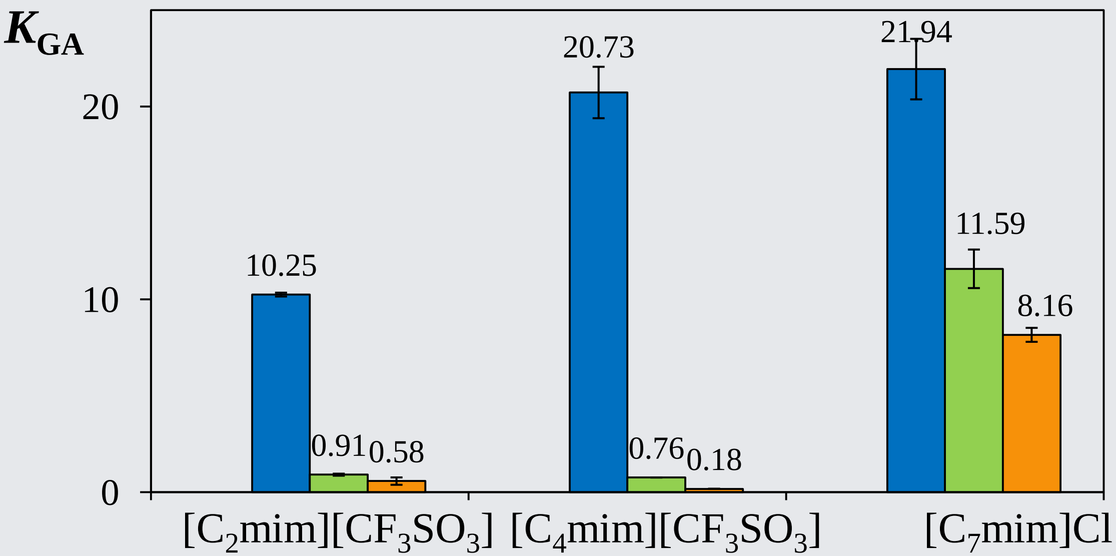
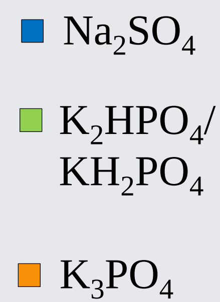
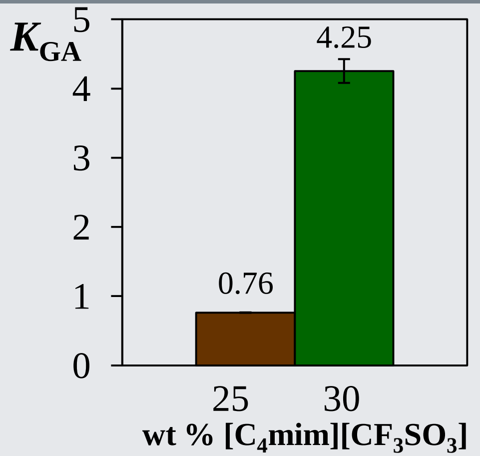
## Effect of pH in the acid gallic partitioning




❖ pH at the salt-rich phase ≈ pH at the IL-rich phase for the same system;

| IL+inorganic salt + water | | $Na_2SO_4$ | $K_2HPO_4/KH_2PO_4$ | $K_3PO_4$ |
|---|---|---|---|---|
| [C$_2$mim][CF$_3$SO$_3$] | Salt-rich phase | 3.32 | 7.28 | 13.09 |
| | IL-rich phase | 2.71 | 7.57 | 13.15 |
| [C$_4$mim][CF$_3$SO$_3$] | Salt-rich phase | 3.04 | 7.10 | 12.85 |
| | IL-rich phase | 3.12 | 7.37 | 13.10 |
| [C$_7$mim]Cl | Salt-rich phase | 4.16 | 7.22 | 12.85 |
| | IL-rich phase | 4.15 | 7.45 | 12.99 |

❖ The cation alkyl chain length does not significantly contributes for differences in pH;

❖ Changing the anion from [CF$_3$SO$_3$]$^-$ to Cl$^-$ guides to slightly differences in the acidity of both aqueous phases.

# 4. Future Work

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❖ Extend this type of study to other phenolic compounds and test more conditions in order to optimize extraction routes;

❖ Determine the pH of both rich phases for some systems already evaluated in this work;

❖ In order to better evaluate the effect of pH on the phenolic compounds extraction it will be important to extend the study for more systems based on different ILs;

❖ Use the knowledge acquired to proceed to more practical and real experiments attempting direct extractions from biomass, such as the extraction of phenolic compounds from wood, plants or wastewater effluents.

# Thank you for your attention!