Assessing Curcumin Solubility in Food-Grade Solvents

Deivis M. Carvalho, Katiuchia P. Takeuchi, Robson M. Geraldine, Celso J de Moura, Julie E. S. Carneiro & Anna Paula M. Santos

A curcumina é extraída de rizomas de açafrão (*Curcuma longa L*), usada como condimento, corante natural e tem demonstrado atividades farmacológicas. A curcumina é agente bioativo e antioxidante, mas é praticamente insolúvel em água, tendo baixa biodisponibilidade. O objetivo desse trabalho foi avaliar a solubilidade da curcumina em água, etanol, glicerol e em misturas com etanol ou glicerol em água. Para as análises de solubilidade, a curcumina em excesso foi adicionada nos solventes, homogeneizada, filtrada e, em seguida, foram determinadas as concentrações. Nos testes realizados, a curcumina apresentou maior solubilidade em glicerol e etanol do que em água e maior solubilidade em etanol do que em glicerol. As interações intermoleculares da curcumina com etanol e água e com glicerol e água proporcionaram aumento significativo da solubilidade da curcumina nas misturas dos solventes, quando comparados com a água pura. Sugere-se que soluções saturadas de curcumina em glicerol ou em etanol podem ser adicionadas em alimentos ou medicamentos de base aquosa, de modo a aumentar a concentração de curcumina solubilizada no meio.

Palavras-chave: *curcumina; solventes; solubilidade.*

Having presented pharmacological activities, curcumin is extracted from turmeric rhizomes (Curcuma longa L) and used as condiment, natural coloring. Curcumin is a bioactive agent and an antioxidant but it is practically water-insoluble, presenting thus low bioavailability. The objective of this study was to assess the curcumin solubility in water, ethanol, glycerol and mixtures with ethanol or glycerol in water. For the solubility analyses, the excess curcumin was added in the solvents, homogenized, filtered subsequently having the concentrations established. The tests conducted presented curcumin with higher solubility in glycerol and ethanol than in water and higher solubility in ethanol than in glycerol. The intermolecular interactions of curcumin with ethanol and water and with glycerol and water provided meaningful increase in curcumin solubility in the mixtures of solvents compared with pure water. Curcumin saturated solutions in glycerol or in ethanol are suggested to be added in water-based food or medicines to increase the concentration of solubilized curcumin.

Keywords: *curcumin; solvents; solubility.*

Introduction

The cultivation of saffron or turmeric (*Curcuma longa* L) has become popular in the world market, the spice is a possible alternative to synthetic colors, can be used as seasoning and presents medicinal properties [1]. The curcumin extracted from turmeric rhizome is the yellow, orange compound responsible for the coloring which also presents pharmacological activity [2]. The curcumin chemical composition in the market is commonly a mixture of three major curcuminoids (curcumin, desmethoxyl and bis-desmethoxylcurcumin) saffron-derived products in variable proportions [3]. The curcumin molecular formula is $C_{21}H_{20}O_6$, with molecular weight of 368.38 $g.mol^{-1}$. In curcumin chemical structure, the replacement of a methoxyl with a hydrogen atom originates the desmethoxylcurcumin; the replacement of both methoxyl generates the bis-desmethoxylcurcumin.

Curcumin is a powerful bioactive agent and natural antioxidant, but it is practically water-insoluble and presents low bioavailability [4-5]. It is common that a certain substance dissolves another to a limited extent. The maximum quantity of a substance at equilibrium is the substance solubility in the solvent (saturation). The reason for solubility is a natural tendency to disorder and to favor more intense forces between the substances (solute and solvent). The dissolution of a molecular substance in another is limited when molecular forces favor the state of separate substances. Similar substances are mutually soluble. Polar substances tend to solubilize polar substances, while nonpolar substances tend to solubilize nonpolar substances. Interactions such as hydrogen bounds and Van der Waals forces are also extremely important. When two substances present similar types of intermolecular forces, they tend to solubilize mutually [6]. In order to use curcumin in products and processes of both food and pharmaceutical industries, it is important to know and increase its solubility in solvents the products can receive without posing any risks to consumers' health. The objective of this study was to assess curcumin solubility in water, ethanol and glycerol as well as the increase in solubility through mixtures in ethanol or glycerol.

Methodology

The solubility analyses were conducted in room conditioned at 25°C. The solubility was tested in 3 solvents: deionized water (pH 5.8), ethanol P.A. (99.5 %), glycerol P.A. (99.8 %) and in mixtures of water and 2.5%, 5.0% and 10.0% of ethanol or glycerol. The quantity of standard curcumin (Sigma Aldrich, Reference C1386 - 65% Curcumin and 35% other curcuminoids) added was sufficient for excess content in the solvent, exceeding the saturation point. The tests were prepared in glass vials screw cap covered with aluminum foil to avoid light exposition. After curcumin was added to the solvent, the homogenization was carried out through a vibration homogenizer (Biomixer Vortex, model QL-901) for 2 to 3 minutes; subsequently the tubes were placed in a rotating homogenizer (Phoenix, model AP32, Araraquara) for 24 hours. After homogenization, the samples were filtered in filter paper (Unifil blue C42, porosity 2.0 micrometers) at atmospheric pressure [4]. The mixtures with pure glycerol were filtered in syringe filter (Millipore, porous membrane 0.22 micrometers) due to its high viscosity [5].

The methodology applied to establish the concentrations of solubilized curcumin was based on NBR 1362, 1996 [7] altering the stage of preparing the samples and creating a standard curve (absorbance / concentration). Reading were conducted through spectrophotometer (Biospectro, model SP-220, Curitiba). Each solvent or mixture of solvents without the solute was used "white". The samples filtered were analyzed in wave-length of 425 nm to quantify the solubilized curcumin mass for each type of solvent mixture of solvents.

The samples were prepared with 3 repetitions and the spectrophotometer reading were carried out in triplicate. The Analysis of Variance and the Tukey Test ($p \leq 0.05$) were performed to assess the difference in curcumin solubilization in distinguished types and mixture of solvents.

Results and Discussion

The standard curve (Figure 1) designed to establish the concentrations of solubilized curcumin presented a r^2 of 0.9992; the equation of straight line was $y = 0.1443x – 0.0317$.

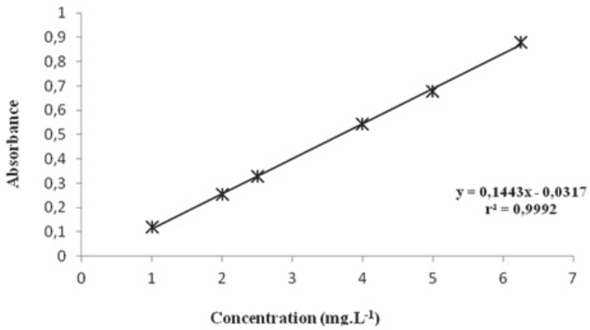

Figure 1. Curcumin standard curve, where “y” is the equation of straight line.

Meaningful difference was indicated for solubilized curcumin mass in water (1.3 $mg.L^{-1}$), ethanol (8895.9 $mg.L^{-1}$) and glycerol (45.6 $mg.L^{-1}$) when comparing pure solvents ($p \leq 0.05$). Pure curcumin presents a slow and low rate of dissolution in water due to its hydrophobicity generating a flowing powder in the surface dissolution area and reducing the contact area for the solvent [5]. Curcumin was 34 times more soluble in glycerol than in water, 6653 times more soluble in ethanol than in water and 195 times more soluble in ethanol than in glycerol. The use of curcumin is allowed as food additive included in the International Numbering System for Food Additives [8-10] as INS 100i. We aimed at assessing curcumin solubility in solvents that can be used as food additives or ingredients, such as Glycerol (INS 422), water and ethanol. Another important factor for studies with glycerol and ethanol is that both are water-soluble. Their molecules interact with curcumin molecules and water molecules acting as dispersant due to their intermediate polarity, which enables the formation of hydrogen bonds. Probably, the presence of 3 hydrogen atoms (electronegativity) in glycerol molecule exerting intramolecular attraction on hydrogen atoms making them less available for intermolecular interactions. As the oxygen is distributed among the 3 carbon atoms, the glycerol dipole moment is lower (0.96 Debye) than ethanol (1.69 Debye) with 1 hydrogen atom in just one extremity of the molecule, forming a more intense dipole. The more positive extremity presents hydrogen atoms probably more available to interact with other molecules. The intermolecular interactions of curcumin with ethanol and water and with glycerol and water acting as dispersant provide curcumin with increased solubility in mixtures of solvents compared with pure water (Figure 2). The mixture of water and 10% glycerol increased curcumin solubility in 72% and the mixture of water with 10% de ethanol increased curcumin solubility in 150%. The ethanol molecule has a more dipolar nature which probably provides it with better performance as curcumin dispersant in water than in glycerol.

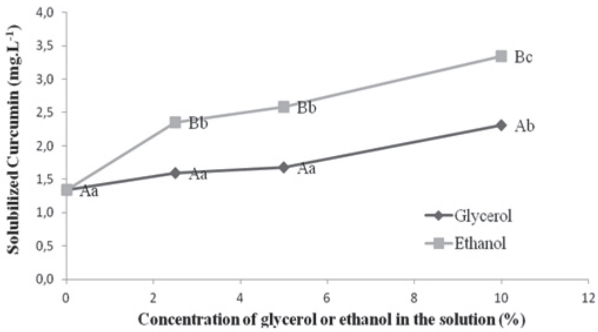

Figure 2. Concentration of solubilized curcumin in mixtures of water and glycerol or water and ethanol ($mg.L^{-1}$). Different letters (A, B) represent meaningful difference ($p \leq 0.05$) between glycerol and ethanol. Different letters (a, b, c) represent meaningful difference ($p \leq 0.05$) as glycerol or ethanol concentration increased.

Cretu, Dima and Bahrim also observed ethanol as most effective through studies with two groups of microemulsions with water, curcumin and vegetable oils, one group for ethanol as surfactant co-agent and another group for glycerol [11].

Results suggest that solutions of saturated curcumin in glycerol or ethanol can be applied in water-based food or medicines to increase the concentration of solubilized curcumin in the environment and possibly boosting its activity either as food coloring or pharmacological agent.

Conclusion

Curcumin presented higher solubility in ethanol followed by glycerol and water. The mixture of saturated curcumin and glycerol or ethanol represent meaningful increase in water solubility compared with pure curcumin in water; ethanol proved the most effective substance.

Acknowledgements

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