International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 16, Special Issue 3, 2024

Original Article

IMIDAZOLIUM-BASED IONIC LIQUIDS FOR THE SELECTIVE SEPARATION OF TOCOTRIENOL HOMOLOGUES FROM PALM FATTY ACID DISTILLATE VIA LIQUID-LIQUID EXTRACTION

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Received: 22 Nov 2023, Revised and Accepted: 10 Jun 2024

ABSTRACT

Objective: Tocotrienols have now stepped into the limelight of vitamin E research and have proven to have some exceptional benefits that are not shared by their “older” tocopherol siblings. Unlike tocopherols, tocotrienols are able to inhibit cholesterol biosynthesis, have specific neuroprotective activities stronger antioxidant effects, antihypertensive and anti-cancer. The purpose of this study was to carry out selective separation of tocotrienols homologues from Palm Fatty Acid Distillate (PFAD) by liquid-liquid extraction, using Ionic liquids (ILs) as extractants in the presence of diluent.

Methods: Four kinds of imidazolium-based ILs that used are 1-butyl-3-methylimidazolium chloride ([Bmim]Cl), 1-Butyl-3-methylimidazolium acetate ([Bmim]Ac), 1-Hexyl-3-methylimidazolium chloride ([Hmim]Cl) and 1-Ethyl-3-methylimidazolium chloride ([Emim]C]). The extraction is carried out by creating a two-phase system between ILs and PFAD in n-hexane. Quantification of extracted tocotrienols was performed using High-Performance liquid Chromatography (HPLC) with a C18 column, mobile phase methanol: water (97.5:2.5), flow rate 1 ml/min and Ultraviolet (UV) detector at 295 nm.

Results: The results showed that the concentration (extraction efficiency) of tocotrienols extracted using ILs in order were [Bmim] Ac 1611.09 mg/Kg (75.41%) and [Hmim][Cl] 1603.39 mg/Kg (75.05%), [Bmim]Cl 1523.60 mg/Kg (71.32%) and [Emim]Cl 1174.24 mg/Kg (54.96%).

Conclusion: [Bmim]Ac yielded the highest tocotrienols concentration and extraction efficiency.

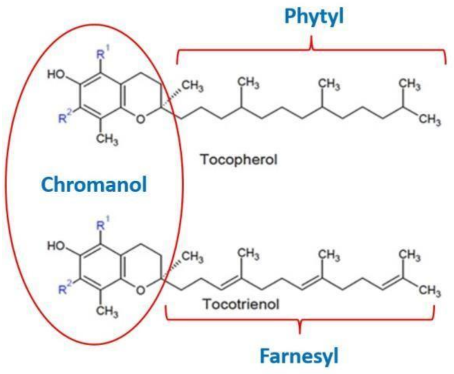
Keywords: Ionic liquids, Green solvent extraction, Palm fatty acid distillate, Tocotrienols

DOI: https://dx.doi.org/10.22159/ijap.2024.v16s3.13 Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Vitamin E is synthesized naturally in plants as four homologs, alpha, beta, gamma and delta based on the number and position of methyl groups attached to the chromanol ring (fig. 1). Tocopherols have a saturated side chain (pythyl) while tocotrienols have an unsaturated side chain (farnesyl) with three double bonds [1]. The unsaturated side chains of tocotrienols make them shorter in size, resulting in more efficient penetration into tissue [2]. Vitamin E products on the market generally contain tocopherols because there have been many studies related to these compounds. In recent years, interest in tocotrienol (vitamin E homologous) has increased due to its distinct health benefits and superiority to tocopherols [3]. Antioxidant test and free radical scavenging effects studies show that tocotrienols are superior to tocopherols, due to their better distribution in the fatty layer of cell membranes [4]. Unlike tocopherols, tocotrienols are able to inhibit cholesterol biosynthesis and also have specific neuroprotective effects [5]. The study showed that α-tocotrienol has antioxidant activity 40-60 times stronger than α-tocopherol in liver microsomes [6] and has unique anti-carcinogenic properties [7]. Interest in tocotrienols is also increasing in the food, cosmetic and clinical dermatology industries because of their light-protective effects and strong antioxidants [8]. When compared to synthetic products, natural vitamin E has greater market interest and acceptance. There is some research evidence showing that the potency of natural tocotrienols is greater than that of synthetic products [9].

Deodorizer Distillate (DD) is a by-product from the oil refining process which contains several high-value ingredients such as plant sterols, squalene and natural vitamin E. In the deodorization process, vitamin E is lost up to 15-57% in palm oil. The levels of vitamin E in the distillates can be 0.8%, and therefore, this by-product represents a potential source for the recovery of these valuable compounds [11]. Nowadays, industry refines enormous amounts of Crude Palm Oil (CPO), wherein 100 tons of CPO produces about 3.66 ton PFAD [12]. However, the availability of abundant stocks in Indonesia makes PFAD a potential raw material for producing tocotrienols.



Isomer	R¹	R²
α-	CH3	CH3
β-	CH3	H
γ-	H	CH3
δ-	H	H

Fig. 1: Chemical structures of vitamin E homologs. Adapted and modified from Ref [10]

Since tocotrienols are always present in mixtures with different structurally related compounds, particularly fatty acids, the currently developed methods for the separation of tocotrienols from DD involve multiple steps [13], such as esterification, saponification, liquid-liquid extraction, crystallization, distillation [14], ion-exchange, and adsorption [15]. Comparatively, typical organic solvents provide low selectivity (20–28% extraction efficiency), whereas adsorption and ion-exchange suffer from low-capacity outcomes and excessive solvent consumption [16]. Because of the risks associated with flammability, volatility, toxicity, and other factors, many organic solvents that adhere to "green chemical" principles are subject to regulatory restrictions. There is growing awareness of the issue and pressure to reduce or completely stop using hazardous organic solvents [17]. Another method for processing and technology developments in the recovery of valuable minor components in palm oil and other natural sources include short path distillation [18], molecular distillation [19] pressurized liquid extraction [20] and supercritical carbon dioxide extraction [21]. These techniques, however, can only be used under severe operating conditions, some with temperatures approaching 250 °C and pressure close to 65MPa, which will require high capital expenditure.

Different neoteric solvents, especially ILs, have received significant attention from both academia and industry. ILs, generally comprised of asymmetric organic cation (e. g., imidazolium, pyridinium, etc.) and anion, feature unique physicochemical properties including low vapor pressure, non-flammability, wide liquid range, flexible structure tunability and green solvent [22]. ILs have been revealed to have the strong ability of interacting with organic molecules through various mechanisms (e. g.,π-π, dispersion, ionic exchange, hydrogen bonding) [23]. Moreover, these interactions can be finely adjusted by the change of ILs's cation or anion task-specifically, thus often bringing on elevated separation efficiency as compared to the traditional organic solvents [24]. The tocotrienol homologues have different hydrogen-bond acidities that stem from their structural differences, so it is reasonable to speculate that they are likely to be separated with each other effectively by some specific kinds of ILs via hydrogen-bonding interactions mainly.

In systems that contain compounds with aromatic rings or phenolic structures, as tocotrienols in this study, imidazolium-and pyridinium-based ILs typically perform great extraction efficiency [25, 26]. Using a biphasic system of [C$_4$MIM]-based ILs and hexane, Ren and colleagues [27] reported the selective separation of α-tocopherol from its homologues (β-, γ-and δ-); in this system, the separation efficiency is linked with the H-bond basicity of the ILs. Additionally, they demonstrated how well [C$_2$MIM]-based ILs could extract α-tocopherol (with a selectivity of 29.6 and a recovery efficiency of 92%), using methyl linoleate as a model component of DD that was diluted in hexane [28]. According to recent publications, Qin *et al.* [29] used [C$_6$MIM] Acetate to successfully extract tocopherol homologs with a recovery rate of 90–98% from soybean and corn oil deodorizer distillates. This is explained by the robust π-π contact between the nitrogen-based heterocycle cations and the aromatic ring. Imidazolium-based ILs have shown to be particularly appealing and adaptable among the many ILs due to their simple accessibility, excellent stability, and simple recycling [30].

This study was designed to investigate the use of PFAD as sources of vitamin E to be extracted using the different kinds of imidazolium-based ion liquids, classified as a tocotrienol-rich fraction.

MATERIALS AND METHODS

Sample material

Palm Fatty Acid Distillate (PFAD) were contributed from one of palm oil companies in Indonesia

Chemical and reagent

1-butyl-3-methylimidazolium chloride ([C4mim][Cl]), 1-Butyl-3-methylimidazolium acetate ([C$_4$mim][Ac]), 1-Hexyl-3-methylimidazolium chloride ([C$_6$mim][Cl]) and 1-Ethyl-3-methylimidazolium chloride ([C$_2$mim][Cl]), n-hexane, methanol for liquid chromatography and sodium sulfate were purchased from merck (Darmstadt, Germany). Bidistilled water pro injection was obtained from IkaPharmindo Putramas (Jakarta, Indonesia).

Identification and quantification of tocotrienols and tocopherols in pfad

0.25 g of PFAD was put into a 5 ml volumetric flask and methanol was added. The solution was pipetted 0.5 ml into a 10 ml flask and added methanol to the mark. The final solution was filtered with a membrane diameter 0.2 micrometers and ready to be injected into HPLC. Identification of vitamin E homologs in PFAD was done by comparing with the standard.

Preparation of Ionic liquids

Weighed ionic liquid material then dissolved with methanol until dissolved and homogeneous to obtain a concentration of 0.5 M.

Quantification of total tocotrienols in PFAD

0.5 g PFAD dissolved in 5 ml of methanol, then the solution was diluted 20 times with methanol. Take 2 ml solution and filtered using a 0.2 micrometer membrane and injected into HPLC. The tocotrienols concentration is calculated based on the standard regression curve.

Extraction procedure

0.5 gram of PFAD was dissolved in 5 ml of hexane and then stirred until dissolved. Furthermore, ionic liquid with the same volume of 5 ml was added to this solution and stirred for 3 h at 200 rpm at room temperature. This two-phase liquid was then centrifuged at 3000 rpm for 3 min and two phases were formed and separated (the upper phase was n-hexane and the lower phase was ILs). Extract and raffinate samples were carefully taken with a syringe without breaking the liquid phase boundary. The ILs phase was then added sodium sulfate and reextracted with 2.5 ml n-hexane for 3 times. The re extraction method used was using a vortex for 3 min followed by centrifugation at 3000 rpm for 3 min. The hexane phase was collected and then taken 1 ml dried using nitrogen gas flow and added 2 ml methanol. Furthermore, the solution was filtered with a membrane with a diameter of 0.2 micrometers and ready to be injected into HPLC. The injected volume of the sample is 80 µl on a 20 µl loop.

HPLC analysis

The HPLC used was an Agilent 1260 infinity with quaternary pump. The column used was Atlantis C18 (5µm, 4.6 mm×250 mm). The mobile phase was methanol: water (97.5: 2.5 v/v), flow rate 1 ml/min. Tocotrienol detection was performed using a UV detector at a wavelength of 295 nm. The concentration of extracted tocotrienols was calculated using the regression curve of the homologous standard of tocotrienol. Standard concentrations made were in the range of 20-200 ppm. Extraction efficiency calculated by comparing with the concentration of total tocotrienols in PFAD.

$$\text{Extraction Efficiency (\%)} = \frac{\text{amount of tocotrienols in extract}}{\text{Total amount of tocotrienols in PFAD}} \text{ x } 100\% \ldots (1)$$

RESULTS AND DISCUSSION

Profile of vitamin E isomers in PFAD

Identification of isomer types and quantification of vitamin E concentration in PFAD must be done to be able to calculate the concentration of tocotrienols from the extraction results. Fig. 2 displays vitamin E isomers found in PFAD samples based on retention time in standard chromatograms. These include δ-, βγ-, α-tocotrienol, and α-tocopherol, with βγ-tocotrienol being the most abundant homologs. The beta and gamma homologs with the HPLC system used were unable to be separated due to their very similar polarity. Following that, these isomers were employed as reference mixtures to determine the tocotrienols total concentration from the extraction process. After measurement, the total concentration of tocotrienol in the PFAD sample was 2136 ppm.

The effect of different cation

The extraction of tocotrienols in PFAD using four types of imidazolium-based ILs is shown in table 1. By varying the number of substituent groups and the length of their alkyl chains within the imidazolium ring, particularly at the 1-and 3-positions, the imidazolium-based cation can be made more diverse. Thus, while fixing the chosen anion of Cl$^-$, the effects of the length of the substituent group's alkyl chain in the imidazolium ring on the extraction efficiency were examined. [C_2MIm]$^+$, [C_4MIm]$^+$, and [C_6MIm]$^+$are the three imidazolium-based cations that were introduced to examine the impact of the length of substituent groups in extraction efficiency. The extraction efficiency to tocotrienols with ILs with three cations and Cl$^-$ anion are listed in table 1. It is evident that as the imidazolium ring's substituent groups increase, so does the extraction efficiency, [C_6MIm]Cl>[C_4MIm]Cl>[C_2MIm]Cl (fig. 3).

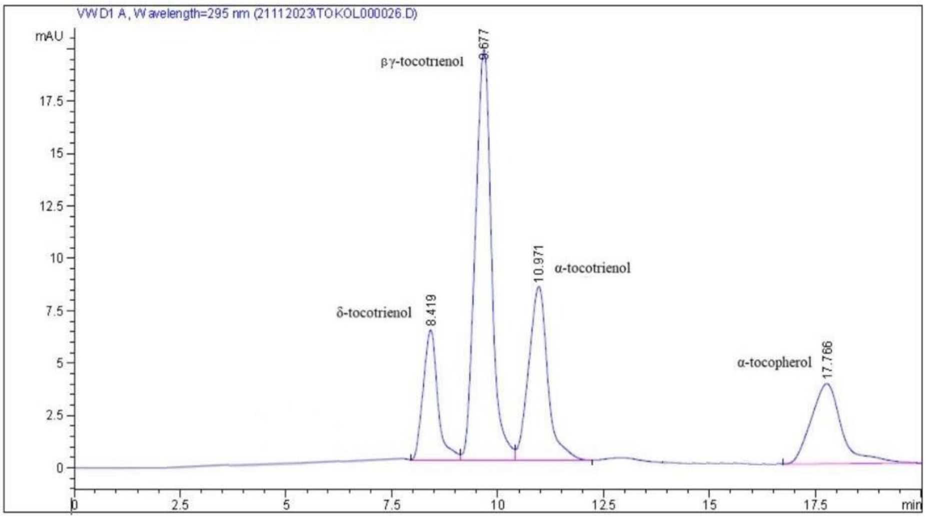


Fig. 2: Retention time of vitamin E homologues in standard chromatogram

Table 1: The extraction efficiency to tocotrienols with ILs

No	ILs	Concentration of tocotrienols (mg/Kg)	Extraction efficiency (%)±SD
1	[C_2MIm]Cl	1174.24	54.96±2.5
2	[C_4MIm]Cl	1523.60	71.32±2.1
3	[C_6MIm]Cl	1603.39	75.05±3.2
4	[C_4MIm]Ac	1611.09	75.41±2.7

Data was presented in mean+SD, n=3

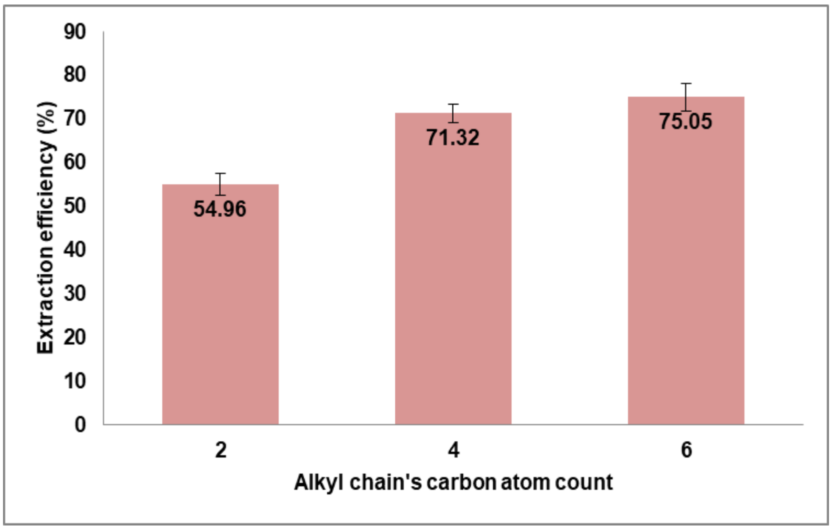


Fig. 3: Extraction efficiency of ILs with different length of chain alkyl

The results of this extraction efficiency are in line with research conducted by Qin, l *et al.* [29]. He has determined the solubility parameter δ To comprehend the increased partition coefficient of methyl linoleate and α-tocopherol from C2 to C8 (fig. 4). δ drops when the chain alkyl length changes from C2 to C8. Similarly, the difference in δ (Δδ) between ILs methyl linoleate and α-tocopherol implies that ILs made of longer-chain cations will have a greater ability to dissolve methyl linoleate and α-tocopherol [31]. As demonstrated, the van der Waals (vdW) interaction energies, Hydrogen Bond (HB) interaction energies, and corresponding Hydrogen Bond donor strength (HB_don3) nearly remain unchanged as the length of the alkyl substituent increases from C2 to C8, suggesting that neither the vdW interaction nor the hydrogen bond play a major role in the rapidly increasing partition coefficient of α-tocopherol for various imidazolium cations.

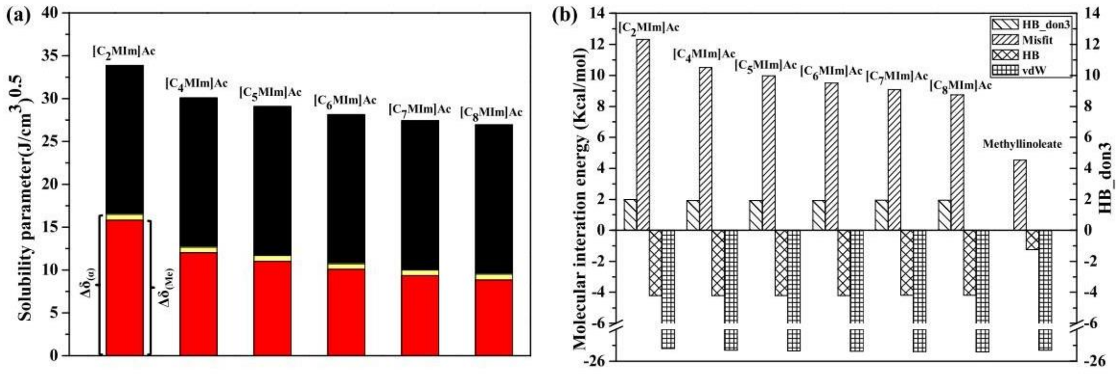


Fig. 4: Different ILs' s Solubility parameters (a) and their molecular interaction energies with α-tocopherol (b) calculated by Materials studio and COSMO-RS, respectively (Adapted with permission from Ref [29]

The effect of different anion

In general, the anion structure greatly affects how well extraction efficiency of ILs. The anions' hydrogen bond acceptor (HB_acc3), one of the most helpful characteristics for estimating the strength (basicity) of the hydrogen-bonding (HB) acceptor [32]. Consequently, it may be said that the anion's greater HB acceptor capacity is advantageous for the extraction efficiency. Furthermore, it showed that the anion with the stronger HB acceptor capacity could cause the IL to be less soluble in fatty acid, which would be advantageous for the extraction process. An anion with a greater HB accepter capacity is preferred, since it influences both the solubility of IL in the raffinate and the selectivity to α-tocopherol [29]. [C$_4$MIM]Ac has a greater Hydrogen Bond acceptor (HB_acc3) value than [C$_4$MIM]Ac (table 2), this is in accordance with the experiments that have been carried out. The extraction results of two ionic liquids that have the same cation but different anions, namely chloride and acetate, can be seen that the acetate anion produces greater extraction efficiency. Polarity is one of the most significant intrinsic characteristics of ILs since it serves as a primary indicator of the ILs ability to dissolve, and most solvents have been categorized based on their capacity to dissolve polar or charged species [33].

Therefore, an evaluation of the ILs Kamlet-Taft polarity parameters was conducted in order to ascertain the likely factor impacting their extractability. Table 2 displayed the results for the α (donating hydrogen bonds), β (accepting hydrogen bonds), and π* (dipole/polarizability). Therefore, the Kamlet-Taft polarity parameters of the ILs were useful in elucidating the likely factor impacting the extractability of ILs. Table 2 displayed the results for the α (donating hydrogen bonds), β (accepting hydrogen bonds), and π* (dipole/polarizability) of two ILs with different anions [34]. Tocotrienols is insoluble in water due to the lengthy tail alkyl groups in its structure (fig. 1). Additionally, because Tocotrienols also contains one phenolic hydroxyl group, tocols and ILs can interact through a hydrogen bond, making ILs an effective solvent for dissolving tocotrienols. With the highest α value and the greatest hydrogen-bond ability, it is expected that [C$_4$MIM]Ac will have the higher extraction efficiency.

Table 2: Predicted parameters by COSMO-RS [29] and the calculated kamlet–taft [34]

ILs	HB_acc3	S	Solubility (X) (lg	α	β	π*
[C$_4$MIM]Cl	36.6278	3.7698	-3.2343	0.32	0.95	1.13
[C$_4$MIM]Ac	38.9278	7.0219	-3.3773	0.36	0.85	1.06

Hidrogen Bond Acceptor (HB acc3), Selectivity (S), hydrogen bond donating (HBD) ability (α), hydrogen bond accepting (HBA) ability (β), and dipolarity/polarisability (π*)

CONCLUSION

Tocotrienols are hydrophobic compounds due to their long alkyl branch chains. This results in ILs that have longer alkyl chains being more capable of extracting tocotrienols from PFAD. The polarity of the anions that make up the ILs also affects the extraction results because it affects the taft chamlet parameters of the ILs formed. ILs with greater Hydrogen Bond Donating (HBD) ability (α) values result in greater extraction efficiency. [C$_4$MIM]Ac was able to produce the greatest efficiency among the other 3 imidazolium-based ILs in this study.

ACKNOWLEDGMENT

The authors would like to acknowledge Badan Pengelola Dana Perkebunan Kelapa Sawit, Ministry of Finance of Republic Indonesia for financial support throughout Grant Riset Sawit 2023 Program (PRJ-03/DPKS/DIT. IV/2023). We also thank the Research Organization for Health, National Research and Innovation Agency (BRIN) for administrative assistants.

AUTHORS CONTRIBUTIONS

Dian Maria Ulfa: Handled sample preparation: performed the experiments and managed research administration; Abdul Munim: Assisted in interpreting the results; Siti Irma Rahmawati: Supervised the research and validated the findings; Masteria Yunovilsa Putra: Supervised the research; Asep Bayu: Designed and planned the experiments; provided financial support for the research. All authors offered critical feedback and contributed to the research, data analysis, and manuscript preparation.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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