



EQUILIBRIUM THERMODYNAMICS AND MASS TRANSFER PARAMETERS ESTIMATION OF THE PRODUCTS OF SYNTHESIS OF PIPERONAL BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

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ABSTRACT: The moment technique from pulse chromatography is applied to obtain information about equilibrium and mass transfer parameters in the separation of piperonal in mixture with safrole, isosafrole and terpinolene, compounds present in the synthesis of piperonal from essential oil of *Piper hispidinervum* C.DC (long pepper). In this paper, the adsorption and mass transfer phenomena of these compounds were studied using C₁₈ as stationary phase, and ethanol/water 70/30 (v/v) at 35 °C as mobile phase. The values of partition equilibrium constant, mass transfer parameters and axial dispersion coefficients are obtained, and show the piperonal as less retained specie.

KEYWORDS: Safrole; Long pepper; Adsorption; C₁₈; HPLC.

1. INTRODUCTION

Piperonal [3,4-(methylenedioxy)benzaldehyde] is applied to obtain various products in the pharmaceutical industry (Torri *et al.*, 1984; Santos *et al.*, 2004). Its synthesis from *Piper hispidinervum* presents 84.9% purity, and other compounds such as terpinolene, safrole, *cis-trans*-isosafrole (Cremasco and Braga, 2012). One

of separation technique possible to employ in its separation from organic compounds is high performance liquid chromatography (HPLC). This technique is ruled by equilibrium and mass transfer phenomena. In adsorption process with linear isotherm, the pulse chromatography can be describe by material balances in mobile and stationary phases by appropriate differential equations, and to obtained the first (μ) and second moments (σ^2).

In this case, it is possible to obtain porosities of bed and particles, as well as mass transfer information and equilibrium partition constant (Schneider and Smith, 1968; Suzuki and Smith, 1971; Heynes, 1975; Harlick and Tezel, 2000, 2003; Cremasco *et al.*, 2001; Chihara *et al.*, 2005). The first and second moment from pulse chromatography are (Cremasco and Wang, 2012), respectively,

$$\mu = \frac{L}{u} \left[1 + \left(\frac{1 - \varepsilon}{\varepsilon} \right) K \right] + \frac{t_0}{2} \quad (1)$$

$$\begin{aligned} \sigma^2 = & \left(\frac{2L}{u} \right) \left(\frac{E_b}{u^2} \right) \left[1 + \left(\frac{1 - \varepsilon}{\varepsilon} \right) K \right]^2 + \\ & + \left(\frac{2L}{u} \right) \left(\frac{1 - \varepsilon}{\varepsilon} \right) K^2 \left(\frac{d_p}{6k_f} + \frac{d_p^2}{60D_{eff}} \right) + \frac{t_0^2}{12} \end{aligned} \quad (2)$$

with

$$K = \varepsilon_p + (1 - \varepsilon_p)k_p \quad (3)$$

and (Piatkowski *et al.*, 2003)

$$D_{eff} = \varepsilon_p D_p + (1 - \varepsilon_p)k_p D_s \quad (4)$$

with: L , effective length column; E_b , axial dispersion coefficient; u , liquid interstitial velocity; k_f , film mass transfer coefficient; D_p , pore diffusion coefficient; D_s , surface diffusion coefficient; D_{eff} , effective diffusion coefficient; ε , bed porosity; ε_p , adsorbent porosity; d_p , adsorbent particle diameter; k_p , partition equilibrium constant. The values of free diffusion (D_{AB}) can be calculated by appropriated correlation (Cremasco, 2015), such as Siddiqui and Lucas' equation (1986):

$$D_{AB} = 2.98 \times 10^{-7} \left(\frac{T}{V_{bA}^{0.5473} \mu^{1.026}} \right) \quad (5)$$

where T is absolute temperature (K); V_{bA} , molar volume at normal boiling point ($\text{cm}^3 \text{mol}^{-1}$); dynamic viscosity (cP). The pore diffusion and convective mass transfer coefficients from Mackie and Meares (1955) expression (Piatkowski *et al.*, 2003) and Wilson and Geankoplis (1966), respectively,

$$D_p = \frac{\varepsilon_p}{(2 - \varepsilon_p)^2} D_{AB} \quad (6)$$

$$\frac{d_p k_f}{D_{AB}} = \frac{1.09}{\varepsilon} \left(\frac{\varepsilon u d_p}{D_{AB}} \right)^{1/3} \quad (7)$$

The axial dispersion coefficient can be calculated by correlations present in Literature, such as that ones presented in Table 1 (Starquit, 2004). From Equations 1 and 2 it is possible to write (Ramos and Cremasco, 2015):

$$\gamma = \alpha u + \beta \quad (8)$$

With

$$\alpha = 2 \left(\frac{1 - \varepsilon}{\varepsilon} \right) \frac{1}{K} \left[1 + \left(\frac{\varepsilon}{1 - \varepsilon} \right) \frac{1}{K} \right]^{-2} \left(\frac{d_p^2}{60 D_{eff}} \right) \quad (9)$$

and

$$(10)$$

$$\beta = 2 \left(\frac{E_b}{u} \right)$$

Table 1. Equations for E_b (based on Starquit, 2004).

Author	Equation	Observation
Chung and Wen (1968)	$\frac{E_b}{\varepsilon u d_p} = \frac{\varepsilon}{0.2 + 0.0011 Re_p^{0.68}} \quad (11)$	$Re_p = \frac{\varepsilon u d_p}{\nu}$ $0,001 < Re_p < 0,1$
Koch and Brady (1985)	$\frac{E_b}{\varepsilon u d_p} = \varepsilon \left[\frac{3}{4} + \frac{\pi^2}{6} (1 - \varepsilon) \ln(Pe_{M_p}) + \frac{1}{Pe_{M_p}} \right] \quad (12)$	$Pe_{M_p} = \frac{\varepsilon u d_p}{D_{AB}}$ $Pe_{M_p} \gg 1$
Gunn (1987)	$\frac{E_b}{\varepsilon u d_p} = \left(\frac{Z_p (1-p)^2 + Z_p^2 p (1-p)^3 (e^{-q} - 1)}{\tau Pe_{M_p}} \right) + \frac{\varepsilon}{\tau Pe_{M_p}} \quad (13)$ with $Z_p = \frac{Pe_{M_p}}{4\alpha_l^2 (1-\varepsilon)}$; $q = \frac{1}{p(1-p)Z_p}$; $p = 0.17 + 0.33e^{(-24/Re_p)}$; $\alpha_l = 2.405$ e $\tau = 1.4$	$0.03 < Re_p < 500$
Athayle et al. (1992)	$\frac{E_b}{\varepsilon u d_p} = \left(\frac{Pe_{MP}}{1-\varepsilon} \right)^{1/6} \quad (14)$	$7 < Pe_{M_p} < 320$ $Re_p < 1$

The partition equilibrium constant, k_p , is obtained from the first moment by Equation 1 as function of interstitial velocity (u), or (Schulte and Epping, 2005):

$$t_R = \frac{L}{\varepsilon u} [\varepsilon_t + (1 - \varepsilon_t)k_p] \quad (15)$$

In this work, the strategy of calculus, stationary phase and experimental system are those ones founded in Ramos and Cremasco (2015). While these authors employed the mobile phase composed by acetonitrila and water at 25 °C; ethanol and water at 35 °C is the mobile phase used in the present work. Thus, this work intends to obtain the values of partition equilibrium constant (k_p), as well as mass transfer parameters D_{eff} , D_s , E_b under condition of infinite dilution to piperonal, safrole, isosafrole and terpinolene.

2. MATERIALS AND METHODS

The experiments were done in chromatograph Shimadzu, with system controller, detector UV and two pumps, models CBM-20A/UFLC. Analytical column (25 cm x 0.46 cm) and semi-preparative column (25 cm x 1.00 cm) were used, with silica C₁₈ Vydac 150HC, particle size 20 μm, particle porosity 0.357, as stationary phase. The total porosity of the analytical and semipreparative columns are 0.686 and 0.593 (Ramos and Cremasco, 2015).

The standards of piperonal (99%) and safrole (99.7%) were obtained from Sigma-Aldrich, USA; the isosafrole (99.5%), ChemService, USA; terpinolene (>85%), in Fluka, USA. Mobile phase was composed by ethanol, grade HPLC, obtained from J. T. Baker, USA and water Milli Q (18.2 mΩ), whose ratio was 70/30 (v/v). Solutions were injected in chromatographic system at 35 °C and wave length 245 nm.

The partition equilibrium constant and mass transfer parameters have been estimated from pulse method with solution 0.20 g L⁻¹ of the mixture piperonal/safrole/terpinolene. All the injections were 20 μL and flow rates were 0.6-1.4 mL min⁻¹ in analytical column and 4.0-6.0 mL min⁻¹ in semi-preparative column (Ramos and Cremasco, 2015). The molecular diffusion coefficient (Table 2) values were calculated from Equation 6.

Table 2. Free diffusion coefficients in ethanol-water at 35 °C.

Compound	piperonal	safrole	isosafrole	terpinolene
D_{AB} (cm ² s ⁻¹)	72.21 x 10 ⁻⁵	60.03 x 10 ⁻⁵	54.86 x 10 ⁻⁵	43.42 x 10 ⁻⁵

3. RESULTS AND DISCUSSION

3.1 Partition Equilibrium Constant

By straight angular coefficient, t_R versus $L/\epsilon u$, from Equation 15 it is possible to obtain partition equilibrium constant, whose values are in the Table 3. The results presented in this table show that piperonal is the less retained compound. Besides, the selectivity ($\alpha = k_{pj}/k_{p1}$) results a good separation between piperonal and other components.

Table 3. Partition equilibrium constants.

Compound	k_p	R^2	α_{j1}
piperonal (1)	0.512	0.9997	–
safrole (2)	2.586	0.9997	5.051
isosafrole (3)	2.923	0.9996	5.709
terpinolene (4)	8.408	0.9996	16.422

component j: 2, 3, 4.

3.2 Determination of Axial Dispersion and Mass Transfer Coefficients

Effective diffusion and axial dispersion coefficients were obtained from slope and intercept of straight line described by Equation 8. The results are presented in Table 4. The linear relationship of γ versus u to piperonal ($R^2 = 0.9857$), safrole ($R^2 = 0.9845$), isosafrole ($R^2 = 0.8950$), and terpinolene ($R^2 = 0.8912$). Pore diffusion

coefficients, D_p , present in Table 4, was calculated from Equation 6. Surface diffusion coefficient D_s has been calculated from Equation 4, considering D_p in Table 4. Due to magnitude of D_s , it is cannot negligible when someone considers to model the adsorption phenomenon in similar case of this work.

Table 4. Mass transfer parameters: ethanol/water at 35 °C.

Compound	D_p (cm ² s ⁻¹)	D_{eff} (cm ² s ⁻¹)	D_s (cm ² s ⁻¹)	E_b (cm ² s ⁻¹)
piperonal	9.55 x 10 ⁻⁷	5.93 x 10 ⁻⁶	7.64 x 10 ⁻⁷	3.81 x 10 ⁻⁷ u
safrole	7.94 x 10 ⁻⁷	1.32 x 10 ⁻⁶	6.26 x 10 ⁻⁷	4.00 x 10 ⁻⁷ u
isosafrole	7.26 x 10 ⁻⁷	1.94 x 10 ⁻⁶	8.95 x 10 ⁻⁷	6.52 x 10 ⁻⁷ u
terpinolene	5.74 x 10 ⁻⁷	2.63 x 10 ⁻⁶	4.49 x 10 ⁻⁷	5.65 x 10 ⁻⁷ u

The experimental results for axial dispersion coefficient can be compared with that ones showed in Table 1. Considering that, in this paper, the Reynolds number varies from 1.1 x 10⁻² up 1.6 x 10⁻², Table 5 presents this comparison by relative mean deviation, or (Ramos and Cremasco, 2015).

$$RMD = \left(\frac{E_{bexp.} - E_{bmodel}}{E_{bmodel}} \right) \times 100\% \quad (9)$$

Table 5. Relative mean deviation for E_b experimental (%).

	piperonal	safrole	isosafrole	terpinolene
Chung and Wen (1968)	- 3.15	- 7.84	- 43.45	- 34.75
Koch and Brady (1985)	- 46.92	- 43.40	- 63.43	- 52.30
Gunn (1987)	- 16.72	- 17.32	- 48.23	- 37.17
Athayle et al. (1992)	- 0.46	- 2.32	- 39.16	- 27.01

The results presented in Table 5 show the Athayle *et al.* (1992) as the correlation indicate to describe the values of axial dispersion coefficient for conditions studied in this work. Similar conclusion was obtained by Ramos and Cremasco (2015) using different mobile phase.

In order to analysis the mobile phase effect on mass transfer parameters, it is presented the Table 6, founded in Ramos and Cremasco (2015), that used acetonitrila/water (70/30, v/v) at 25 °C as mobile phase.

Table 6. Mass transfer parameters: acetonitrile/water at 25 °C (Ramos and Cremasco, 2015).

Compound	D_p (cm² s⁻¹)	D_{eff} (cm² s⁻¹)	D_s (cm² s⁻¹)	E_b (cm² s⁻¹)
piperonal	21.50 x 10 ⁻⁷	1.66 x 10 ⁻⁶	15.88 x 10 ⁻⁷	3.45 x 10 ⁻⁷ u
safrole	17.87 x 10 ⁻⁷	2.80 x 10 ⁻⁶	10.72 x 10 ⁻⁷	3.49 x 10 ⁻⁷ u
isosafrole	16.33 x 10 ⁻⁷	3.01 x 10 ⁻⁶	10.93 x 10 ⁻⁷	4.16 x 10 ⁻⁷ u
terpinolene	12.93 x 10 ⁻⁷	5.47 x 10 ⁻⁶	6.31 x 10 ⁻⁷	4.00 x 10 ⁻⁷ u

Comparing Table 4 with Table 6, the effect of mobile phase on dispersion axial doesn't present a big difference between both mobile phases, indicating the majority effect ruled by eluent velocity. However, despites on temperature influence, the crucial effect lies in diffusities. The high values presents by acetonitrile/water at 25 °C is due to viscosity effect of the solution, because while ethanol/water at 35 °C solution has $\mu = 1.387$ mPa.s; acetonitrile/water at 25 °C solution has $\mu = 0.609$ mPa.s.

4. CONCLUSION

The use of silica C₁₈, particle size 20 µm, particle porosity 0.357, and a solution of ethanol/water 70/30 (v/v) at 35 °C as mobile phase can be employed in the separation of piperonal from a mixture of safrole, isosafrole and terpinolene. Besides, the present work shows that is possible to use the moment method from pulse chromatography, since the adsorption can be describe by linear isotherm to obtain information of the thermodynamics equilibrium and mass transfer.

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