Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/jopr

Original Article

Total and partial solubility parameters prediction: Lornoxicam in individual solvents

Meena Kharwade [a,*], *C.V.S. Subrahmanyam* [b], *P.R. Sathesh Babu* [c]

[a] *Assistant Professor, Department of Pharmaceutics, Gokaraju Rangaraju College of Pharmacy, Bachupally, Hyderabad 500090, Andhra Pradesh, India*

[b] *Principal and Professor, Department of Pharmaceutics, Gokaraju Rangaraju College of Pharmacy, Bachupally, Hyderabad 500090, Andhra Pradesh, India*

[c] *Professor, Department of Pharmaceutics, Gokaraju Rangaraju College of Pharmacy, Bachupally, Hyderabad 500090, Andhra Pradesh, India*

ARTICLE INFO

Article history:
Received 12 September 2012
Accepted 14 December 2012
Available online 15 June 2013

Keywords:
Lornoxicam
Solubility
Flory–Huggins size correction
Partial parameters

ABSTRACT

Background: The solubility behavior of lornoxicam was used to predict its solubility parameter in untested solvents of several chemical classes varying from nonpolar to highly polar in nature.

Methods: Supersaturated solution of lornoxicam was shaken in a water bath for 72 h at 25 °C. The drug content was determined after attaining the equilibrium. The extended Hansen's method was applied for analyzing the solubility datum and partial solubility parameters were obtained for knowing the solute–solvent interaction. The method applied regression analysis of logarithm of the experimental mole fraction solubility of the drug against the partial solubility parameters of the solvent.

Results: A correlation was up to 90% using Flory–Huggins size correction term B, in the prediction of lornoxicam solubility. The four parameter approach involving proton-donor and proton-acceptor parameters was used in fitting the solubility data (R^2 = 84%). Further, the 'B' term coupled with four-parameter approach was result in 2% improved in the correlation. The total solubility parameter obtained by this method was 11.10 H, which was closer to the value obtained by Van Krevelan method (11.69 H).

Conclusion: The ensuing partial solubility parameters obtained are δ_{2d} = 9.03 H; δ_{2P} = 5.40 H; δ_{2a} = 3.27 H; δ_{2b} = 1.93 H gives insights into the interaction capabilities of the drug. As $\delta_{2a} > \delta_{2b}$, proves lornoxicam is a Lewis acid i.e. a better proton donor which are in favor with its chemical structure. By various methods of datum analysis, the solubility parameter of lornoxicam was consigned at 11.10 H.

1. Introduction

Solubility parameter of drug molecules has received considerable interest by the pharmaceutical scientist.[1] The solubility parameter, δ_T, is an intrinsic physicochemical property of a substance, helps in explaining the interaction between drug and solvent molecules and in selecting the right solvent for optimum level of solubility in preformulation. The solubility

* *Corresponding author*. Tel.: +91 9989483660; fax: +91 4023040860.
E-mail address: meenakharwade@yahoo.com (M. Kharwade).

0974-6943/$ – see front matter
http://dx.doi.org/10.1016/j.jopr.2012.12.004

parameter has been used to explain fast prediction of basic properties of materials, solvent selection for organic reactions, selection of polymer surfactant combination, prediction of adhesion of film coating to tablets, dosage from technology and design,[2–5] correlation with anti bacterial activity of antibiotics,[6,7] selection of co-formers for co-crystal,[8] and HPLC.[9]

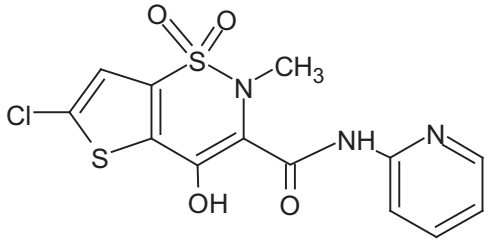
Substances with similar values for δ are possibly miscible due to the balance of energy of mixing released by interactions within the substances and between the substances.[10] The closer is δ_T values of drug and of solvent, the higher would be its solubility.[11] The separation of total solubility parameter (δ_T) of drug into partial solubility parameters may provide greater insights on the nature interactions.

Hansen defined three partial parameters, δ_d (London dispersion forces), δ_p (Keesom dipolar interactions), and δ_h (generalized electron transfer bonding including hydrogen bonding and acid base interaction).[12] These are related by Equation (1).

$$\delta_T^2 = \delta_d^2 + \delta_p^2 + \delta_h^2 \quad (1)$$

where δ_T is the total solubility parameter.[13] The partial solubility parameters of solvents are found to play a role in the solubilization of the drug molecules, which in turn depends on the drug's chemical structure. The extended Hansen's approach, the Flory–Huggins size correction term, and the four parameter approach were proposed methods to obtain partial solubility parameters of drug substances.[14,15]

Lornoxicam is a non-steroidal anti-inflammatory drug (NSAID) used in rheumatoid arthritis, osteoarthritis, and joint pains.[16,17] The structure of lornoxicam is given below.



Lornoxicam structure indicates that the molecule is highly aromatic and no functional group much to the aqueous solubility. It is essential to assess relative role of nonpolar, polar, and hydrogen bonding, with its total solubility parameter. Present communication reports the solubility behavior of lornoxicam in individual solvents ranging from nonpolar (hexane), semi-polar (alcohol) to polar solvent (water) by using the current approaches. The additional support was obtained from the theoretical group contribution methods.[18,19]

2. Materials and methods

2.1. Materials

Lornoxicam was gift sample (Hetero Drugs, Hyderabad, India). Solvents and other chemicals were of analytical grade (S.D. fine chemicals Ltd, Mumbai).

2.2. Methods

2.2.1. Solubility determination

The lornoxicam solubility was determined in saturated solutions of pure solvents. The mixtures with excess drug were shaken in an orbital shaker bath held at 25 ± 0.5 °C. The mixtures were filtered after 72 h and diluted with 0.05 N sodium hydroxide solution for drug content estimation using UV–visible spectrophotometer at 376 nm.[20]

2.2.2. Enthalpy of fusion and molar volume

The enthalpy of fusion was determined by differential scanning calorimeter by heating at 2 °C per min and at the fusion temperature of 479.8 °K. These data was taken to calculate the ideal mole fraction solubility of lornoxicam. Melting point was determined in open capillaries.

Experimentally floatation technique was used to determine the molar volume[21] and theoretically by Fedors group contribution approach.[18]

2.2.3. Solubility parameter determination

Theoretically total solubility parameter of lornoxicam was calculated by the methods of Fedors and Hoy[18,19] and partial solubility parameter values using Van Krevelan method.[22] The solubility parameters of the solvents were collected from the literature, shown (Table 1). The solubility parameter (δ_T), for lornoxicam is also calculated by different statistical methods based on the experimental data.

2.2.4. Statistical analysis

Required in-house software was developed using GW-BASIC for solubility calculations. The dependent variables were fitted to the three-parameter equation, Flory–Huggins size

Table 1 – Solubility parameter values for lornoxicam by different methods.

Sl. no.	Method/system	Solubility parameter	
		Hildebrand, H	SI units, $MPa^{1/2}$
1	Fedors[a]	13.77	28.17
2	Hoy's[b]	12.76 δ_{2T} (δ_{2d}, δ_{2p}, δ_{2h})	26.10
3	Van Krevelen method[c]	11.69 (9.08, 3.79, 6.28)	23.90
4	Flory–Huggins size correction term B[d]	11.39 (9.32, 5.87, 2.89)	23.29
5	Four-parameter approach with log (γ_2/A)[e]	10.58 (8.94, 5.66, 0.228)	21.64
6	Four-parameter approach with B[e]	11.10 (9.03, 5.40, 3.55)	22.70
6	Earlier published work[f]	13.2	27.0

a Estimated from the Fedors molar attraction constants.
b Estimated from the Hoy's substituent method.
c Estimated from the fragmental constants for partial parameters.
d Log (γ_2/A) replaced by B, in three parameter approach, Equation (8).
e Extended Hansen's approach, Equations (10) and (11).
f Taken from reference.[27]