Data in Brief 16 (2018) 135–140

Contents lists available at ScienceDirect

Data in Brief

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

Data Article

Experimental data of co-crystals of Etravirine and L-tartaric acid

Mikal Rekdal [a], Aravind pai [c,1], Muddukrishna BS [b,*]

[a] Department of Chemical Engineering, Norwegian University of Science and Technology, 7491 Trondheim, Norway
[b] Department of Pharmaceutical Quality Assurance, Manipal College of Pharmaceutical Sciences, Manipal University, Manipal, Karnataka 576104, India
[c] Department of Pharmaceutical Chemistry, Manipal College of Pharmaceutical Sciences, Manipal University, Manipal, Karnataka 576104, India

ARTICLE INFO

Article history:
Received 21 August 2017
Received in revised form
2 November 2017
Accepted 3 November 2017
Available online 7 November 2017

Keywords:
Etravirine
Co-crystals
HPLC
FTIR instrument
DSC instrument

ABSTRACT

Etravirine is a drug used alongside other medication in the treatment of HIV and is a non-nucleoside reverse transcriptase inhibitor. It is a BCS class IV drug, having low solubility and high permeability (Drugbank, https://www.drugbank.ca/drugs/DB06414) [1]. As a result, large doses of the drug are required for treatment. Two pills have to be taken twice a day, making it a "pill burden" (Intelence, http://www.intelence.com/hcp/dosing/administration-options) [2]. Therefore, attempts of co-crystallizing Etravirine are attractive as the solubility of the drug tends to increase in this solid form (Schultheiss and Newman, 2009) [3].

In this study Etravirine co-crystals were synthesized in the molar ratios 1:1, 1:2 and 2:1 with L-tartaric acid as the co-former. Both slow evaporation and physical mixture was performed to mix the components. DSC values of final products are presented as well as FTIR spectra to observe the altered intermolecular interactions. A chemical stability test was performed after seven days using area under curve data from an HPLC instrument.

* Corresponding author. Fax: +91 0820 2571998.
E-mail address: krishna.mbs@manipal.edu (M. BS).
[1] Fax: +91 0820 2571998.

https://doi.org/10.1016/j.dib.2017.11.019

Specifications Table

Subject area	*Pharmacy*
More specific subject area	*Pharmaceutical co-crystals*
Type of data	*Table and figure*
How data was acquired	*Fourier transform infrared (FTIR, Shimadzu FTIR-8300), differential scanning calorimeter (DSC, Shimadzu DSC-60) and high performance liquid chromatography (HPLC, Shimadzu LC-10 series) was used to analyze the product.*
Data format	*Analyzed, processed*
Experimental factors	– *Prepared co-crystals were stored in ambient conditions prior to analysis* – *Saturated solution was diluted by a factor of ten for solubility analysis within appropriate range*
Experimental features	*Preparation of co-crystals of Etravirine and L-tartaric acid in molar ratios 1:1, 1:2 and 2:1 with slow evaporation method. Solid state characterization of products using DSC and FTIR in addition to chemical stability analysis.*
Data source location	*Manipal, Karnataka, India*
Data accessibility	*Data are available in article*

Value of the Data

- Mixture of L-tartaric acid and Etravirine shows different IR spectra compared to pure drug.
- Further solubility studies of the co-crystals could investigate possible improved drug performance.
- Chemical stability proved for molar ratio 1:1 and 1:2 of Etravirine and L-tartaric acid.

1. Data

Data in this article shows the characteristics of products prepared from different molar ratios of Etravirine and L-tartaric acid. Table 3 shows the melting points of pure reactants and of the product samples and Fig. 1 displays the complementary thermograms. Fig. 2 displays the FITR spectra of the samples. All three sample batches prepared by slow evaporation method show a broadening of the primary amine peak (3300–3500 cm^{-1}) whereas the physical mixture does not. Chemical stability data is shown in Fig. 3 and Table 4 where the retention peak for Etravirine is the only area of significant size for both 0 and 7 days.

2. Experimental design, materials, and methods

2.1. Materials

Etravirine was received from Apotex Research PVT LTD, Bangalore. L-tartaric acid was purchased from Sigma-Aldrich, Mumbai. HPLC grade acetonitrile was obtained and analytical grade methanol was obtained from FINAR Limited, Ahmedabad and acetone from Merck Life Sciences Private Limited, Mumbai. A Milli-Q purification system (Siemens AG, Germany) was used in the laboratory to obtain HPLC grade water.

L-tartaric acid was selected as co-former after promising results in increased solubility with DL-tartaric acid as co-former from a research study performed at Manipal College of Pharmaceutical Sciences during the fall of 2016 [4]. Etravirine has 2 hydrogen bond donor sites and 7 hydrogen bond acceptor sites resulting in a high probability of co-crystal formation with co-formers.

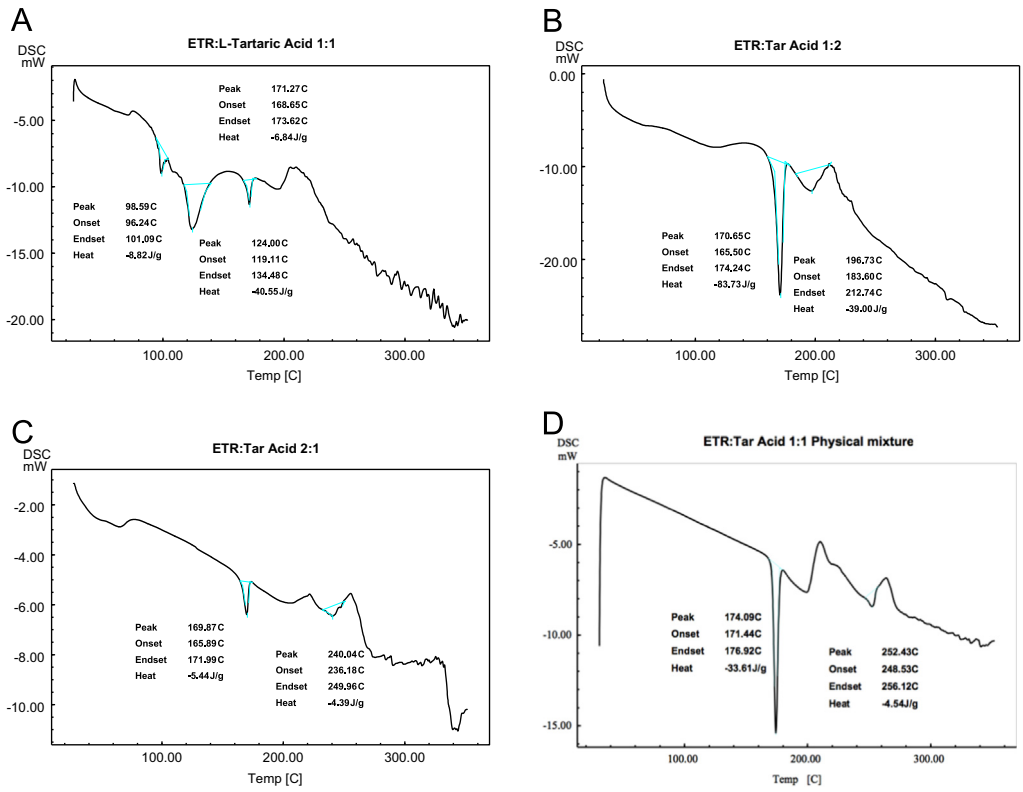

Fig. 1. Thermograms from DSC analysis of products of Etravirine: L-tartaric acid (A) 1:1 by slow evaporation method, (B) 1:2 by slow evaporation method, (C) 2:1 by slow evaporation and (D) 1:1 by physical mixture.

2.2. Co-crystal preparation

Co-crystals were prepared in molar ratios 1:1, 1:2 and 2:1 of Etravirine and L-tartaric acid respectively through slow evaporation method. Desired amount of co-crystal component was weighed and saturated solutions of the components were prepared separately by adding approximately 1 mL solvent. The solvent used was acetone: methanol (50:50% v/v). The saturated solutions were mixed in a common vial and vortexed for 10 minutes. After, the solution was spread evenly on a petri dish and covered with aluminum foil with holes. The solution evaporated at room temperature until the sample was completely dry. The petri dish was scraped and the co-crystals were collected and stored for further analysis. 500 mg of co-crystals were produced in triplicate batches ($n=3$) for each molar ratio as described in Table 1.

A single physical mixture sample of molar ratio 1:1 was also prepared in a plastic vial by mixing with a micro spatula for two minutes and then shaking the vial manually for five minutes.

2.3. Analysis

1. DSC
   Shimadzu DSC-60 was used for obtaining DSC values. A single DSC sample consisting of all three batches was analyzed for each molar ratio. A sample of the physical mixture was also prepared, making 4 samples in total. 5 mg of each sample was placed in an aluminum bottom and crimped with an aluminum top. The test ran in the temperature range 30–350 °C with a temperature increase of 10 °C/min.

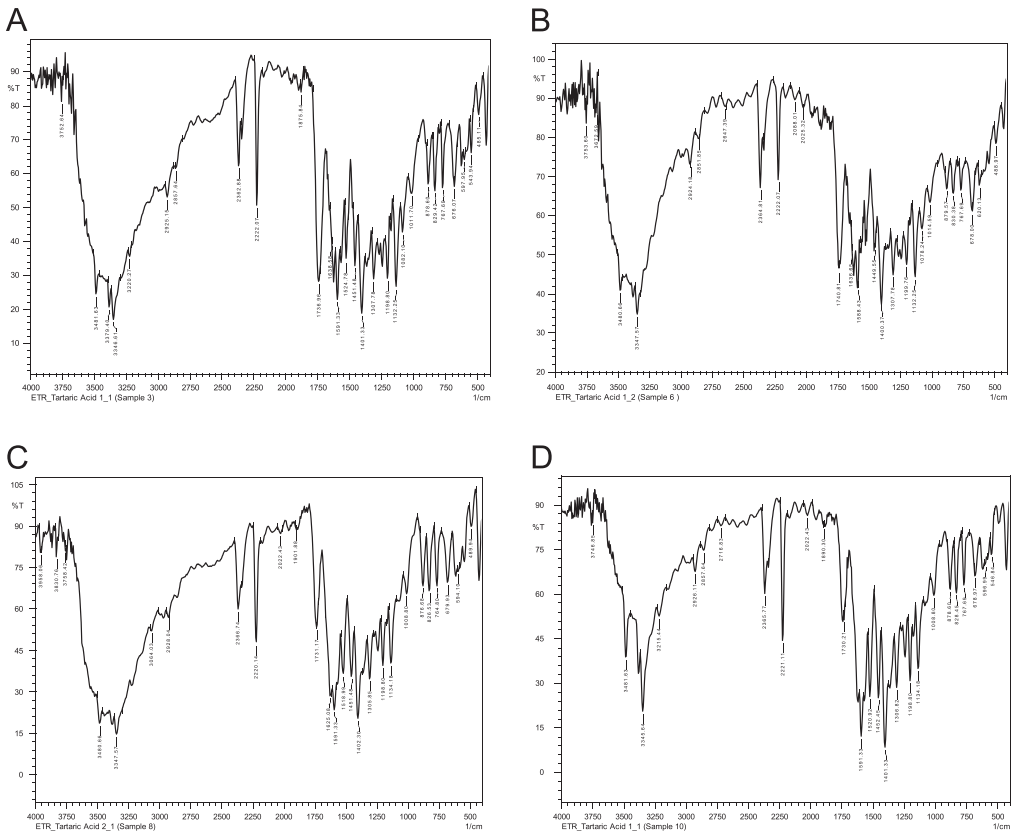

Fig. 2. FTIR spectra of samples containing Etravirine: L-tartaric acid in molar ratios (A) 1:1 by slow evaporation method, (B) 1:2 by slow evaporation method, (C) 2:1 by slow evaporation* and (D) 1:1 by physical mixture. *Only one of the three batches of molar ratio 2:1 showed a broadened peak around 3500–3300 cm^{-1}.

2. FTIR

   A Shimadzu FTIR-8300 was used to acquire the FTIR spectra of the co-crystals. One FTIR sample per batch was prepared in addition to the physical mixture making 10 samples in total. The samples were dispersed in KBr which was then grinded to a disk by applying pressure. The measured range was 4000–500 cm^{-1} with 25 scans.

3. HPLC

   The co-crystal purity was analyzed with a Shimadzu LC-10 series chromatographic system. The system contained a controller unit (SCL-10A VP), a degasser unit (DGU-20A5), a quaternary gradient pump (LC-20AD), a refrigerated auto sampler (SIL-20AC HT) and a PDA detector (SPD-20A). The buffer solution was filtered using a vacuum-filtration apparatus (Alltech Associates) with a 0.45 μm filter (Pall Life Sciences). The mobile phase was degassed by sonication in Equitron ultrasonic bath. For the stationary phase a Hypersil BDS C_{18} (150×4.6 mm×5 μm) column was used and the mobile phase was a mixture of acetonitrile: phosphate buffer (60:40% v/v). The flow rate was 1 mL/min and detection wavelength at 304 nm at 30 °C.

2.4. HPLC sample preparation

The equivalent of 10 mg Etravirine in each co-crystal form was weighed out from a mixture of product batches with the same molar ratios. A stock solution was created by adding amount from Table 2 in 10 mL acetonitrile: methanol (50:50% v/v). 0.5 mL was pipetted from stock and diluted to

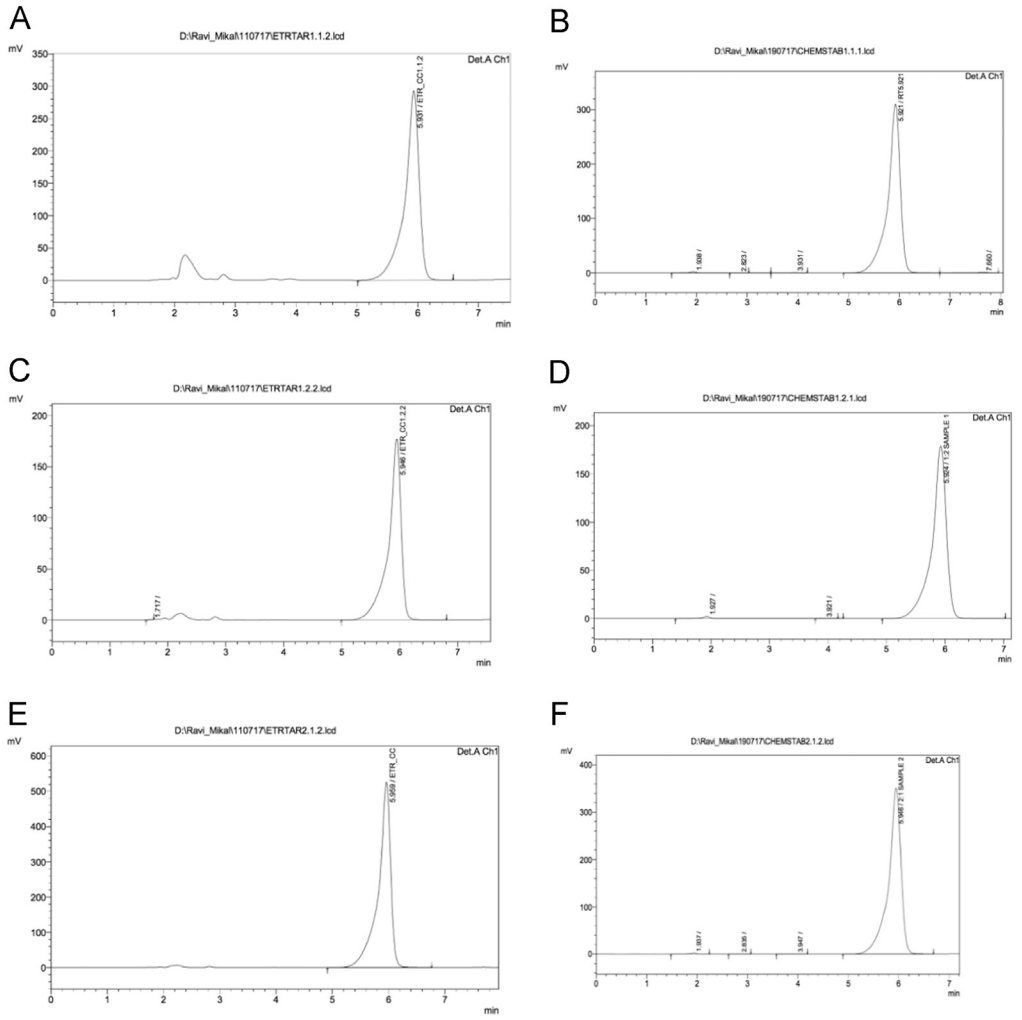

Fig. 3. Chromatograms obtained from chemical stability analysis. A) 1:1, 0 days, B) 1:1, 7 days C) 1:2, 0 days D) 1:2, 7 days E) 2:1, 0 days F) 2:1, 7 days.

Table 1
Mass needed for 500 mg co-crystals in different ratios and number(name) of samples.

Etravirine:L-tartaric acid ratio	Etravirine [mg]	L-tartaric acid [mg]	No. of samples prepared
1:1	371.7	128.3	3
1:2	296.0	204.0	3
2:1	426.5	73.5	3
1:1 physical mix.	371.7	128.3	1

Table 2
Mass of co-crystals needed for the equivalent amount of 10 mg Etravirine.

ETR:TAR composition	Mass co-crystals weighed [mg]
1:1	13.5
1:2	16.9
2:1	11.7

Table 3
Literature values for melting points of components and DSC values for the co-crystal preparations. ETR is Etravirine, TAR is L-tartaric acid and CC stands for co-crystal.

Sample	Melting endotherms [°C]
Etravirine	260.36 [5]
L-tartaric acid	171–174 [6]
1:1 ETR:TAR CC	95.59 & 124.00 & 171.27
1:2 ETR:TAR CC	170.65 & 196.73
2:1 ETR:TAR CC	169.87 & 240.04
1:1 ETR:TAR physical mix	174.09 & 252.43

Table 4
HPLC data for average area under curve for the Etravirine peak initially and after 7 days, as well as percentage assay.

Co-crystal sample	Average area under curve, 0 days ($n=3$)	Average area under curve, 7 days ($n=2$)	% Assay
1:1	4827348	5333824	110,5
1:2	2663206	3063559	115,0
2:1	7999479	6047109	75,6

10 mL with the same solvent. 0.3 mL of diluted solution was further diluted with 1.2 mL acetonitrile: phosphate buffer (60:40% v/v). The product analysis was performed in triplicate ($n=3$) for each molar ratio.

2.5. Stability studies

After 7 days, an additional HPLC test was run as described above on the co-crystals to examine their chemical stability and the possible appearance of degradation products. Samples were prepared in duplicates ($n=2$) for each molar ratio.

Acknowledgments

The author would like to thank student Ravi Ramchandra Choudhari for helping as well as Manipal College of Pharmaceutical Science, Manipal University for providing the materials and instruments to conduct this work.

Transparency document. Supporting information

Transparency data associated with this article can be found in the online version at https://doi.org/10.1016/j.dib.2017.11.019.

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