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” (Intelicence, http://www.intelicence.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.
## 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. Analyzed, processed |
| Data format                  |                                 |
| 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 FTIR 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.
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. 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. 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 ground 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 C₁₈ (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 of samples prepared.

| 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                          |
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.

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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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