COMPARATIVE SOLUBILITY STUDIES BETWEEN TOFACITINIB CITRATE AND TOFACITINIB FREE BASE SIMULATING BCS CONDITIONS.

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INTRODUCTION & OBJECTIVES

The absorption of an Active Pharmaceutical Ingredient (API) can be modulated by controlling its dissolution rate. The aim of this study was to determine the solubility behaviour of tofacitinib citrate and tofacitinib free base in the physiological pH range to help to develop a new drug product.

To achieve this purpose, two different solubility studies were performed:

- A BCS solubility study of tofacitinib citrate and base at different pHs: 1.2, 4.5, 6.8, 5.0, 6.0, 4.0, 7.4 and 8.0.
- A kinetic solubility study in order to determine the dissolution profile of both active substances at different pHs: 1.2, 4.5, 6.8, 7.4, and 8.0.

MATERIAL & METHODS

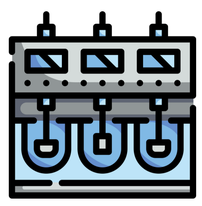
- Tofacitinib citrate (Hinye Pharmaceuticals Batch: 211101)
- Tofacitinib free base (Hinye Pharmaceuticals Batch: 220301)

Highest approved strength in USA
(22.0 mg of tofacitinib base, equivalent to 35.53 mg of tofacitinib citrate)

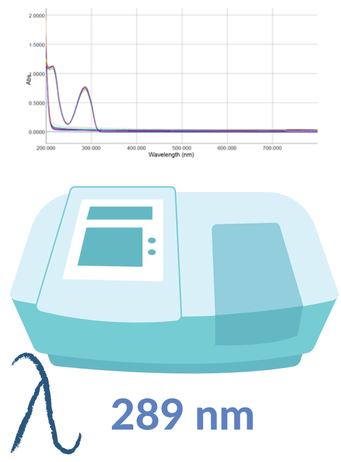
SOLUBILITY STUDY

- 250 mL of media
- Different pH studied (HCl 0,1 M, 4.0, 4,5, 5.0, 6.0, 6.8, 7.4 and 8.0)
- Time: 2 hours stirring at 150 RPM
- Temperature: 37 °C

KINETIC SOLUBILITY

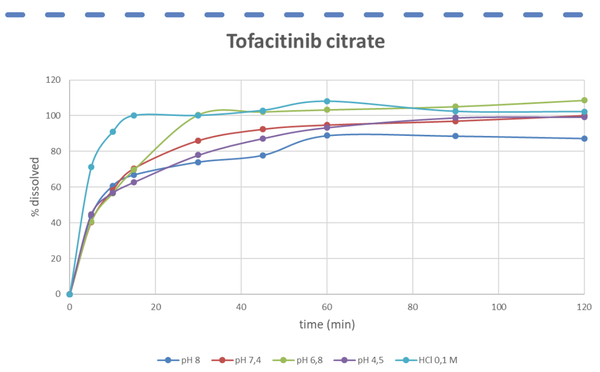


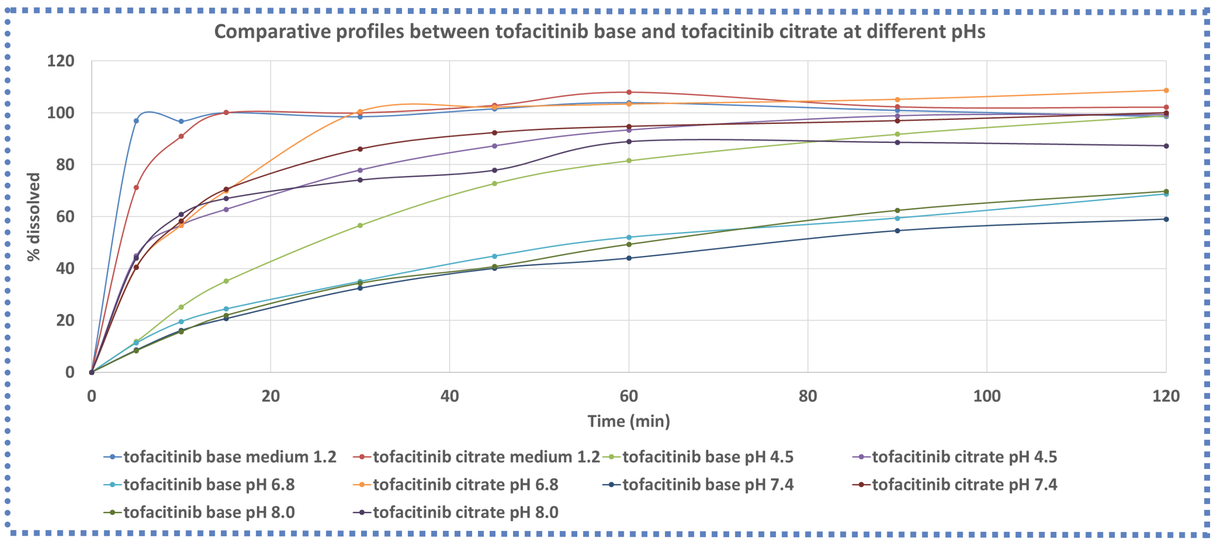
- Volume: 900 mL
- Different pH studied (HCl 0,1 M, 4,5, 6.8, 7.4 and 8.0)
- Sampling time: 5,10,15,30,45,60,90 and 120 min.
- Conditions: paddles, 37 °C at 50 rpm

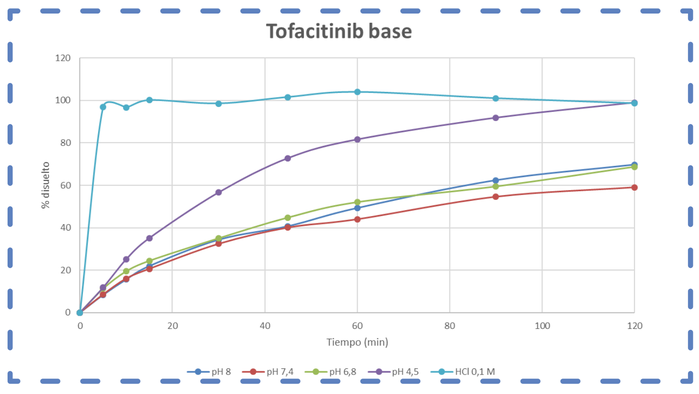


RESULTS & DISCUSSION

The results obtained from de BCS solubility study show that both API can be solubilized in a short time (1 hour at pH 1.2 and 4, and 2 hours at the remained pHs) at 22 mg dose of tofacitinib in all the studied pH. However, for tofacitinib base 22 hours were necessary to dissolve all the dose at pH 6.0 and 6.8.







Tofacitinib citrate and tofacitinib base were dissolved in a short period of time at acid conditions.

However, when the pH is increased, the solubility of both active substances decreases, and in some cases they were not completely solubilised at the time established in the methodology.

CONCLUSIONS

1. Both actives (tofacitinib citrate and base) complies with the BCS study (high dose in 250 mL at different pH's).
2. The kinetic solubility decreases as the pH of the medium increases, and it is faster in tofacitinib citrate than in tofacitinib base.

-European Pharmacopoeia 10th edition. (07/2010:51701). Available on 1.Both actives (tofacitinib citrate and base) accomplish with the BCS study (high dose in 250 mL at different pH's). The kinetic solubility decreases as the pH of the medium increases, and it is faster in tofacitinib citrate than in tofacitinib base. [consulted the 05/05/2022].

-International Council on Harmonisation. Biopharmaceutics classification system-based biowaivers M9. Available on https://www.ich.org/sites/default/files/M9_Guideline_Step4_2019_1116.pdf [consulted the 05/21/2022].

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