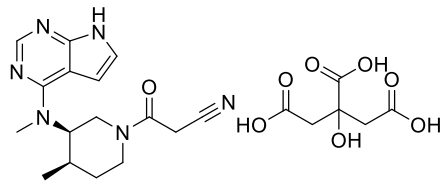
Product data sheet

MedKoo Cat#: 100951 Name: Tofacitinib citrate CAS#: 540737-29-9 (citrate) Chemical Formula: $C_{22}H_{28}N_6O_8$ Molecular Weight: 504.5	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Tofacitinib, also known as tasocitinib, CP-690550, is a Janus kinase (JAK) inhibitor. Tofacitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. JAK enzymes transmit cytokine signaling through pairing of JAKs (e.g., JAK1/JAK3, JAK1/JAK2, JAK1/TyK2, JAK2/JAK2). Tofacitinib inhibited the in vitro activities of JAK1/JAK2, JAK1/JAK3, and JAK2/JAK2 combinations with IC50 of 406, 56, and 1377 nM, respectively.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	47.51	94.17
DMSO:PBS (pH 7.2) (1:1)	0.5	0.99
DMF	5.0	9.91
Water	3.33	6.60

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.98 mL	9.91 mL	19.82 mL
5 mM	0.40 mL	1.98 mL	3.96 mL
10 mM	0.20 mL	0.99 mL	1.98 mL
50 mM	0.04 mL	0.20 mL	0.40 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Hawerkamp HC, Domdey A, Radau L, Sewerin P, Oláh P, Homey B, Meller S. Tofacitinib downregulates antiviral immune defence in keratinocytes and reduces T cell activation. Arthritis Res Ther. 2021 May 21;23(1):144. doi: 10.1186/s13075-021-02509-8. PMID: 34020693; PMCID: PMC8138978.
2. Wong J, Wall M, Corboy GP, Taubenheim N, Gregory GP, Opat S, Shortt J. Failure of tofacitinib to achieve an objective response in a DDX3X-MLLT10 T-lymphoblastic leukemia with activating JAK3 mutations. Cold Spring Harb Mol Case Stud. 2020 Aug 25;6(4):a004994. doi: 10.1101/mcs.a004994. PMID: 32843425; PMCID: PMC7476415.

In vivo study

1. Novais FO, Nguyen BT, Scott P. Granzyme B Inhibition by Tofacitinib Blocks the Pathology Induced by CD8 T Cells in Cutaneous Leishmaniasis. J Invest Dermatol. 2021 Mar;141(3):575-585. doi: 10.1016/j.jid.2020.07.011. Epub 2020 Jul 30. PMID: 32738245; PMCID: PMC7855313.

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2. Pérez-Baos S, Gratal P, Barrasa JI, Lamuedra A, Sánchez-Pernaute O, Herrero-Beaumont G, Largo R. Inhibition of pSTAT1 by tofacitinib accounts for the early improvement of experimental chronic synovitis. J Inflamm (Lond). 2019 Jan 29;16:2. doi: 10.1186/s12950-019-0206-2. PMID: 30728752; PMCID: PMC6352431.

7. Bioactivity

Biological target:

Tofacitinib is an orally available JAK3/2/1 inhibitor with IC50s of 1, 20, and 112 nM, respectively.

In vitro activity

Initially, this study tested the cell viability of keratinocytes, synoviocytes, and T cells in the presence of tofacitinib in a range of concentrations (Supplemental Fig. 1). After confirming that cell viability is not affected by tofacitinib, this study subjected RNA from keratinocytes treated with 600 nM tofacitinib or untreated to DNA MicroArray. To display a broad overview of differentially regulated genes, a heatmap is shown in Fig. 1a. The presence of tofacitinib quite drastically changes the overall gene expression pattern. Blue depicts upregulated genes, while red shows downregulated genes. A number of antiviral genes are downregulated (such as MX1, MX2, OAS1), while antimicrobial genes such as S100A8 and S100A9 (lower end of heat map) seem to only be minimally affected by JAK inhibition (Fig. 1a).

Reference: Arthritis Res Ther. 2021; 23: 144. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8138978/

In vivo activity

Here this study used mouse models to ask if tofacitinib is able to block pathology induced by cytolytic CD8 T cells while sparing protective Th1 responses. Collectively, these series of experiments suggest tofacitinib is an inhibitor that should be considered for the treatment of CL (cutaneous leishmaniasis). The use of host-directed therapies that block inflammatory responses might be considered problematic in infectious diseases, since it is possible that protective responses might simultaneously be dampened. Since Leishmania killing requires the development of a Th1 response, blocking either IL-12 or IFN-γ might lead to uncontrolled parasite growth. However, this study found that tofacitinib had a mild impact on IFN-γ production by CD4 T cells stimulated with IL-12 and IL-18, and in vivo tofacitinib treatment had no impact on the production of IFN-γ during infection. Furthermore, in CL this study has identified an immunopathologic response that can be blocked without affecting parasite control. Thus, tofacitinib inhibited CD8 T cell mediated pathology, while Th1 responses remained intact. Thus, tofacitinib, used in combination with anti-parasitic drugs, would be a successful and to this study's knowledge a previously unreported strategy for the treatment of CL.

Reference: J Invest Dermatol. 2021 Mar; 141(3): 575–585. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7855313/