

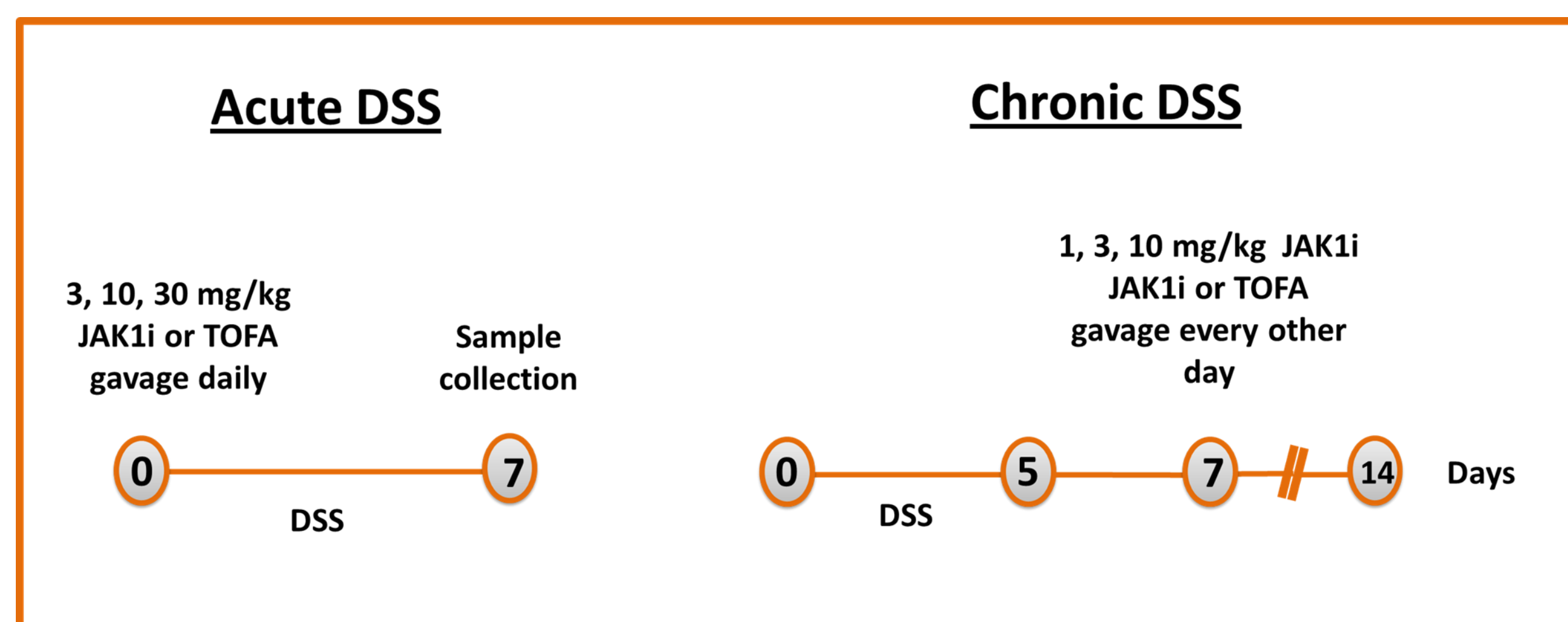
Background

Non-selective Janus Kinase (JAK) inhibitors such as tofacitinib have shown efficacy in treatment of ulcerative colitis.

Side effects such challenge the clinical application of tofacitinib.

Aim: to investigate the potency of a selective JAK1 inhibitor (JAK1i, GSK2276186) vs tofacitinib (CP-690,550, Pfizer) in acute and chronic DSS colitis models.

Methods



Female C56/Bl6 mice (8-12 weeks)
DSS 2% in drinking water ad libitum

Fig.1| Schematic overview of acute and chronic DSS-induced colitis experiments: JAK1i vs tofacitinib

Assessments:

Clinical scoring

colon weight-length ratio
diarrhea score
histology and endoscopy score

Other

qPCR colon
ELISA homogenates

Conclusion

- In vivo, 3, 10 or 30 mg/kg JAK1i and tofacitinib did not protect mice from acute DSS colitis.
- Tofacitinib but not JAK1i ameliorated some aspects of the course of a chronic DSS colitis at the highest dose given.
- Data on a different selective JAK1 inhibitor molecule GLPG0634 reported efficacy in a mouse DSS-induced colitis model¹.

1. [http://dx.doi.org/10.1016/S1873-9946\(14\)60194-X](http://dx.doi.org/10.1016/S1873-9946(14)60194-X)

Results

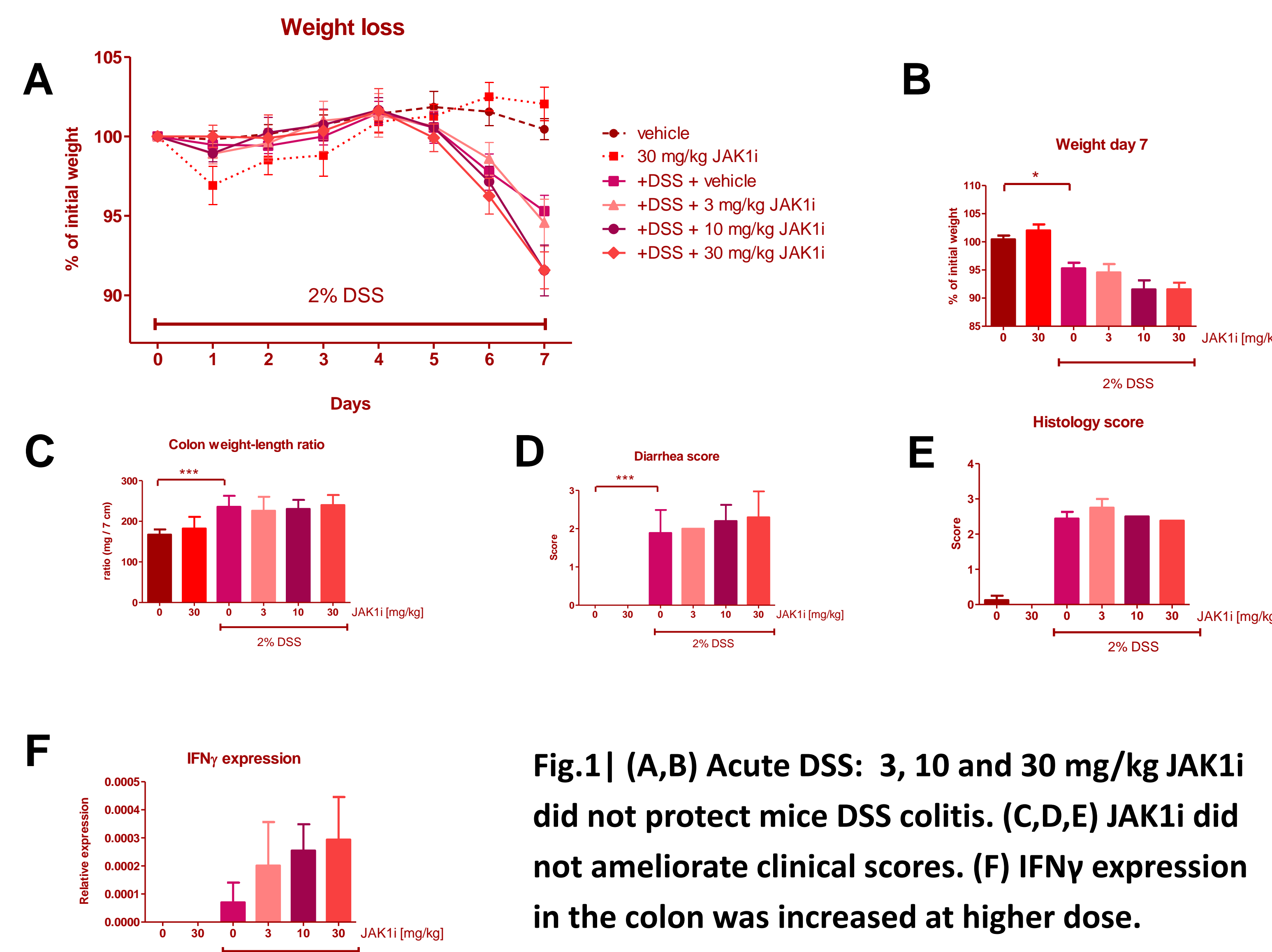


Fig.1| (A,B) Acute DSS: 3, 10 and 30 mg/kg JAK1i did not protect mice DSS colitis. (C,D,E) JAK1i did not ameliorate clinical scores. (F) IFN γ expression in the colon was increased at higher dose.

*** $p < 0.001$; ** $0.001 \leq p \leq 0.01$; * $0.01 < p \leq 0.05$;

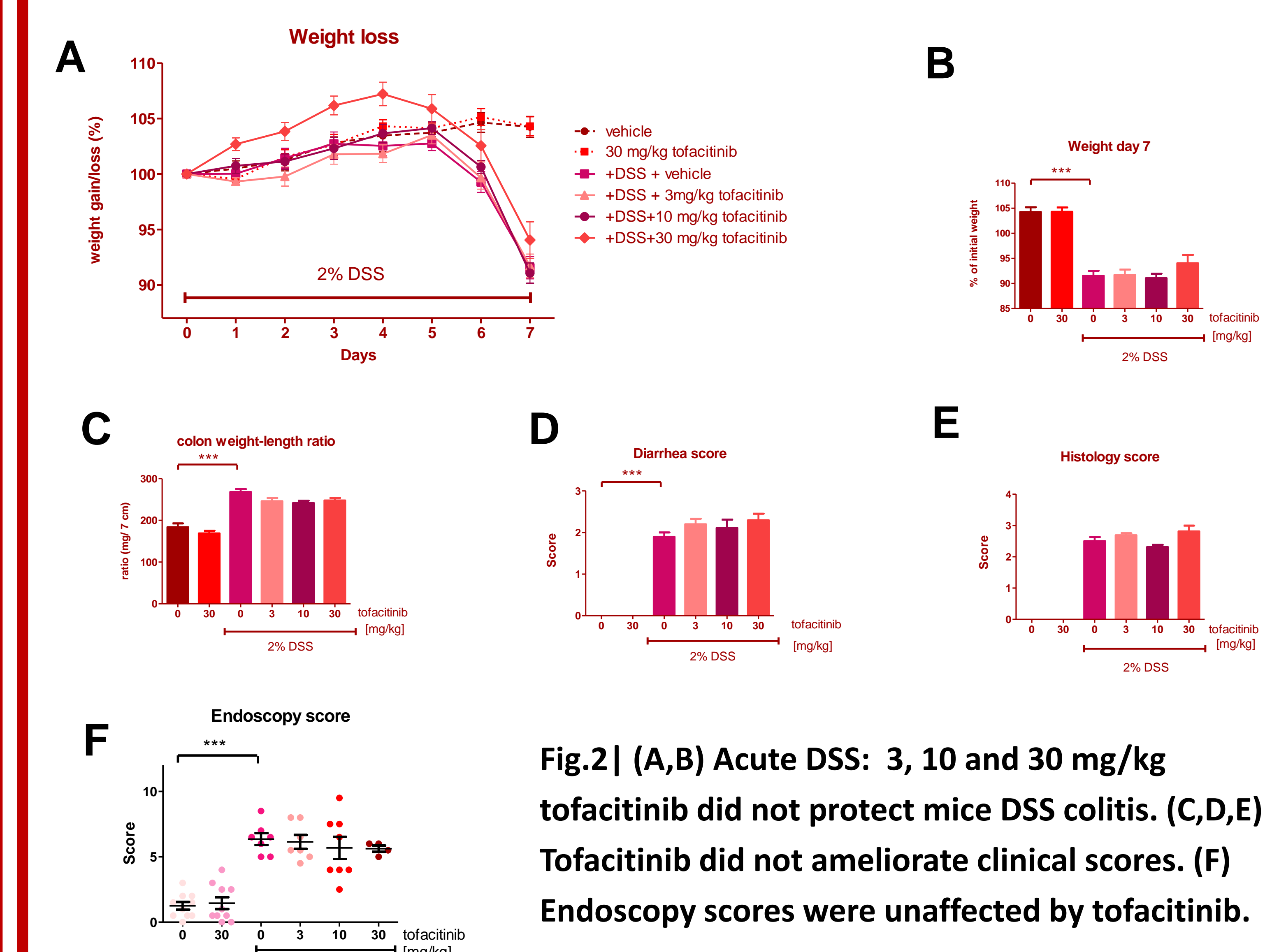


Fig.2| (A,B) Acute DSS: 3, 10 and 30 mg/kg tofacitinib did not protect mice DSS colitis. (C,D,E) Tofacitinib did not ameliorate clinical scores. (F) Endoscopy scores were unaffected by tofacitinib.

*** $p < 0.001$; ** $0.001 \leq p \leq 0.01$; * $0.01 < p \leq 0.05$;

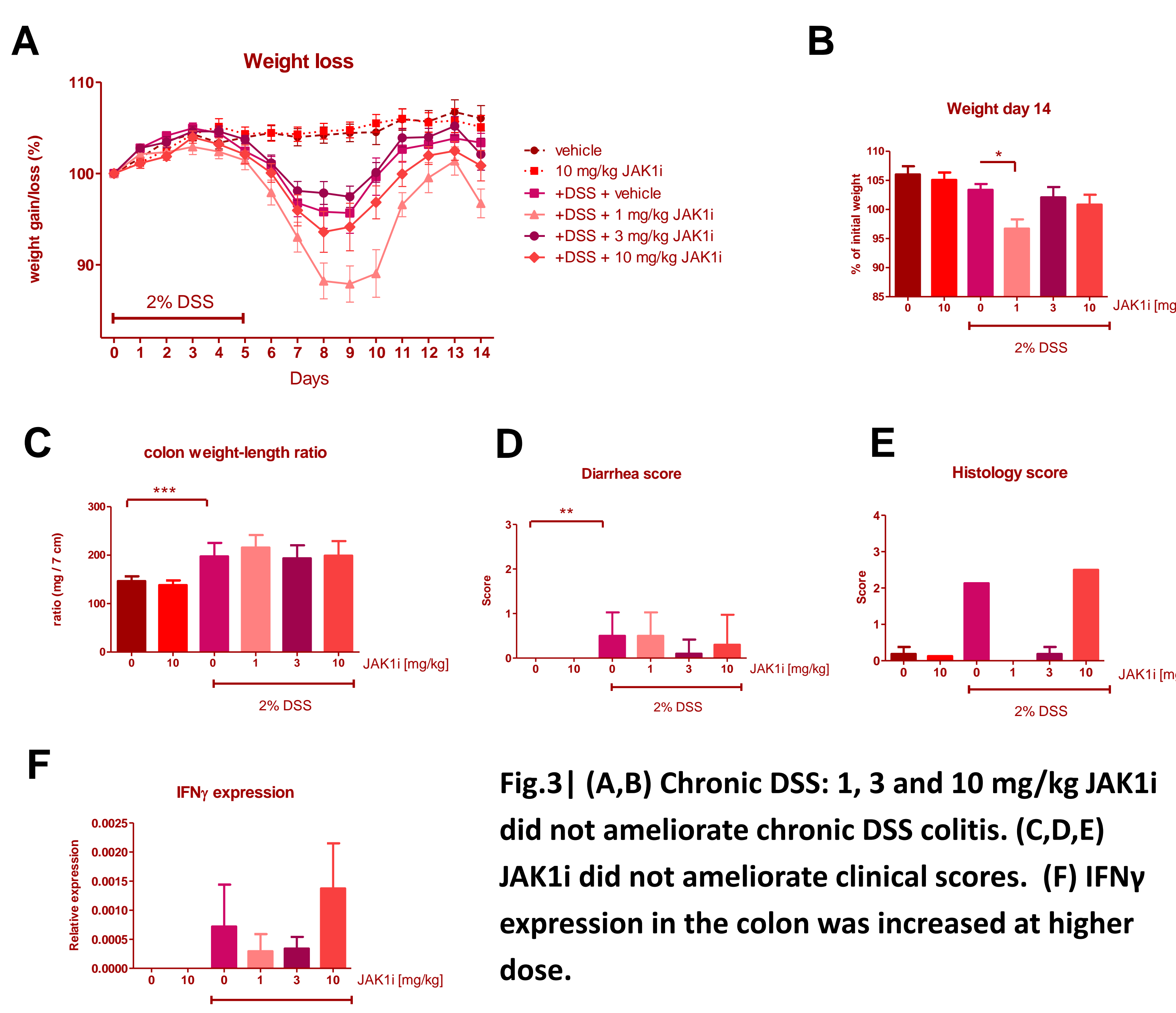


Fig.3| (A,B) Chronic DSS: 1, 3 and 10 mg/kg JAK1i did not ameliorate chronic DSS colitis. (C,D,E) JAK1i did not ameliorate clinical scores. (F) IFN γ expression in the colon was increased at higher dose.

*** $p < 0.001$; ** $0.001 \leq p \leq 0.01$; * $0.01 < p \leq 0.05$;

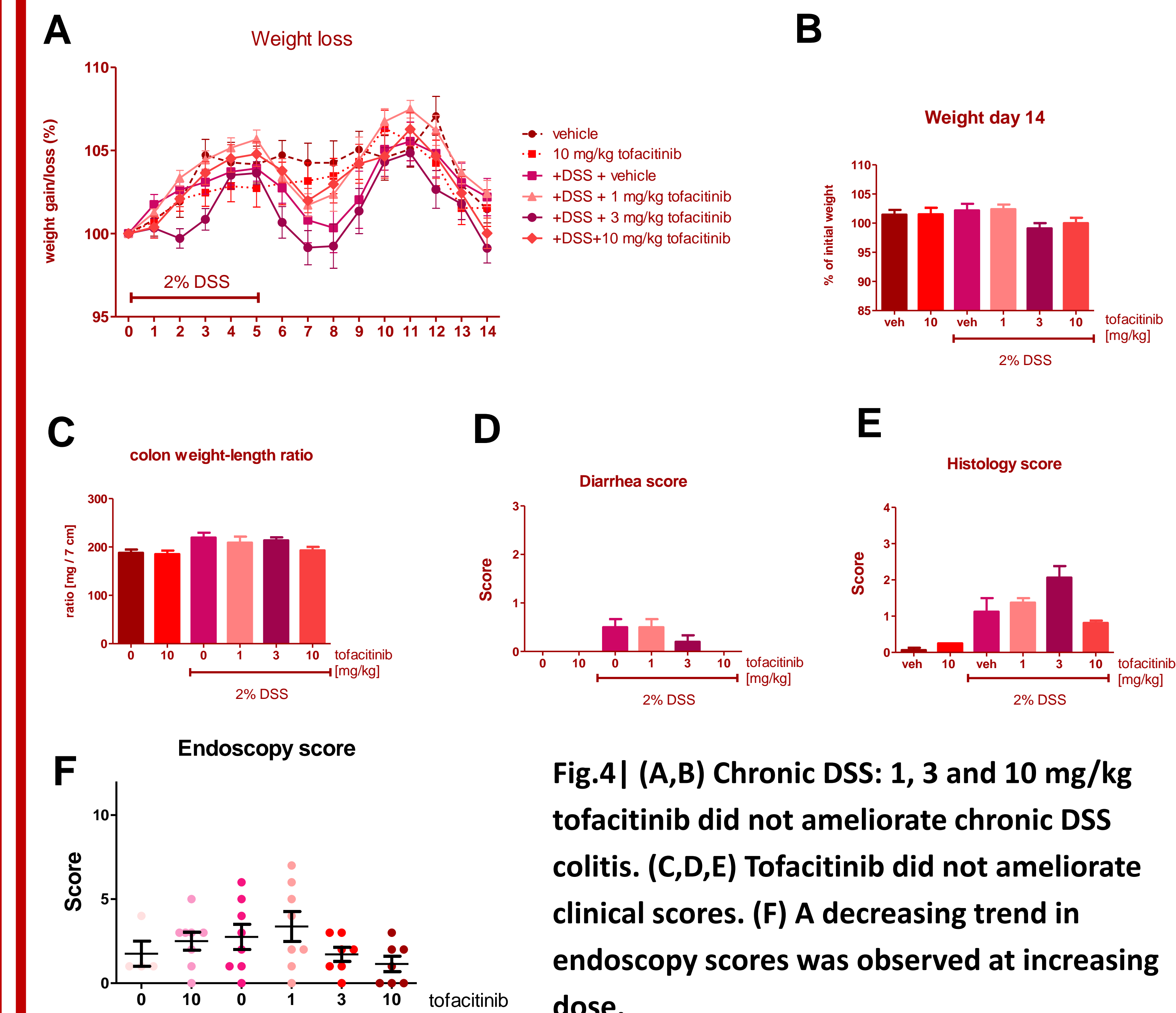


Fig.4| (A,B) Chronic DSS: 1, 3 and 10 mg/kg tofacitinib did not ameliorate chronic DSS colitis. (C,D,E) Tofacitinib did not ameliorate clinical scores. (F) A decreasing trend in endoscopy scores was observed at increasing dose.

*** $p < 0.001$; ** $0.001 \leq p \leq 0.01$; * $0.01 < p \leq 0.05$;