LDN-071, A NOVEL FIRST-IN-CLASS PEPTIDE-BASED PLASMINOGEN ACTIVATOR INHIBITOR 1, SIGNIFICANTLY REDUCES THE SEVERITY OF EXPERIMENTAL COLITIS IN MICE

József Maléth

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A novel peptide-based PAI-1 inhibitor, LDN-071, significantly reduced the severity of DSS-induced experimental colitis in mice across multiple clinical, histological, and inflammatory parameters.

KEY POINTS

- LDN-071 administered orally at 10 mg/bwkg for four consecutive days prevented body weight loss, bloody diarrhoea, colon length decrease, and spleen weight increase in DSS-treated mice.
- Histological analysis showed that LDN-071 significantly impaired DSS-induced transmural inflammation, ulceration, loss of crypt structures, and goblet cell depletion in the colon.
- PAI-1 inhibition with LDN-071 significantly reduced mucosal gene and protein expressions of TNF-α, IL-1β, and IL-6.
- No signs of toxicity were observed in mice exposed to 100 mg/bwkg LDN-071 for seven days, ten times the therapeutic dose tested.
- The authors propose PAI-1 inhibition as a potential novel therapeutic strategy for IBD; LDN-071 is owned by Ladon Therapeutics Ltd.

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