Drug Delivery and Translational Research

Supplementary Information

Oral capsule administration of biomacromolecules that achieves bioavailability and pharmacokinetics comparable to subcutaneous injection in dogs – the BIONDD® technology

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Fig. S1. (a) Illustration of the ex vivo pig stomach model. Pig stomachs acquired directly from the slaughterhouse are cleaned and cut open. The stomach tissue is laid out flat, and a BIONDD® capsule is placed on the inside tissue of the stomach. Water is added dropwise, and the time it takes for the device to actuate (i.e., the capsule to dissolve) is noted. Following device actuation, the spike insertion is visually inspected and photographed. Created in BioRender. Mertz, N. (2026) https://BioRender.com/b26fyf7. The study was carried out under a permit for handling animal byproducts provided by the Ministry of Food, Agriculture and Fisheries of Denmark (license: DK-123-oth-1425482). (b) BIONDD® prototype device after actuation with spike inserted into ex vivo pig stomach tissue. (c) Individual actuation times recorded for the BIONDD® prototype device (n = 6) using the ex vivo pig stomach model. The average actuation time was 130 ± 12 s. Insertion of the spike into the ex vivo pig tissue after device actuation was observed for all of the 6 BIONDD® devices.

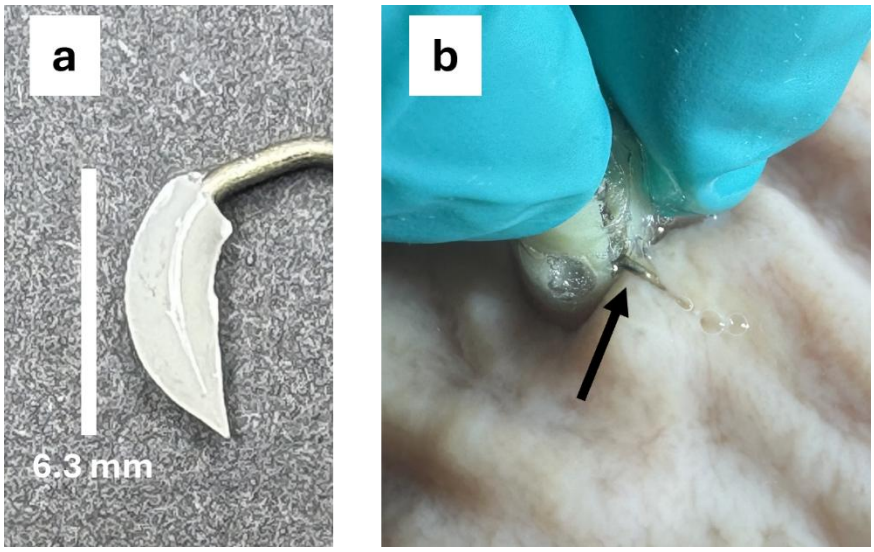

Fig. S2. (a) Biodissolvable spike with a drug load of 6.4 mg lyophilized adalimumab (lyo-adalimumab, Evitria, Zurich, Switzerland) prepared by compression molding of a 65:35 %(w/w) lyo-adalimumab:PEO 200,000 (Poly(ethylene oxide) average M_w 200,000) mixture. (b) Biodissolvable spike (described in (a)) inserted into ex vivo pig stomach tissue after actuation of a BIONDD® device (see method described in Fig. S1a). It should be noted that the spike has been successfully inserted into and is fully covered by the tissue (indicated with arrow).

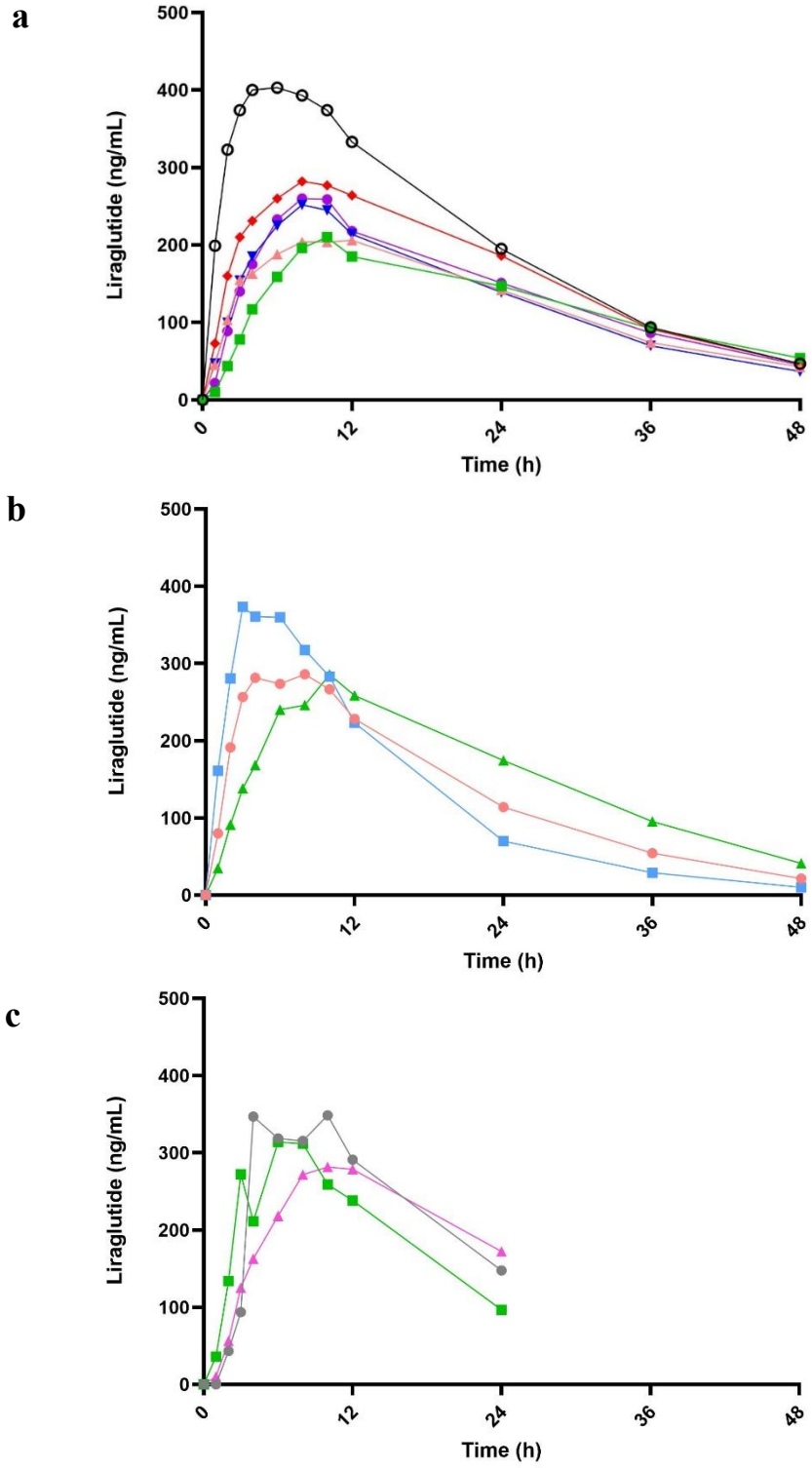

Fig. S3. Individual liraglutide plasma concentrations for dogs. Plasma liraglutide concentrations (ng/mL) after (a) subcutaneous (SC) injection of Victoza® (n =6); (b) intra-wall (IW) injection (n =3) and; (c) IW spike insertion (n = 3) at a dose of 0.4 mg liraglutide per dog are shown. Blood samples were taken up to 48 h after SC injection and IW injection and up to 24 h after IW spike insertion.

Table S1.
Device transit after oral dosing of the BIONDD® capsule to beagle dogs. 12 beagle Marshall dogs were dosed with a size 00 BIONDD® prototype device with a configuration enabling it to contain a biodissolvable spike. At gastroscopies performed 5 min after dosing, 11 of the 12 devices were observed to be inserted in the stomach wall, and these 11 devices were observed to be detached from the stomach wall 24 h after dosing. Fecal monitoring was executed by a Loma IQ 3 metal detector (LOMA SYSTEMS®, Farnborough, UK), specifically calibrated daily for BIONDD® devices following the day of dosing. The animal pens (both feces and bedding material) were checked at least three times daily, and the drain was checked for the presence of devices for up to 5 days. All 12 devices were retrieved within 3 days after oral dosing of the BIONDD® capsule. Nine of the 12 devices were found intact. The remaining 3 of the retrieved devices appeared to have been chewed on by the dogs in the time after excretion and before retrieval.

Days post dosing	**0**	**1**	**2**	**3**	**4**	**5**
Number of retrieved devices	0	4	7	1	0	0
% devices retrieved	0	33%	92%	100%	-	-

Video S1.
UV-Vis imaging. Real-time UV-Vis imaging of liraglutide release (280 nm) and dissolution of the 40:60 %w/w liraglutide:PEG 6000 vehicle (520 nm) after insertion of a spike loaded with 1.00 ± 0.02 mg vehicle (corresponding to a load of 0.4 mg liraglutide) into the porous 2% agarose beads matrix in PBS (pH 7.4) at 37 °C. Replay of images recorded in the entire experiment (3 h).