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Supplementary Materials for

Long-acting reversible contraception by effervescent microneedle patch

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The PDF file includes:

Other Supplementary Material for this manuscript includes the following:

(available at advances.sciencemag.org/cgi/content/full/5/11/eaaw8145/DC1)

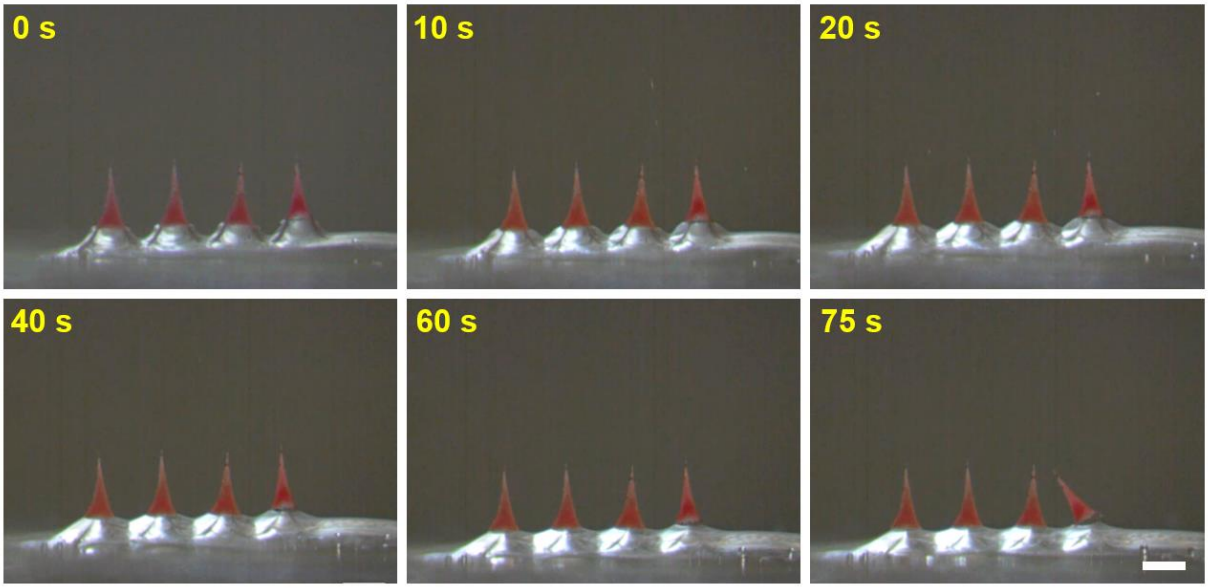

Fig. S1. Representative images of the slow dissolution of an MN patch with PVA/sucrose backing (i.e., noneffervescent) in PBS over time. Scale bar, 500 μm.

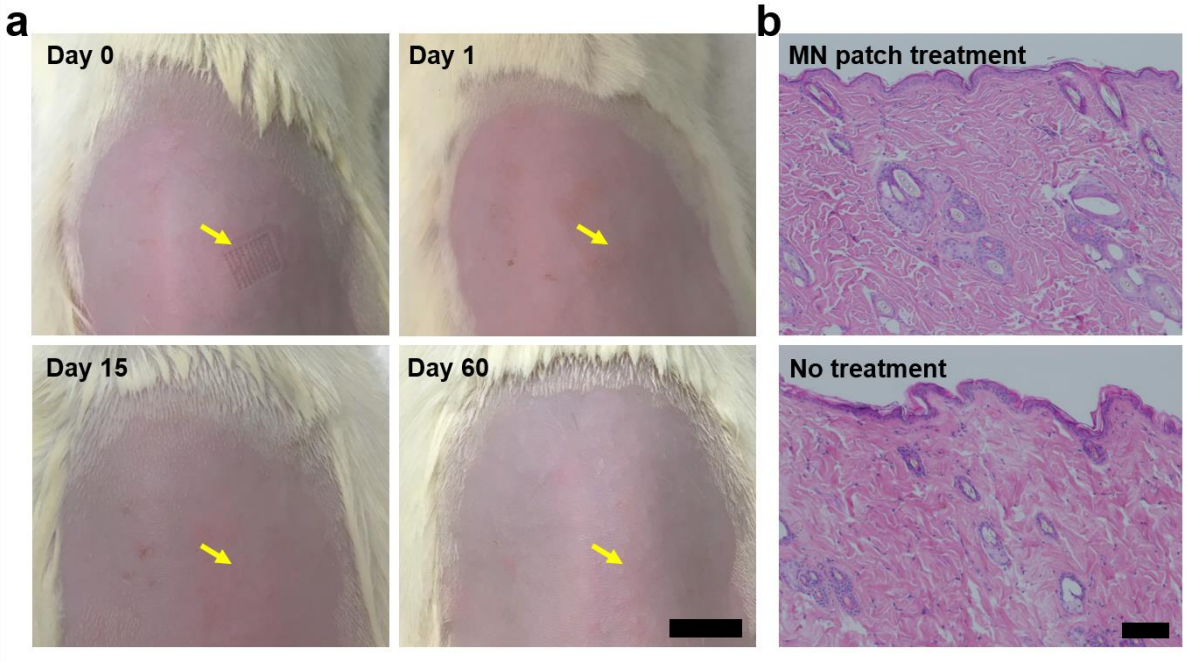

Fig. S2. Local effects of an effervescent MN patch for LNG delivery on rat skin in vivo. The MN patch was applied to skin on Day 0 to administer MNs into skin for slow release of LNG for 60 days. (a) Representative images of rat skin 0, 1, 15 and 60 days after application of an effervescent MN patch containing LNG. The site of MN patch application is shown by a yellow arrow. All images are from the same rat. Scale bar, 1 cm. (b) Representative H&E-stained sections of rat skin with effervescent MN patch treatment or without treatment 60 days after application of the MN patch. Scale bar, 100 μm. (Photo Credit: Wei Li, Georgia Tech.)

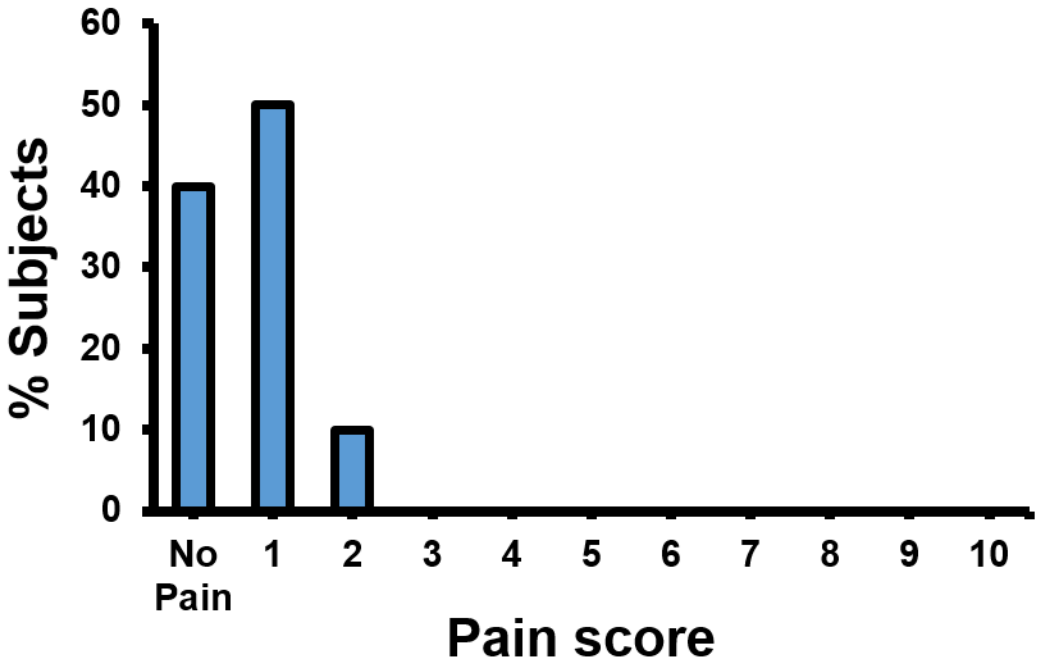

Fig. S3. Assessment of reported pain during MN patch administration scored by participants on a visual analog scale of 0 (no pain) to 10 (pain of a hypodermic injection).

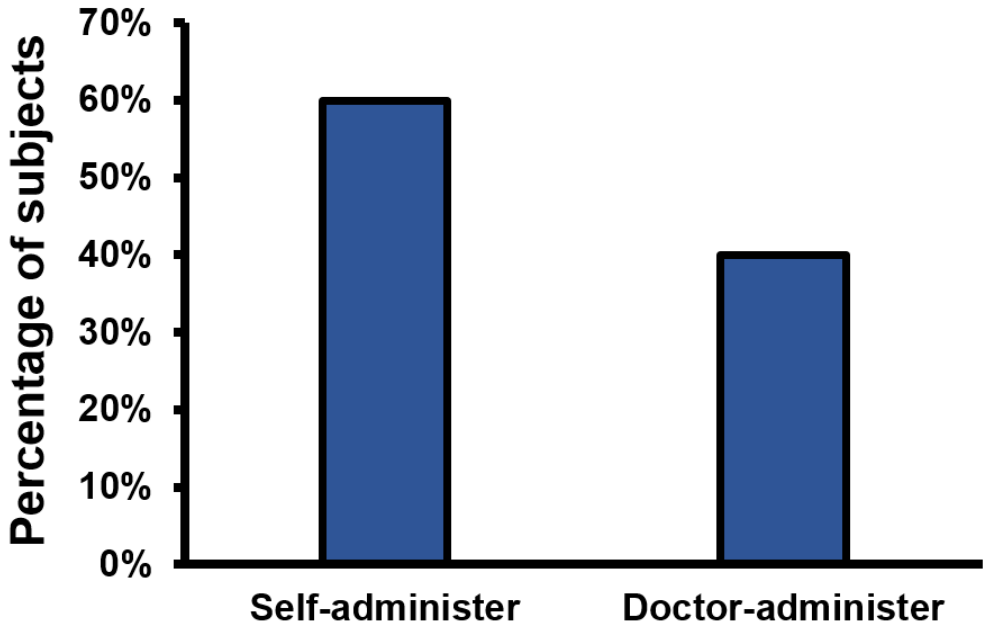

Fig. S4. Percentage of participants showing preference for self-administration or doctor administration for future application of an effervescent MN patch for long-acting contraception.

Table S1. Pharmacokinetic parameters of LNG following administration of effervescent MN patch containing LNG. (mean ± SD)

PK Parameters	LNG-loaded MNs patches administration
T_{max} (h)	98.4 ± 84
C_{max} (ng/mL)	0.83 ± 0.03
$AUC_{(0-t)}$ (ng*h/mL)	480 ± 78
$AUC_{(0-inf)}$ (ng*h/mL)	482 ± 79
Half-life (h)	94.8 ± 30.7
K_e (h^{-1})	0.008 ± 0.003

C_{max}: Maximum plasma concentration. T_{max}: Time of C_{max}. $AUC_{(0-t)}$: Area under the concentration-time curve from time zero to time of last detection. $AUC_{(0-inf)}$: Area under the concentration-time curve from time zero to infinity. The elimination rate constant (K_e) of LNG was estimated using the terminal phase of the plasma concentration versus time profile following intravenous LNG injection, and the data were fit by log-linear regression to estimate the slope (K_e). Half-life = $0.693/K_e$. Microneedle patch dose = 0.28 mg/rat of 200 g each.

Table S2. Summary of the prevalence of skin reactions at different time points after the application of effervescent MN patches to human participants. Percentages indicate the presence of skin reactions[1].

	0 h	1 h	24 h
Pain	10%	0%	0%
Tenderness	0%	0%	0%
Erythema	100%	90%	10%
Swelling	0%	0%	0%

[1]Pain and tenderness were self-reported by subjects. Erythema and swelling were determined by the study investigator.