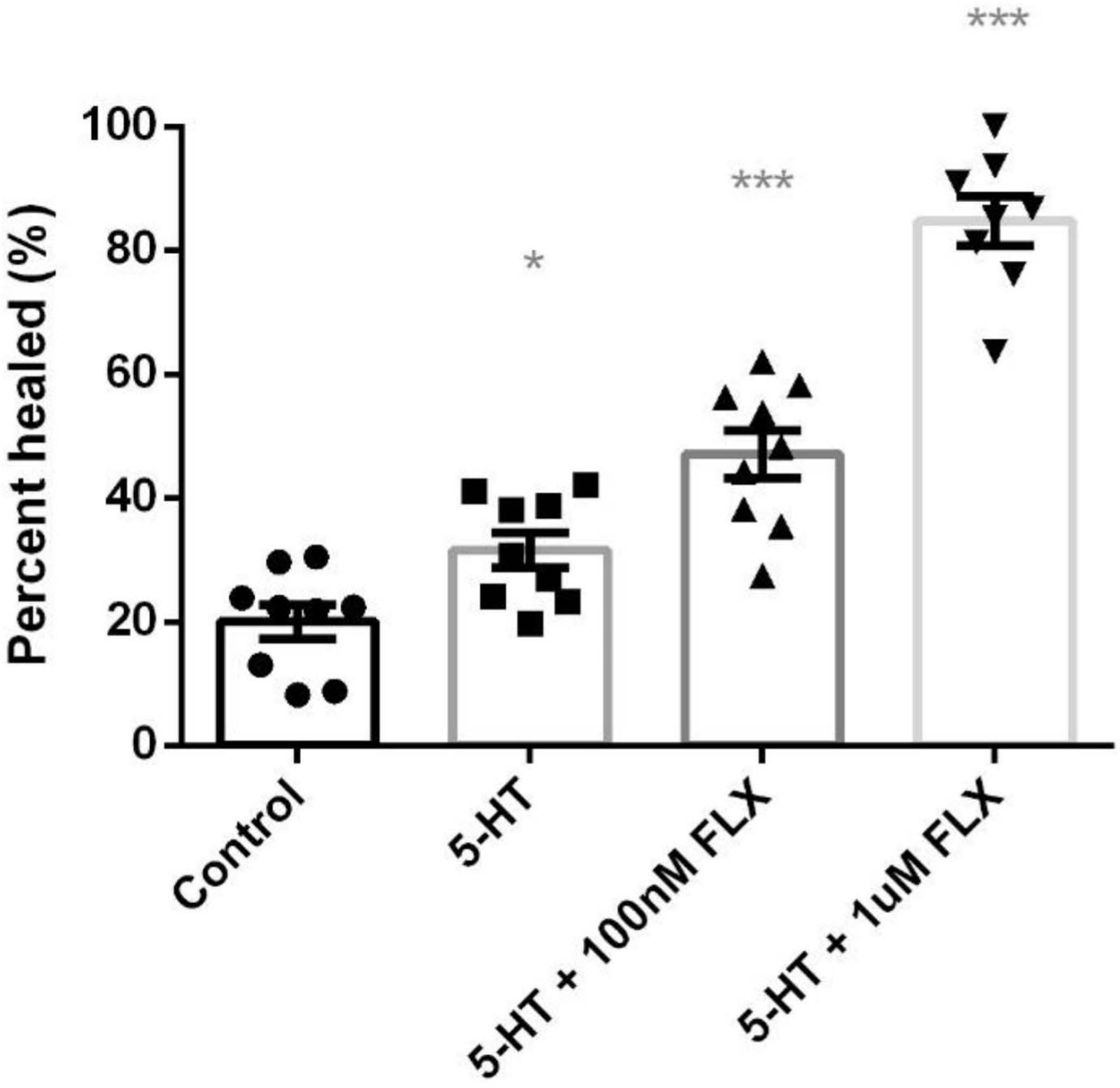
SUPPLEMENTARY DATA

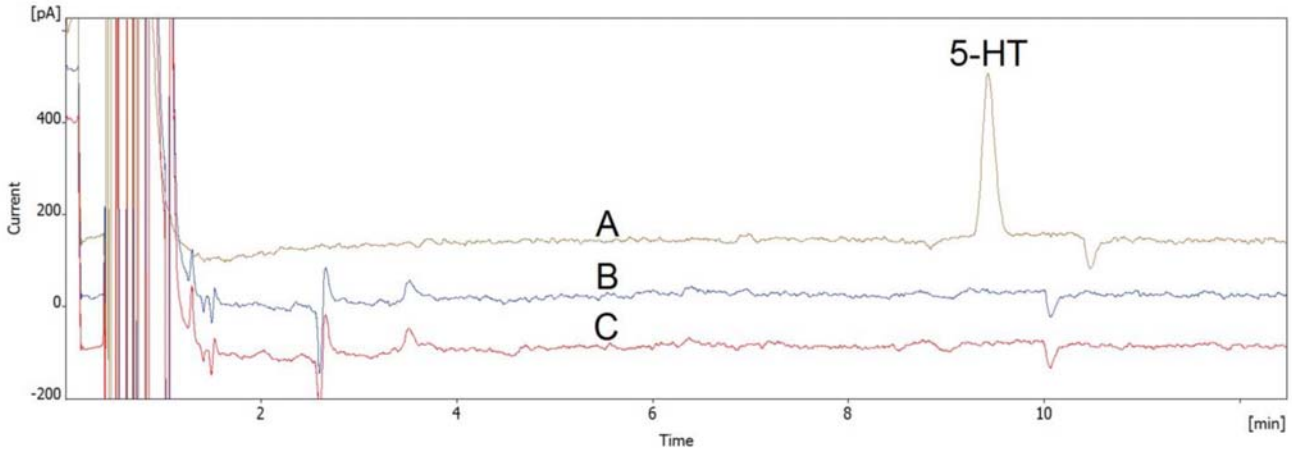
Figure S1: Serotonin and fluoxetine increase re-epithelialization *in vitro*. Scratch wound assays were performed on confluent cultures of D-HEK-Ad keratinocyte cell line originated from type II diabetic patient in the absence/presence of 1μM serotonin (5-HT). Data represented as Mean ± SEM. Kolmogorov-Smirnov tests were performed to confirm normality in data distribution. ANOVA were used to assessed statistical significance. *, $p \leq 0.05$; ***, $p \leq 0.001$.



SUPPLEMENTARY DATA

Figure S2: Neonatal human keratinocytes did not produce serotonin *in vitro*. High performance – liquid chromatography was performed on 24-hour incubation cell culture supernatant samples of primary neonatal keratinocytes (NHK) from 4 different donors. Representative chromatograms of supernatant samples: Orange-A: 33nM 5-HT calibration standard, Blue-B: samples treated with FLX, Red-C: non-treated control sample (A). Individual sample results were listed in table (B). "N/D": not detected. "KGM": Keratinocyte Growth Medium. Lower detection limit: 9.8nM 5-HT.

A



B

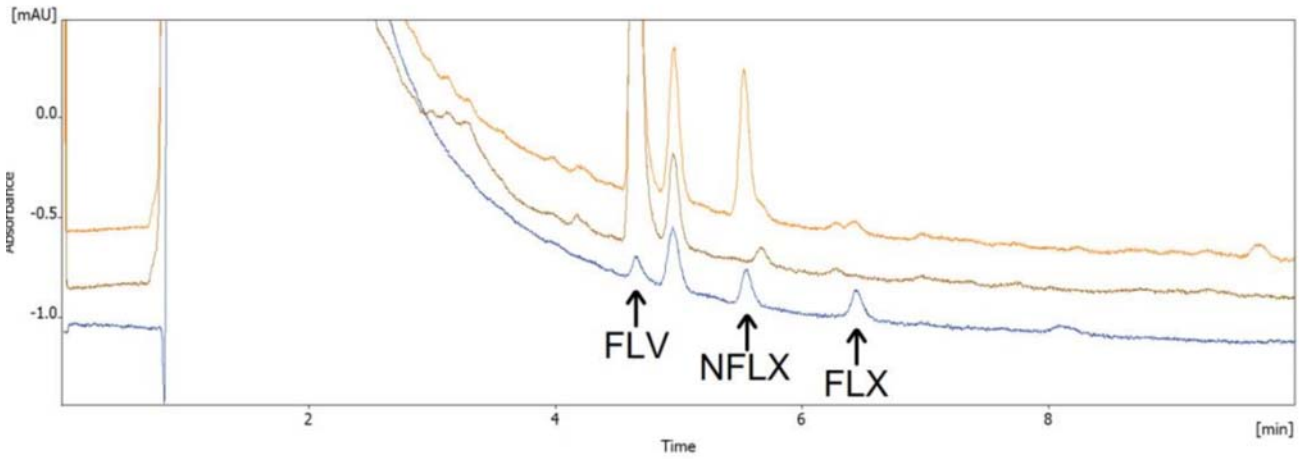
Concentration of serotonin in culture supernatant (nM)	
NHK 1526 p5 - 24 hours control	N/D
NHK 1526 p5 - 24 hours 1 uM FLX	N/D
NHK 1602 p4 - 24 hours control	N/D
NHK 1602 p4 - 24 hours 1 uM FLX	N/D
NHK 1525 p7 - 24 hours control	N/D
NHK 1525 p7 - 24 hours 1 uM FLX	N/D
NHK 1705 p5 - 24 hours control	N/D
NHK 1705 p5 - 24 hours 1 uM FLX	N/D
fresh KGM	N/D

SUPPLEMENTARY DATA

Figure S3: Limited systemic effects of topically applied fluoxetine. High performance –liquid chromatography was performed on plasma samples of mice at day 10 post wounding to quantitate fluoxetine and its metabolite (norfluoxetine). Representative chromatogram of mouse plasma samples. Orange: plasma from a fluoxetine treated mouse collected 12 hours after the final dose. Brown: plasma sample from a control mouse. Blue: a calibration standard containing 2 nM each of fluvoxamine, norfluoxetine, and fluoxetine (A). Quantified concentration of fluoxetine and norfluoxetine in each mouse (B). "N/D": not detected. Excisional biopsy wounds in Db/db mice were treated topically with FLX 0.02% or vehicle control daily. On day 9, the time mice spent in light versus dark chambers was quantified, and percent time not spent in the light chamber is a measure of anxiety (C). Exploration ratio, calculated as the frequency of exploration of a novel versus a known object in mice treated with vehicle control or FLX, was used to evaluate cognitive ability in mice (D).

SUPPLEMENTARY DATA

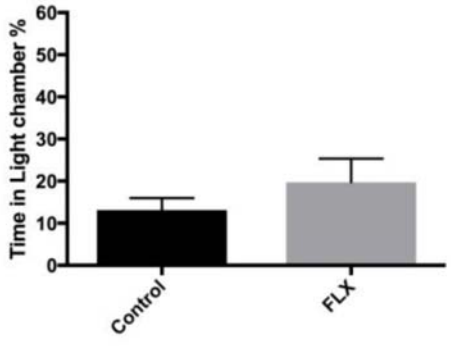
A



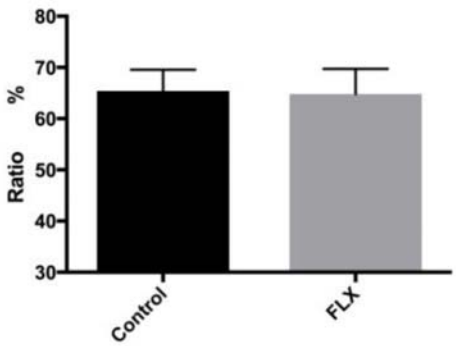
B

Sample Name	Concentration in plasma (ng/mL)		
	[norfluoxetine]	[fluoxetine]	[total]
Control 1	N/D	N/D	N/D
Control 2	N/D	N/D	N/D
Control 3	N/D	N/D	N/D
Control 4	N/D	N/D	N/D
Control 5	N/D	N/D	N/D
Control 6	N/D	N/D	N/D
Control 7	N/D	N/D	N/D
FLX treated 1	52.521	6.994	59.515
FLX treated 2	18.046	5.109	23.155
FLX treated 3	45.453	4.844	50.297
FLX treated 4	35.870	7.245	43.115
FLX treated 5	57.076	7.762	64.838
FLX treated 6	52.974	6.295	59.269
FLX treated 7	21.036	6.610	27.646
AVERAGE FLX IN PLASMA	40.425	6.408	46.834
Standard Deviation	15.832	1.085	16.301

C



D



SUPPLEMENTARY DATA

Figure S4: FLX did not modulate systemic 5-HT concentration. High performance –liquid chromatography was performed on plasma samples of mice at day 10 post wounding to quantitate amount of 5-HT in circulation. Representative chromatogram of mouse plasma samples. Orange-A: 0.330 μM 5-HT calibration standard, Blue-B: plasma sample from a mouse treated with FLX collected at day 10 post wounding, Red-C: plasma sample from a vehicle control-treated mouse collected at day 10 post wounding (A). Data were quantified and presented as bar graphs (B). Data represented as Mean ± SEM. *, $p \leq 0.05$