

Supporting information

From the North Sea to Drug Repurposing, the Antiseizure Activity of Halimide and Plinabulin

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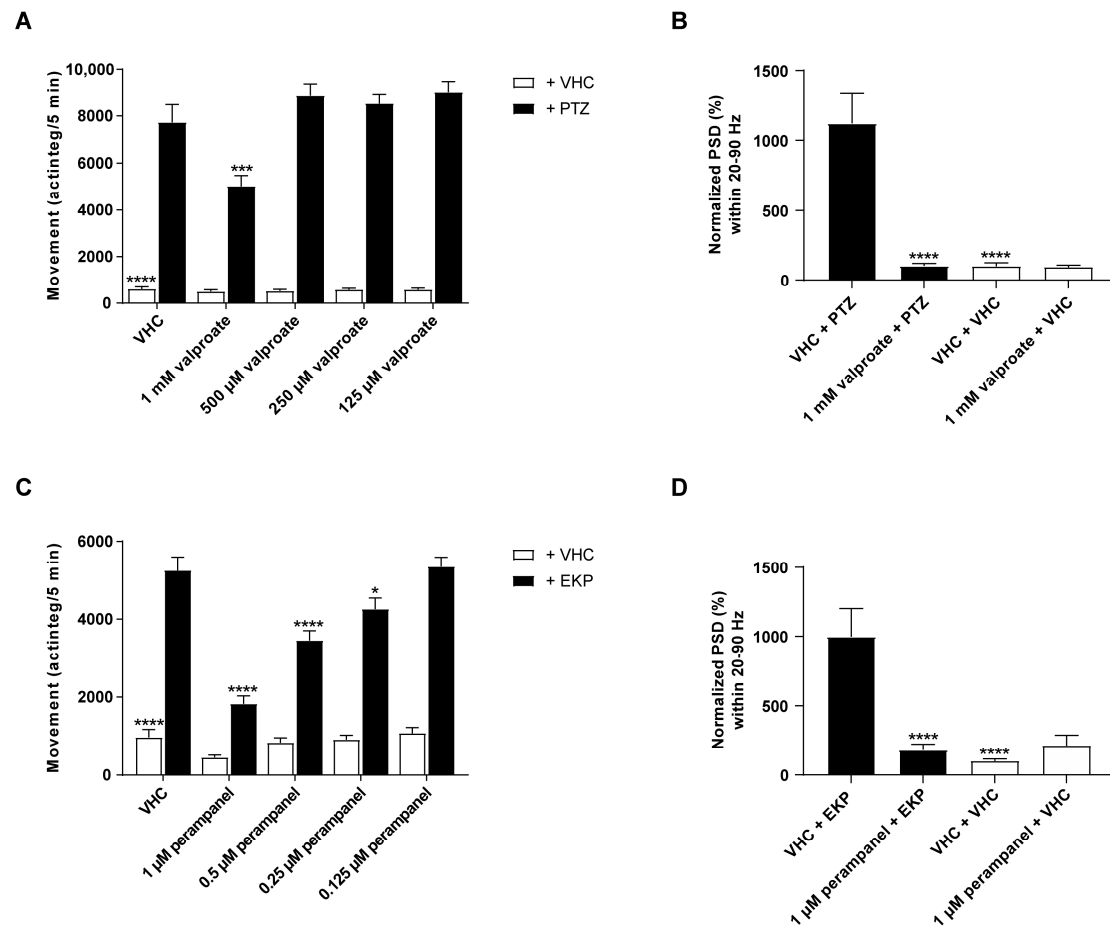


Figure S1: Behavioral and electrophysiological antiseizure analysis of positive controls valproate and perampanel in the zebrafish PTZ and EKP seizure model, respectively. (A, C) Antiseizure activity of valproate and perampanel in the zebrafish pentylenetetrazole (PTZ) and ethyl ketopentenoate (EKP) seizure model, respectively, after a treatment period of 18 h in case of valproate and 2 h in case of perampanel. Behavioral data is expressed as mean actinteg units per 5 min (\pm SEM) during the 30 min recording period (A) and during the 10–25 min recording period (C). (B, D) Antiepileptiform activity of valproate and perampanel in the zebrafish PTZ and EKP seizure model, respectively, after a treatment period of 18 h in case of valproate and 2 h in case of perampanel. Electrophysiological data is normalized against the vehicle (VHC) + VHC control condition and expressed as normalized power spectral density (PSD) (mean \pm SEM) per larva within the 20–90 Hz region. (A, C) Data were pooled from three independent experiments with 8–10 replicate wells per test condition ($n = 28$ –30). (B, D) Number of replicates per test condition were $n = 14$ –17. (A–D) Statistical analysis: one-way ANOVA with Dunnett’s multiple comparison test (GraphPad Prism 9, San Diego, CA, USA). Significance levels: * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$; **** $p \leq 0.0001$.

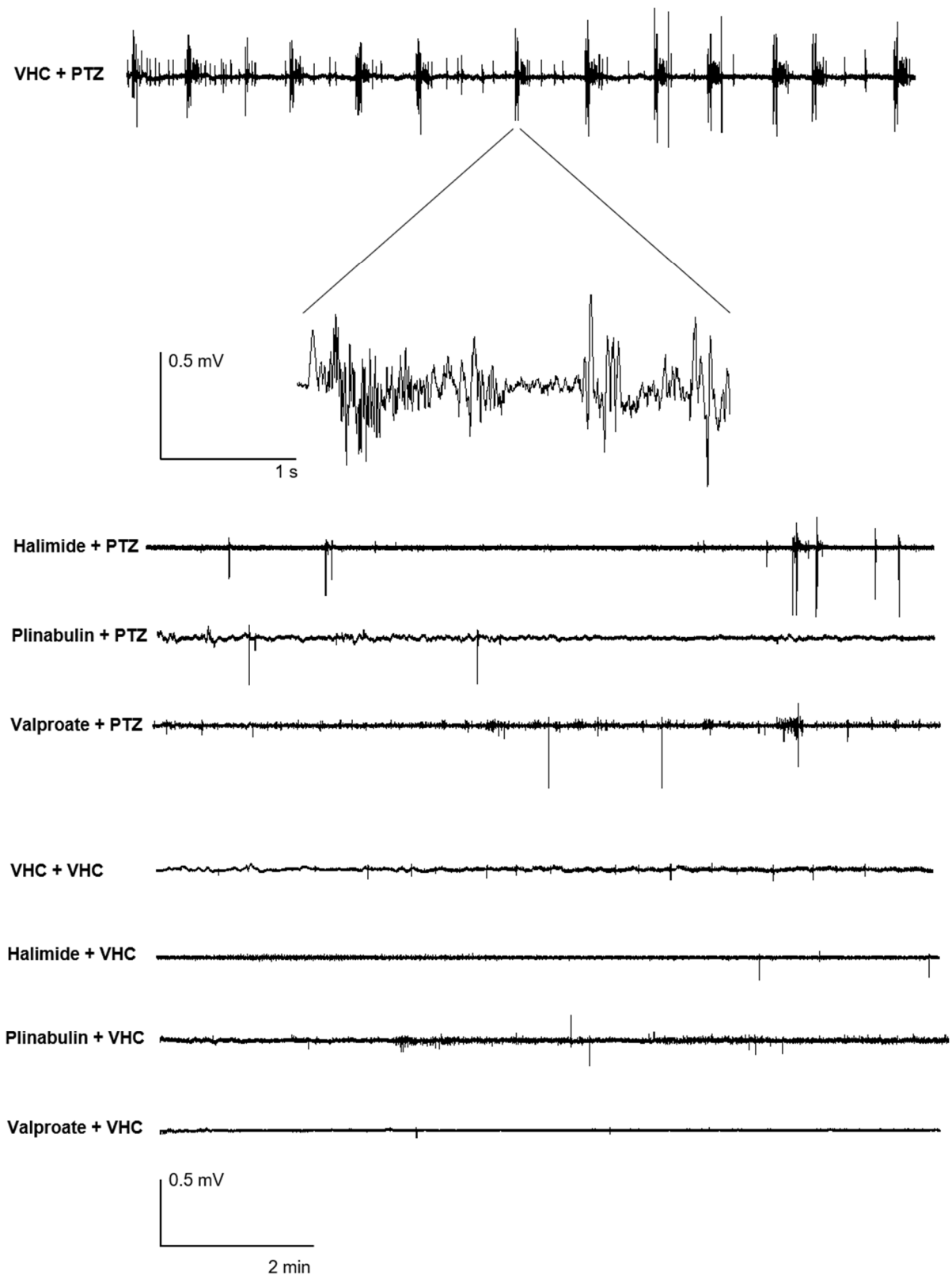


Figure S2: Representative local field potential recordings of the zebrafish PTZ seizure model. 10 min noninvasive local field potential recordings from the optic tectum of larvae pre-exposed to vehicle (VHC) and pentylenetetrazole (PTZ), VHC only, compound and PTZ, or compound and VHC. Test concentration and treatment period used for each compound: 200 $\mu\text{g}/\text{mL}$ halimide (2 h), 10 μM plinabulin (18 h), and 1 mM valproate (18 h).

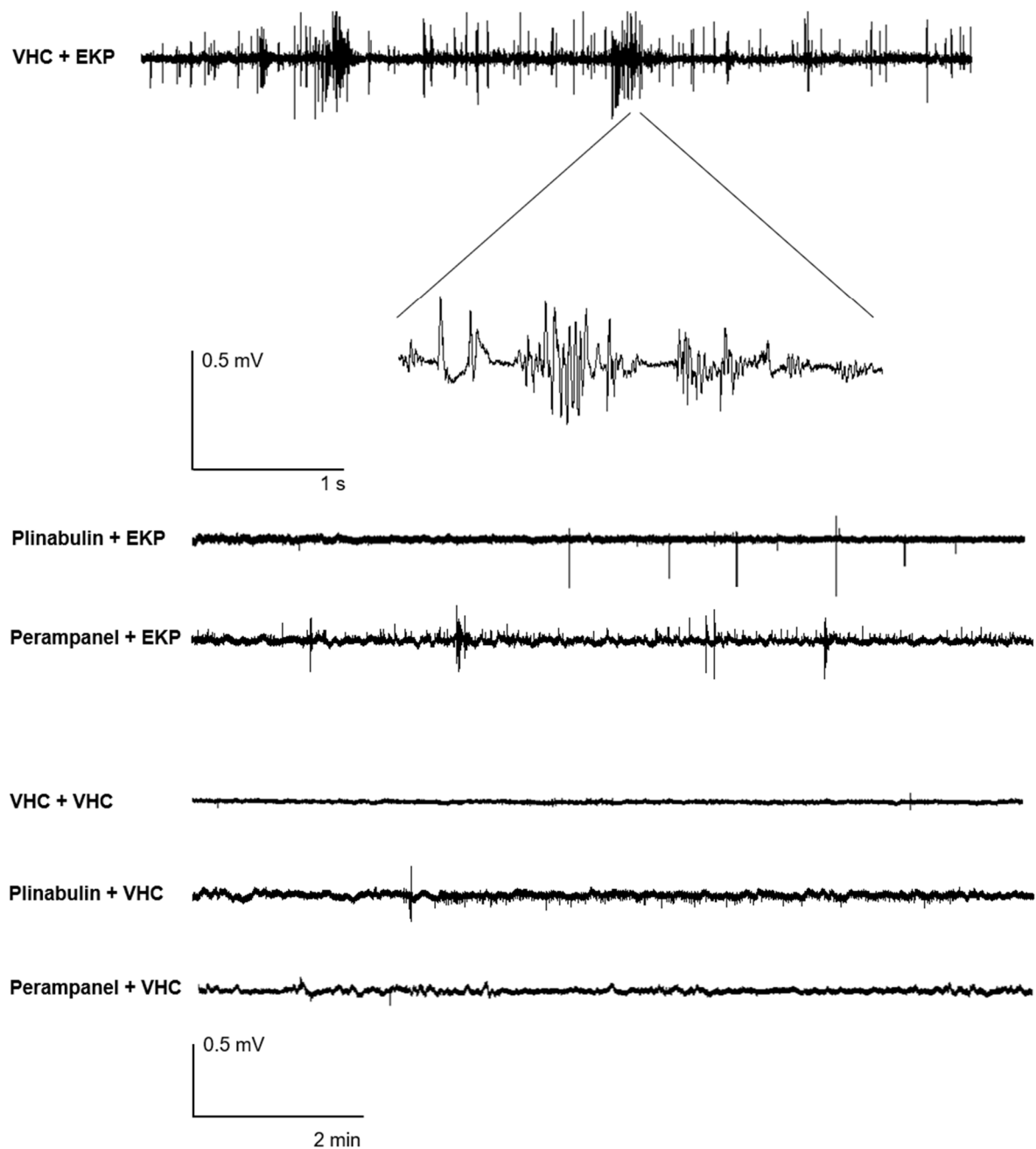


Figure S3: Representative local field potential recordings of the zebrafish EKP seizure model. 10 min noninvasive local field potential recordings from the optic tectum of larvae pre-exposed to vehicle (VHC) and ethyl ketopentenoate (EKP), VHC only, compound and EKP, or compound and VHC. Test concentration and treatment period used for each compound: 10 μ M plinabulin (18 h) and 1 μ M perampanel (2 h).

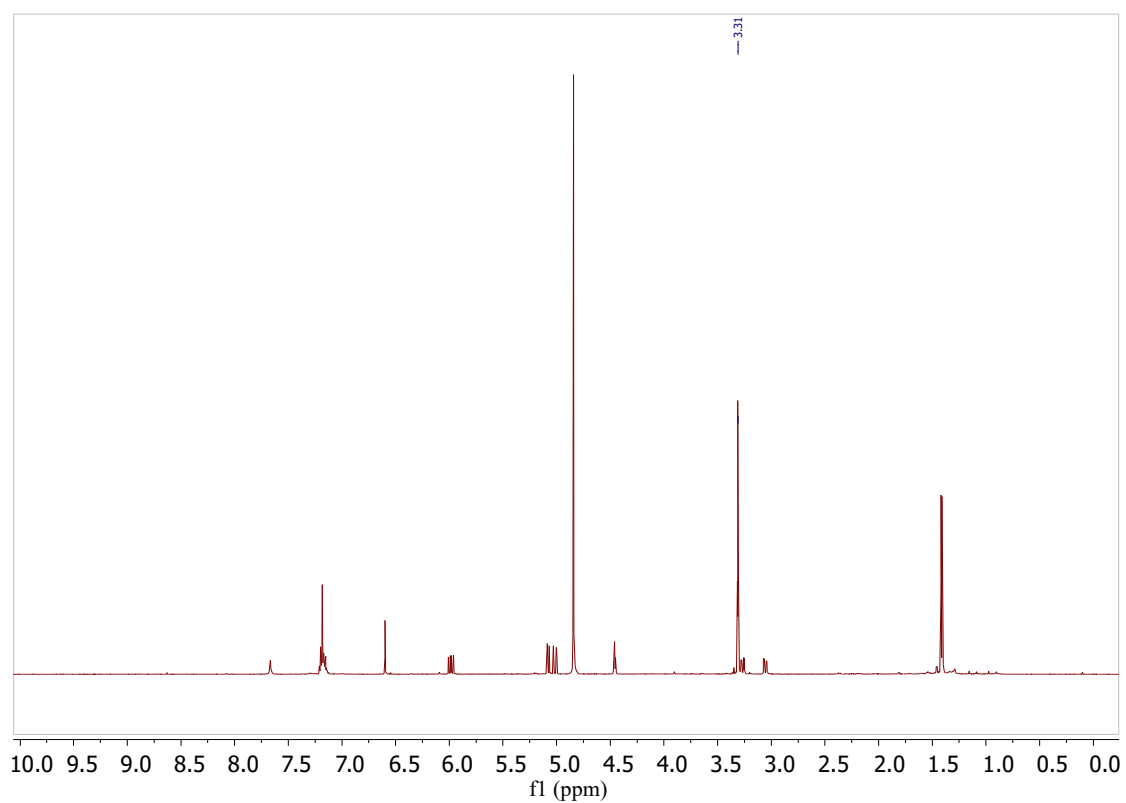


Figure S4: ¹H-NMR (600 MHz, MeOD) of halimide.

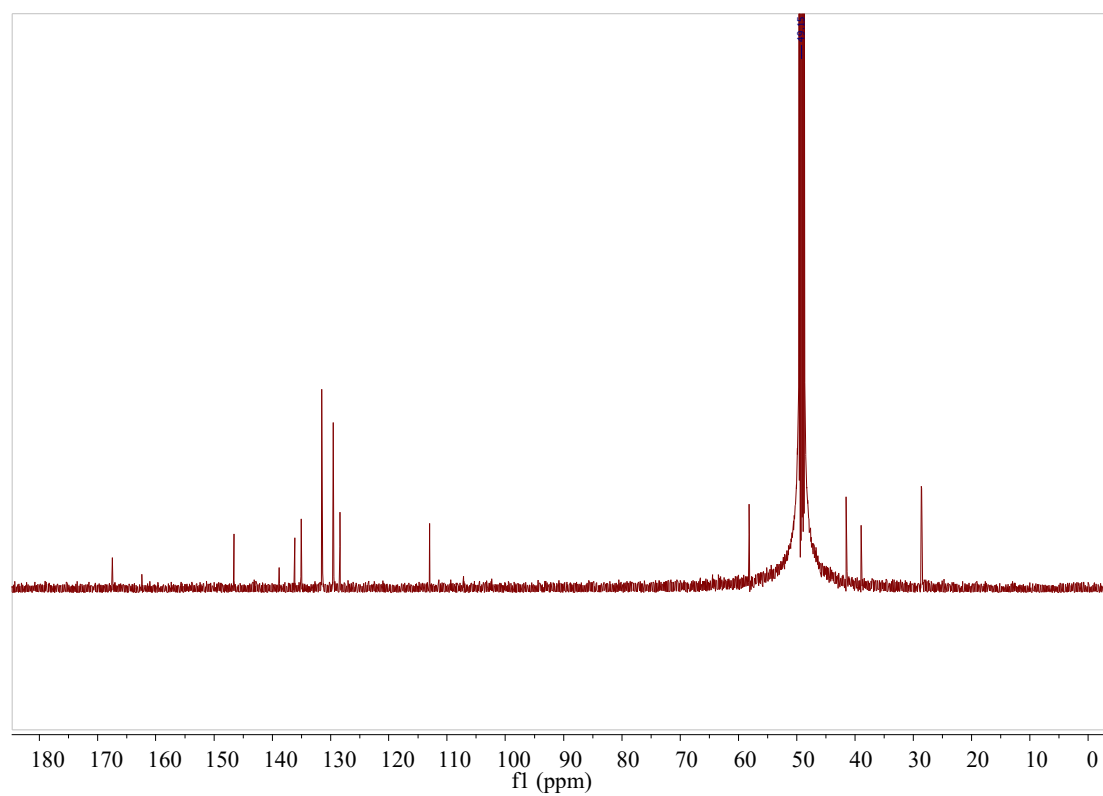


Figure S5: ¹³C-NMR (150 MHz, MeOD) of halimide.