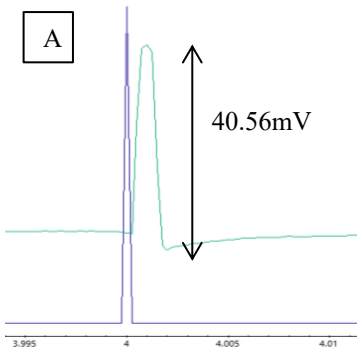
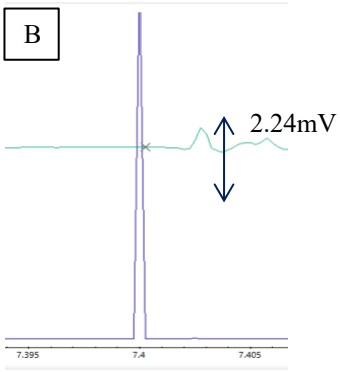
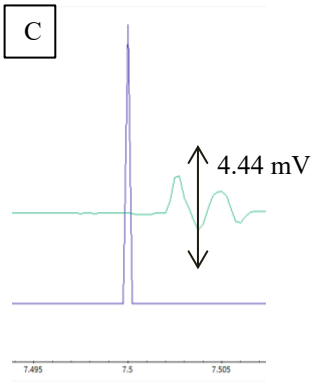
Supplementary material-2

Electrophysiological nerve conduction velocity recordings

The MLA 1204 needle electrodes from AD Instruments were used for the SNCV investigation. For recording purposes, these electrodes were placed at the ankle's medial malleolus area and coupled to the Bio Amp (AD Instruments). The reference electrode and recording electrode were positioned proximally at a distance of one centimeter. The anode was positioned in the third toe, and the cathode in the fifth. On the back of the leg, a ground electrode was positioned. With the AD Instruments PowerLab 16/35 N12128, electric stimuli were reliably supramaximal (8V) at 2 Hz and delivered with a 1 ms pulse width. Beginning with a positive spike diversion was used to quantify the nerve conduction latency (ms). SNCV (m/s) was calculated by dividing the distance between the recording electrodes by the latency of the signal. Using Vernier caliper the distance between recoding electrodes was measured.

The recording electrode was positioned in the plantar region of the paw to perform the MNCV test, whereas the reference electrode was positioned in the fourth toe. The cathode and anode stimulating electrodes were positioned 1 cm proximally in the ankle region for distal stimulation. The cathode and anode were positioned contralaterally at the sciatic notch for proximal stimulation. A ground electrode was positioned beneath the leg's epidermis. At 8V, electric shocks at a frequency of 2 Hz and a pulse width of 1 ms were consistently supramaximal. Using PowerLab, the amplitude was set to 20V and the sampling rate was set to 20 k/s. PowerLab Chart software (Lab Chart Pro v8.1.11) was used to get the data. A negative initial deflection of spike confirms the active electrode adjustment. Latency (ms) of nerve conduction was calculated from the stimulation artifact to the initial negative deflection of spike. MNCV (m/s) was calculated by dividing the distance between the distal and proximal stimulating electrodes by the difference between proximal and distal latencies. The hip was maintained at a right angled position, and the limb was straightened to measure the distance.

Fig. S2a. Sensory nerve conduction amplitude in control and diabetic neuropathic pain rats

		
Control vehicle, 10mL/kg, *i.p.*	IDNP vehicle, 10 mL/kg, *i.p.*	GBP, 10 mg/kg, *i.p.*

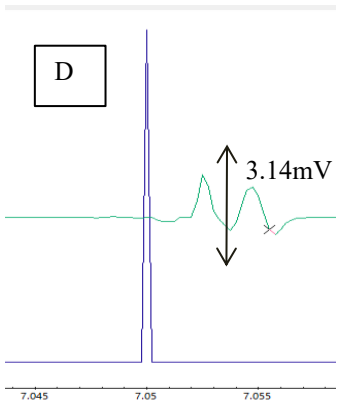
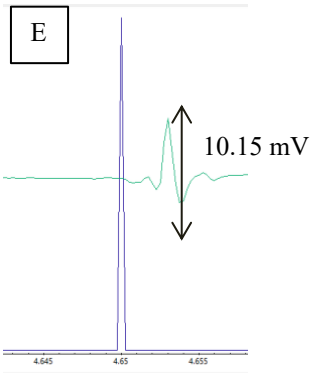
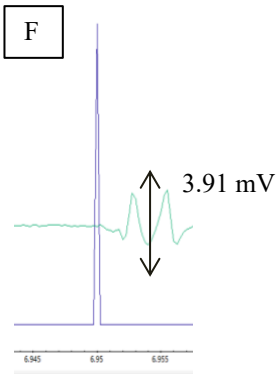
		
LP-211, 3 mg/kg, *i.p.*	LP-211, 3 mg/kg, *i.p.*+ GBP, 10 mg/kg, *i.p.*	Donepezil, 1 mg/kg, *i.p.*

Figure S2a: Difference in the amplitude of the sensory nerve action potential was observed, (A) Control vehicle, 10mL/kg, *i.p.* (B) IDNP vehicle, 10 mL/kg, *i.p.* (C) GBP, 10 mg/kg, *i.p.* (D) LP-211, 3 mg/kg, *i.p*. (E) LP-211, 3 mg/kg, *i.p*.+ GBP, 10 mg/kg, *i.p*. (F) Donepezil, 1 mg/kg, *i.p.* (amplitude of control rats > IDNP rats, LP-211 + GBP > IDNP rats, combination treatment showed improvement).

Fig. S2b. Motor nerve conduction amplitude in control and diabetic neuropathic pain rats

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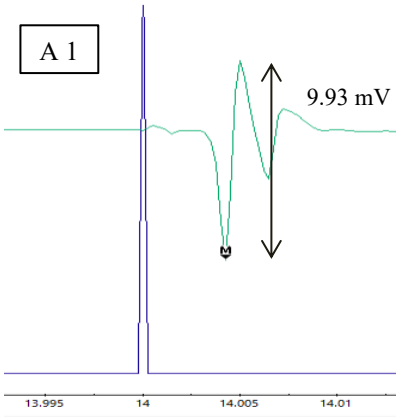
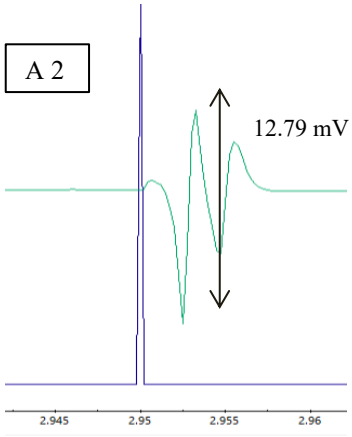
<tr><td> 
</td><td> 
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<tr><td>Proximal motor amplitude of Control vehicle, 10mL/kg, i.p.</td><td>Distal motor amplitude of Control vehicle, 10mL/kg, i.p.</td></tr>
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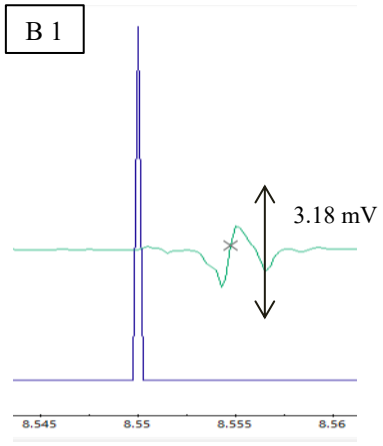
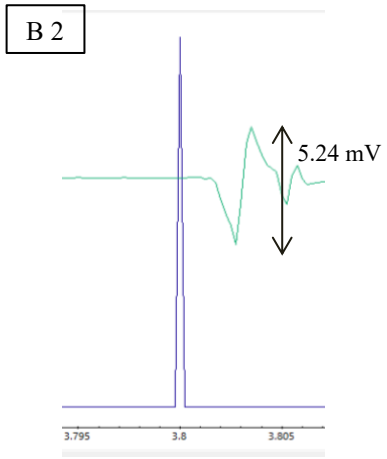
<tr><td> 
</td><td> 
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<tr><td>Proximal motor amplitude of IDNP vehicle, 10 mL/kg, i.p.</td><td>Distal motor amplitude of IDNP vehicle, 10 mL/kg, i.p.</td></tr>
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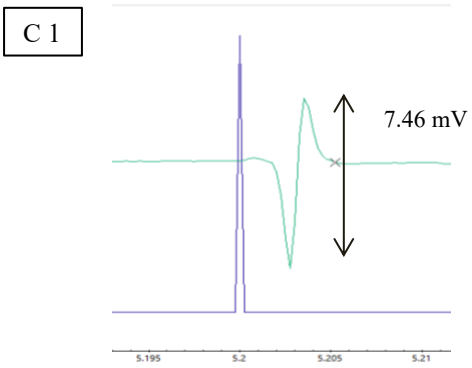
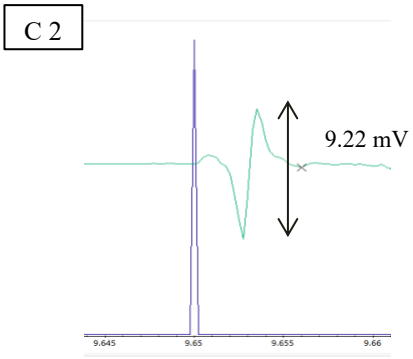
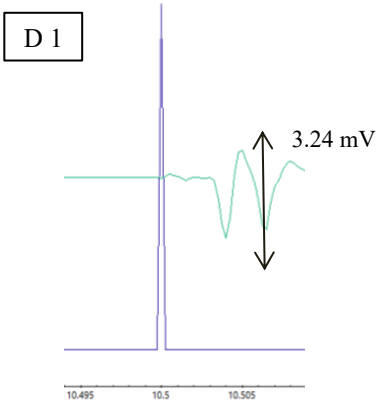


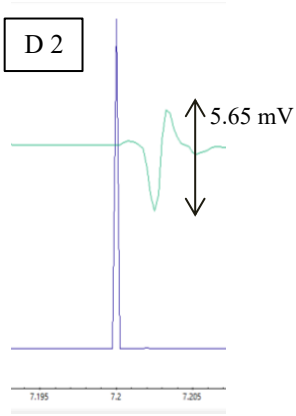
Proximal motor amplitude of GBP, 10 mg/kg, *i.p.*



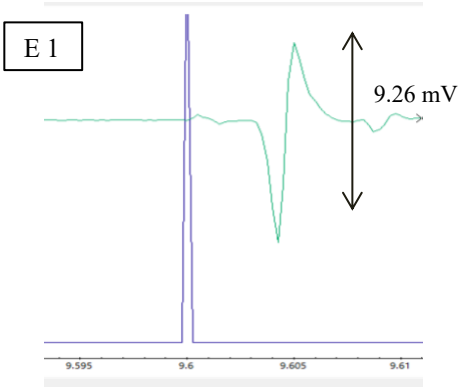
Distal motor amplitude of GBP, 10 mg/kg, *i.p.*



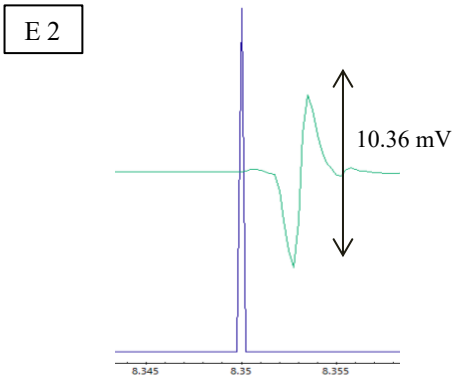
Proximal motor amplitude of LP-211, 3 mg/kg, *i.p.*



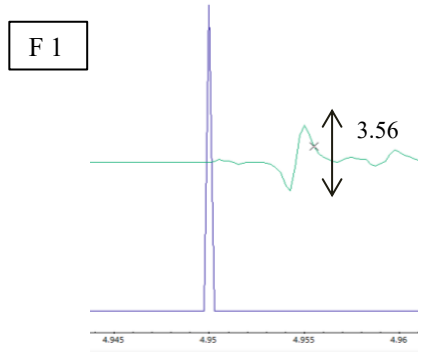
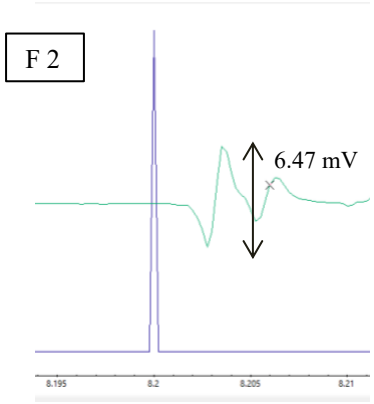
Distal motor amplitude of LP-211, 3 mg/kg, *i.p.*



Proximal motor amplitude of LP-211, 3 mg/kg, *i.p.*+ GBP, 10 mg/kg, *i.p.*



Distal motor amplitude of LP-211, 3 mg/kg, *i.p.*+ GBP, 10 mg/kg, *i.p.*

	
Proximal motor amplitude of Donepezil, 1 mg/kg, *i.p.*	Distal motor amplitude of Donepezil, 1 mg/kg, *i.p.*

Figigure S2b: Difference in the amplitude of the action potential was observed, (A1,A2) Control vehicle, 10mL/kg, *i.p* (B1,B2) IDNP vehicle, 10 mL/kg, *i.p* (C1,C2) GBP, 10 mg/kg, *i.p.* (D1,D2) LP-211, 3 mg/kg, *i.p.* (E1,E2) LP-211, 3 mg/kg, *i.p.*+ GBP, 10 mg/kg, *i.p.* (F1,F2) Donepezil, 1 mg/kg, *i.p.* (amplitude of control rats > IDNP rats, LP-211 + GBP > IDNP rats, combination treatment showed improvement).