

Report : Cardiac Organoid Drug Toxicity Test

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Summary of Experiment

Electrophysiological and impedance-based contractility parameters were evaluated in ACROBiosystems cardiac organoids following treatment with Vehicle, E-4031, and Nifedipine using the CIMFS-96 system.

Compared with the vehicle control group, E-4031 increased Fridericia-corrected field potential duration (FPDcF) and beat period from Dose 1, while spike amplitude decreased at Dose 2. Nifedipine decreased spike amplitude from Dose 1, whereas FPDcF and beat period decreased at Dose 2. Field potential parameters could not be quantified at Dose 3 following treatment with either E-4031 or Nifedipine.

E-4031 decreased impedance amplitude and increased time-to-peak (TTP) and time-to-relaxation (TTR) from Dose 1.

Nifedipine decreased impedance amplitude, TTP, and TTR at Dose 2. Impedance-based contractility parameters could not be quantified at Dose 2 and Dose 3 following E-4031 treatment and at Dose 3 following Nifedipine treatment

Purpose

The purpose of this study was to evaluate electrophysiological and impedance-based contractility parameters in ACROBiosystems cardiac organoids following treatment with Vehicle, E-4031, or Nifedipine using the CIMFS-96 system.

Experimental Overview

Organoid Type	Cardiac organoids (CIPO-HWL01)	Organoid Diameter	1.3 - 1.6 mm
System	CIMFS-96	Cell Chip	CITO-02W16E-10A
Electrode Contact Method	Physical fixation with organoid solutions (holder with silicone net)	Treatment	DW (Vehicle), E-4031, Nifedipine

Experimental Flow

Cardiac Organoid Culture (DIV 0-5):

- Cardiac organoids were cultured in a 37°C, 5% CO₂ incubator for 5 days.

Cell Chip Hydrophilization (DIV 5):

- Cell chips were hydrophilized 1 day before organoid transfer.

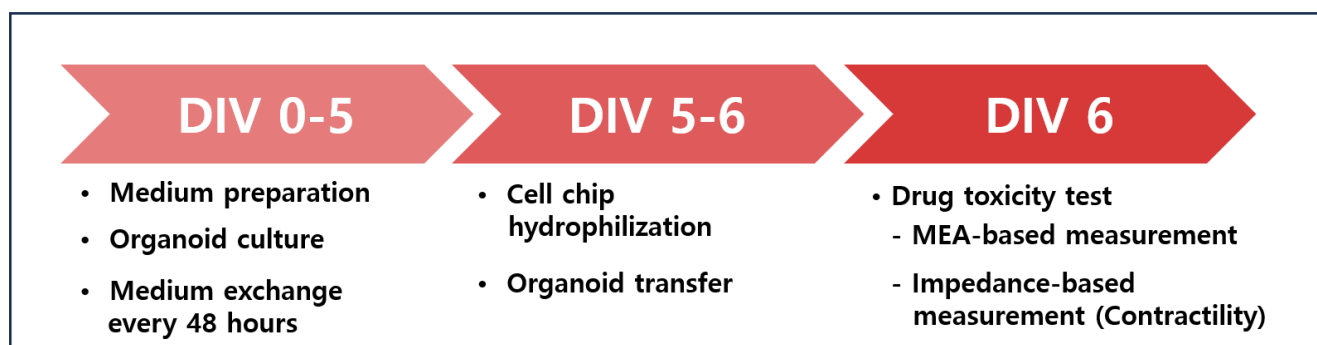
Organoid Transfer (DIV 6):

- Cardiac organoids were transferred onto the MEA cell chip.

Drug Toxicity Test (DIV 6):

- Electrophysiological activity and contractility were evaluated following cumulative administration of low-, medium-, and high-dose compounds using the CIMFS-96 system.



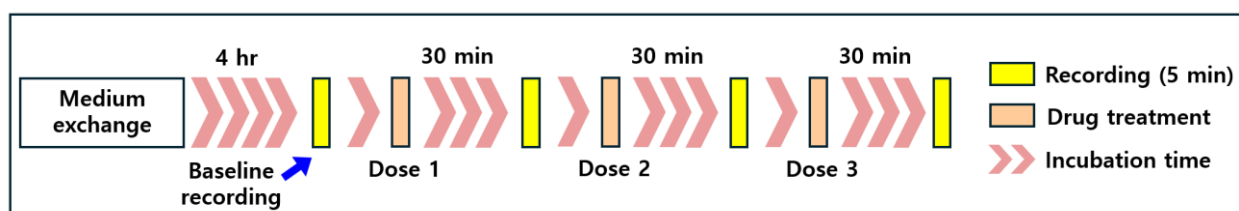


Drug Treatment

- The culture medium should be replaced at least 4 hours before drug treatment.

Drug Treatment and Recording

- Record baseline activity for 5 min before drug treatment.
- Add 80 μ L of a 10 $\times$ compound solution to each well and gently mix by pipetting 4–5 time.
- Incubate for 30 min in a 37°C, 5% CO₂ incubator, then record for 5 min.



Drug Treatment and Recording

- Vehicle control: DW
- Drug: E-4031, Nifedipine

	Baseline	Dose 1	Dose 2	Dose 3
Vehicle (DW, % v/v)	0	0.01	0.01	0.01
E-4031 (μ M)	0	0.1	0.3	1
Nifedipine (μ M)	0	0.01	0.1	1



Results

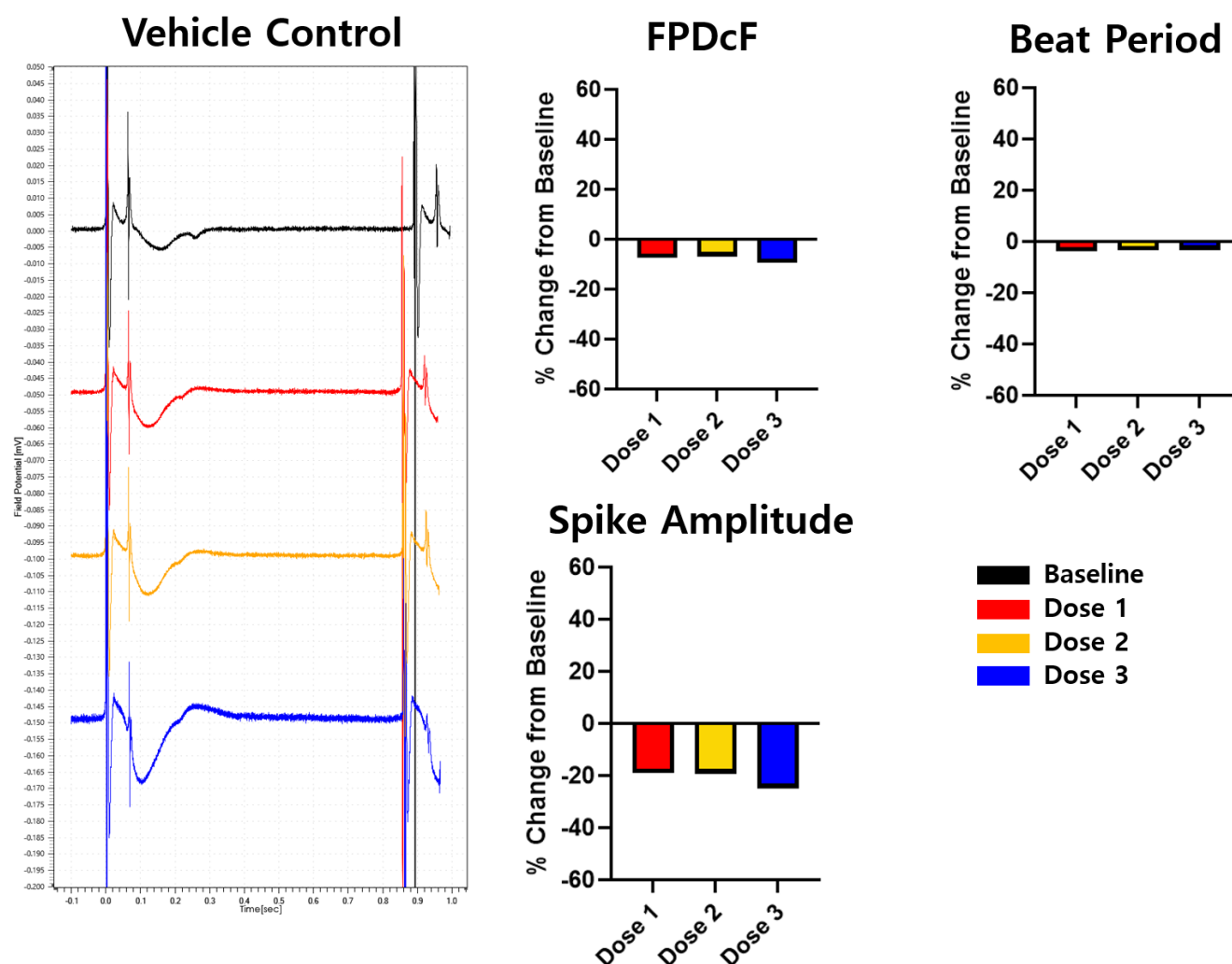


Figure 1. Electrophysiological Characteristics of the Vehicle Control Group.

Quantitative analysis showed that beat period changed by -3.97% , -3.50% , and -3.30% , while FPDcF changed by -7.55% , -6.81% , and -9.53% at Dose 1, Dose 2, and Dose 3, respectively. Spike amplitude decreased by 19.04% , 19.21% , and 24.88% at Dose 1, Dose 2, and Dose 3, respectively, and remained within a similar range throughout the repeated vehicle treatments.

Left panel: Representative field potential traces recorded at baseline and after each cumulative vehicle treatment (Dose 1–3). Right panels: Quantitative analysis of beat period, FPDcF, and spike amplitude, presented as the percentage change from baseline.



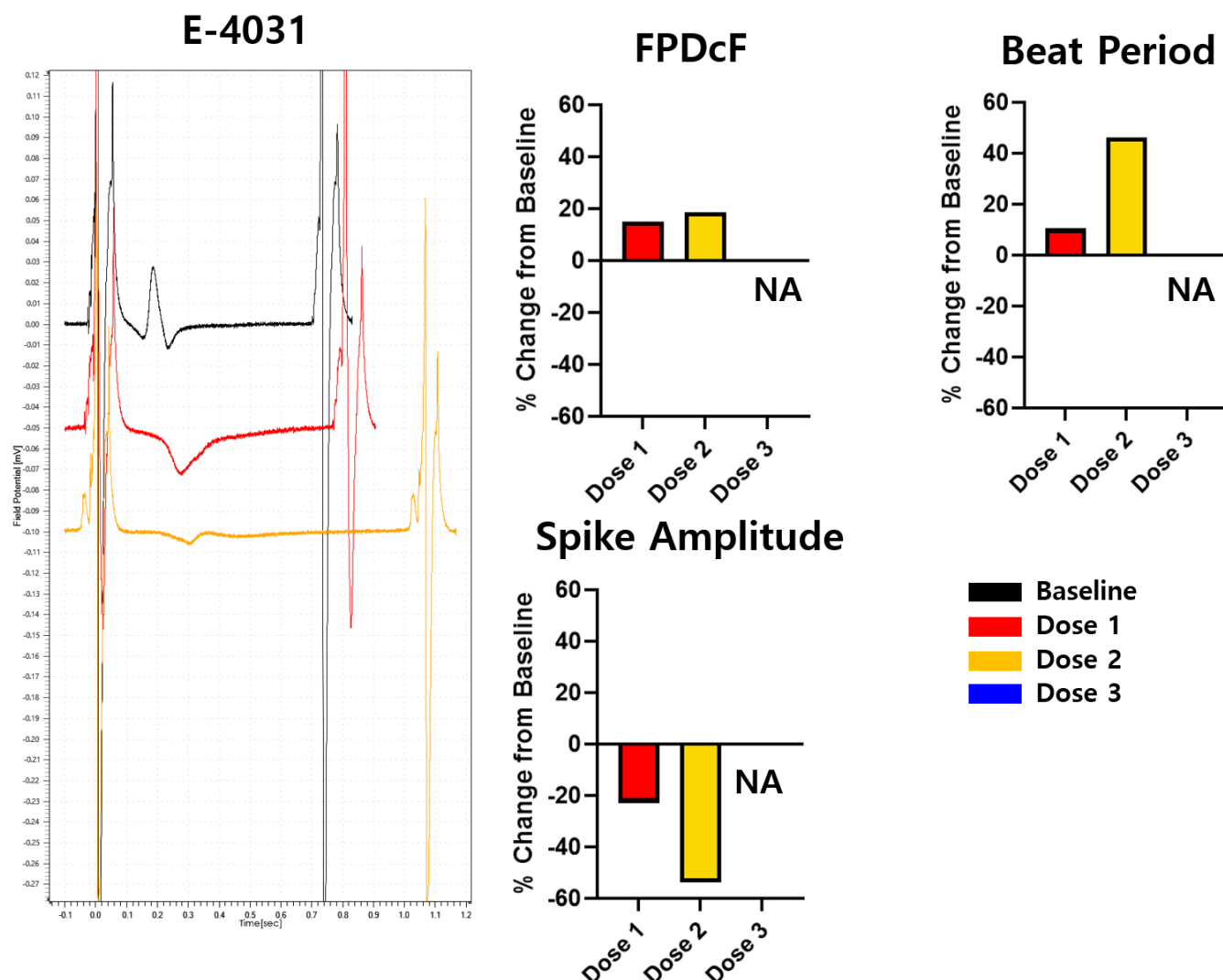


Figure 2. Effects of E-4031 on the Electrophysiological Activity of Cardiac Organoids.

Representative field potential traces showed dose-dependent prolongation of field potential duration (FPD) following cumulative E-4031 treatment. Quantitative analysis demonstrated that FPDcF increased by 15.88% and 18.72% at Dose 1 and Dose 2, respectively, while beat period increased by 10.49% and 46.28%. Spike amplitude decreased by 34.19% and 53.58% at Dose 1 and Dose 2, respectively. At Dose 3, electrophysiological parameters could not be quantified because stable field potential signals were no longer detected.

Left panel: Representative field potential traces recorded at baseline and following cumulative E-4031 treatment. Right panels: Quantitative analysis of FPDcF, beat period, and spike amplitude (change from baseline, %).

NA (Not applicable) indicates that the parameter could not be calculated due to the loss of detectable field potential signals.



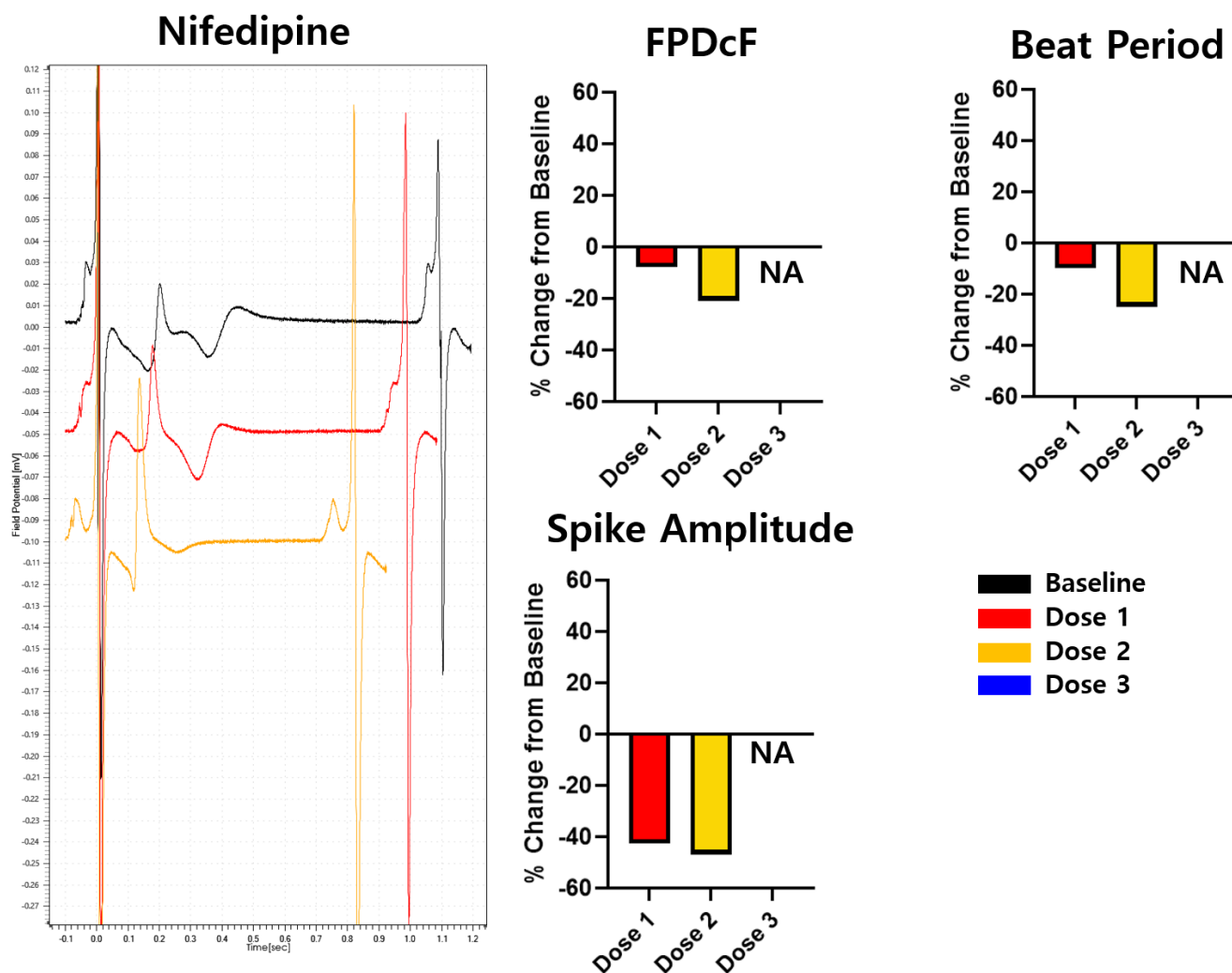


Figure 3. Effects of Nifedipine on the Electrophysiological Activity of Cardiac Organoids.

Representative field potential traces showed shortening of the field potential waveform following cumulative nifedipine treatment. Compared with baseline, FPDcF decreased by 7.95% and 20.91%, and beat period decreased by 9.94% and 24.85% at Dose 1 and Dose 2, respectively. Spike amplitude decreased by 42.68% and 46.83% at Dose 1 and Dose 2, respectively, showing a similar level of reduction at both doses. At Dose 3, stable field potential signals were not detected; therefore, the electrophysiological parameters could not be calculated.

Left panel: Representative field potential traces recorded at baseline and following cumulative Nifedipine treatment. Right panels: Quantitative analysis of FPDcF, beat period, and spike amplitude (change from baseline, %).

NA (Not applicable) indicates that the parameter could not be calculated due to the loss of detectable field potential signals.



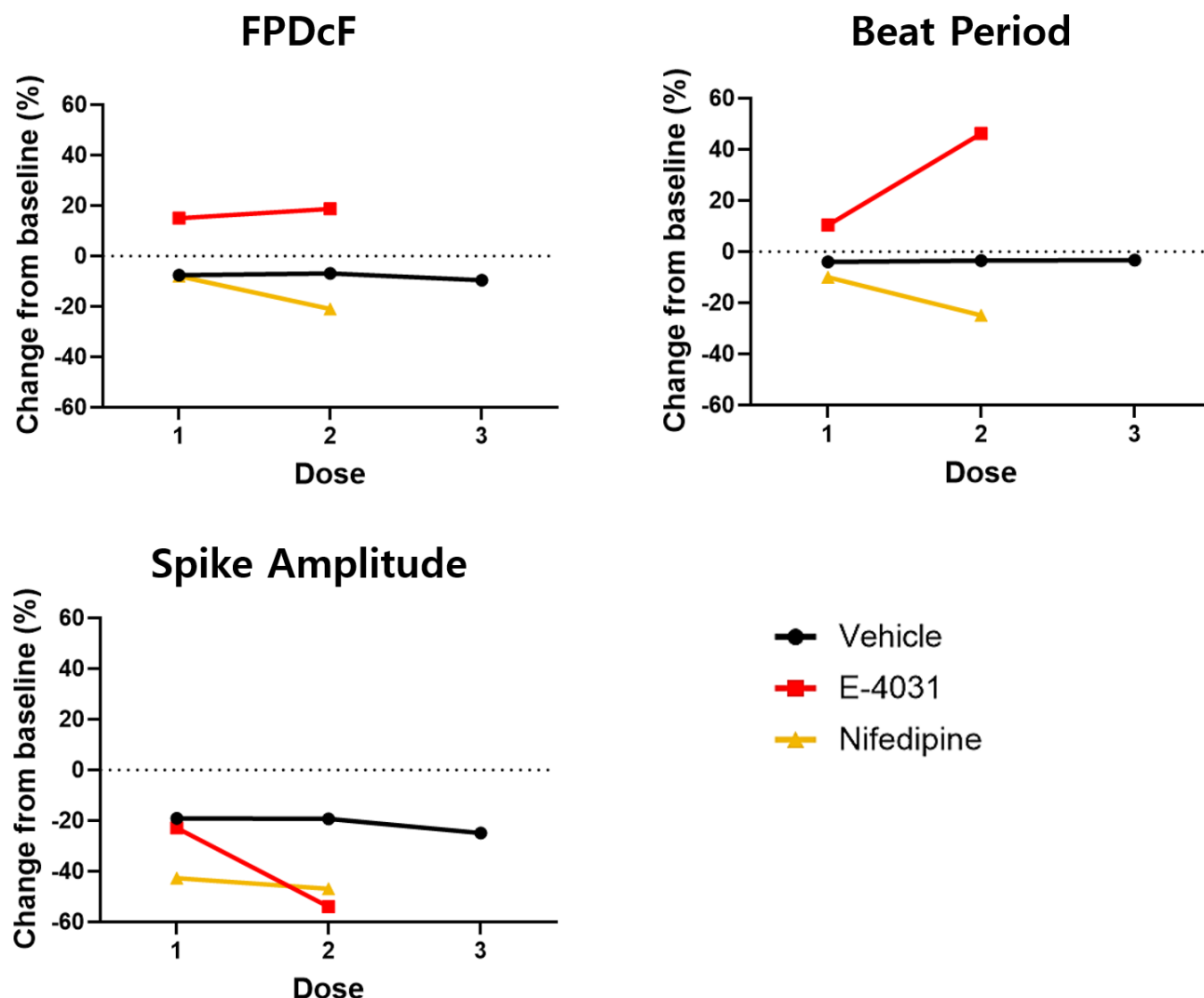


Figure 4. Comparison of Electrophysiological Responses to Drug Treatments in Cardiac Organoids.

Compared with the drug-treated groups, the vehicle group generally exhibited minimal changes in all electrophysiological parameters throughout the experiment. Cumulative E-4031 treatment increased FPDcF and beat period, whereas a marked decrease in spike amplitude was observed at Dose 2. Nifedipine produced marked decreases in FPDcF and beat period at Dose 2, while spike amplitude showed a decreasing trend following treatment. For both E-4031 and Nifedipine, electrophysiological parameters at Dose 3 could not be quantified because stable field potential signals were no longer detected.



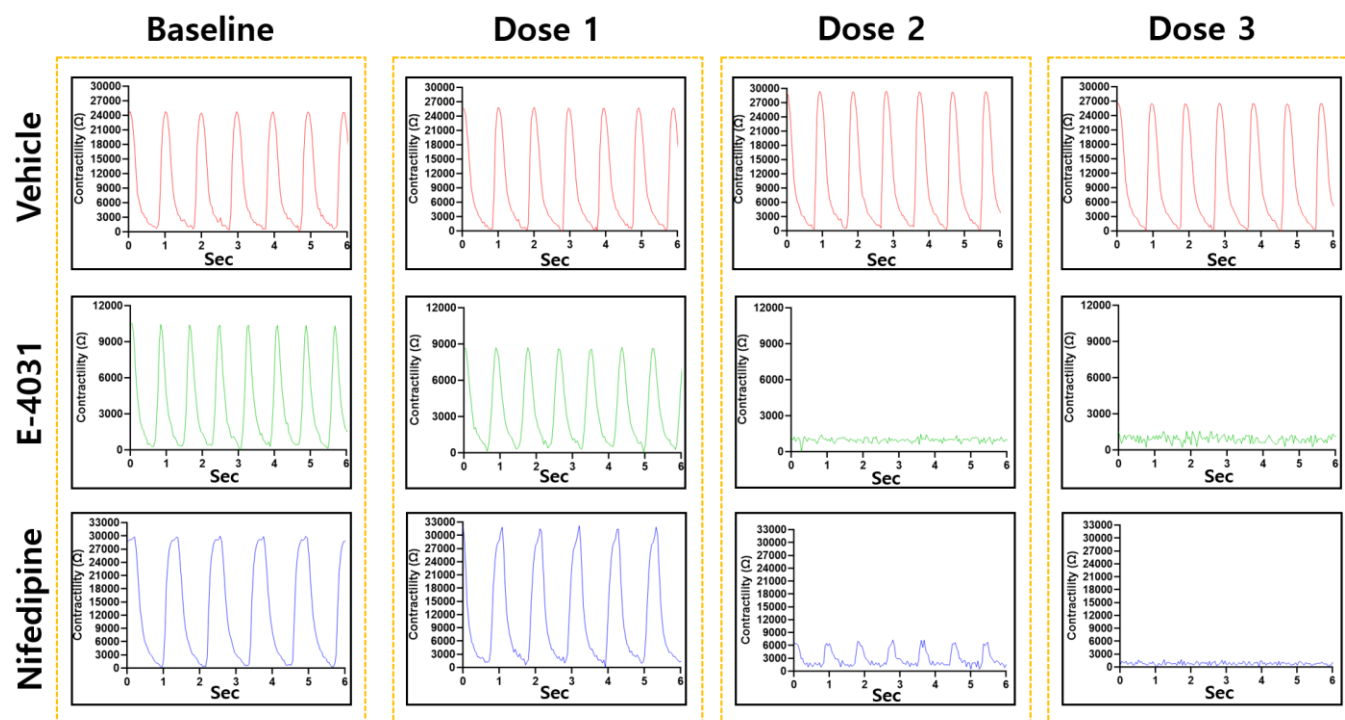


Figure 5. Effects of Vehicle, E-4031, and Nifedipine on Cardiac Organoid Contractility Assessed by Impedance Measurement (3 kHz).

Representative impedance-based contractility recordings of cardiac organoids at 3 kHz following cumulative treatment with vehicle, E-4031, or nifedipine. Vehicle treatment maintained stable contractile waveforms throughout the experiment. In contrast, E-4031 reduced contractile activity after Dose 1, and spontaneous contractions were no longer detected at Dose 2 and Dose 3. Nifedipine also reduced contractile activity in a dose-dependent manner, with a marked decrease in contraction amplitude at Dose 2 and complete loss of detectable contractions at Dose 3.



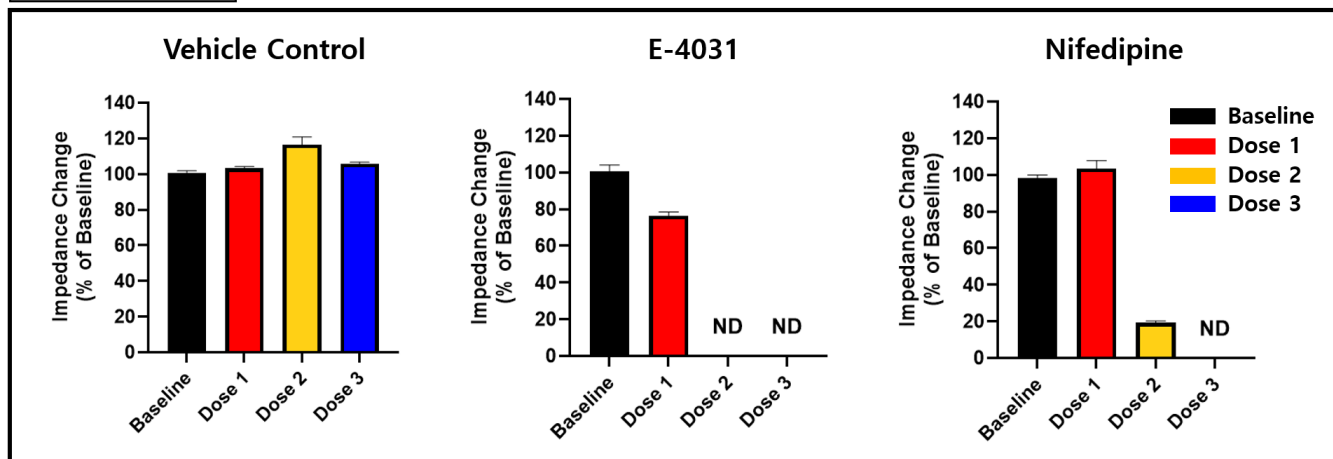
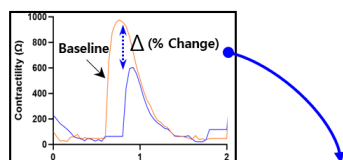


Figure 6. Quantitative Analysis of Impedance-Based Contractility Following Vehicle, E-4031, and Nifedipine Treatment.

Contractility was quantified by measuring the impedance amplitude at 3 kHz and expressed as the percentage relative to the baseline. Compared with baseline, vehicle treatment increased impedance amplitude by 3.34%, 16.60%, and 5.77% at Dose 1, Dose 2, and Dose 3, respectively. In contrast, E-4031 decreased impedance amplitude by 23.60% at Dose 1, while contractile signals were not detected (ND) at Dose 2 and Dose 3. Nifedipine increased impedance amplitude by 3.57% at Dose 1 but decreased it by 80.72% at Dose 2. Contractile signals were not detected (ND) at Dose 3.



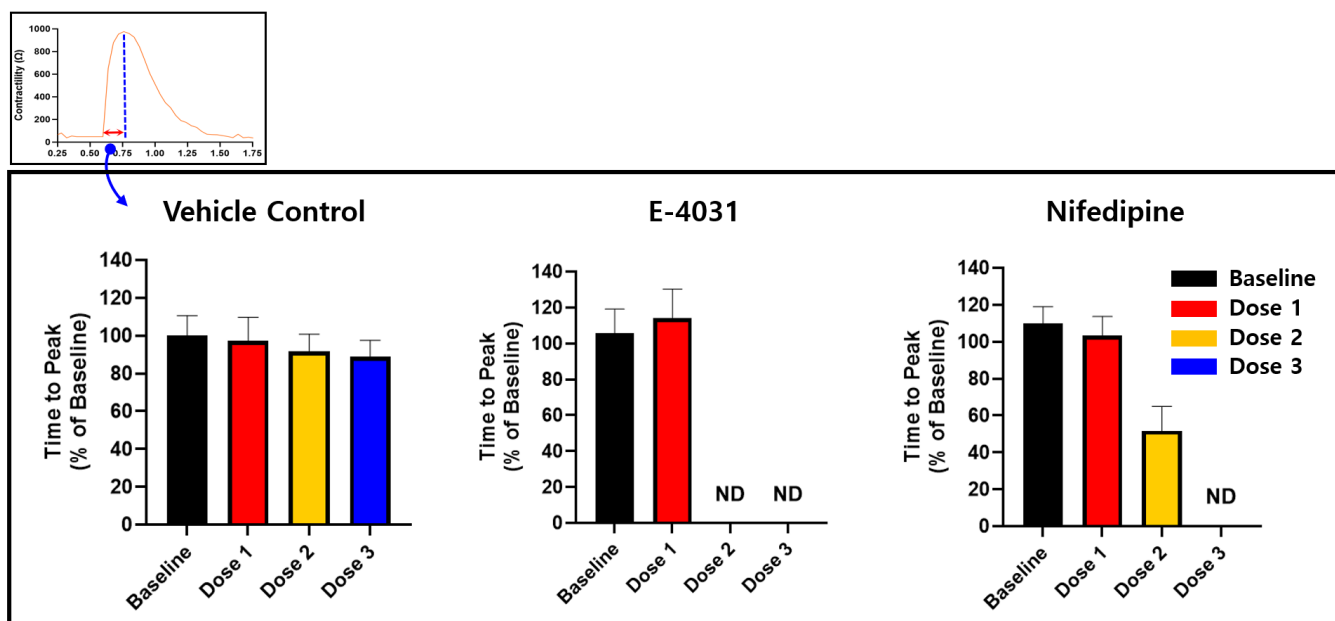


Figure 7. Quantitative Analysis of Time-to-Peak Following Vehicle, E-4031, and Nifedipine Treatment.

Time-to-peak (TTP) was quantified as the time interval from the onset of contraction to the peak impedance signal and expressed as the percentage relative to the baseline. Compared with baseline, vehicle treatment decreased TTP by 2.78%, 8.33%, and 11.11% at Dose 1, Dose 2, and Dose 3, respectively. In contrast, E-4031 increased TTP by 13.89% at Dose 1, while TTP could not be quantified at Dose 2 and Dose 3 because contractile signals were not detected (ND). Nifedipine decreased TTP by 6.67% at Dose 1 and 53.33% at Dose 2. TTP could not be quantified at Dose 3 because contractile signals were not detected (ND).



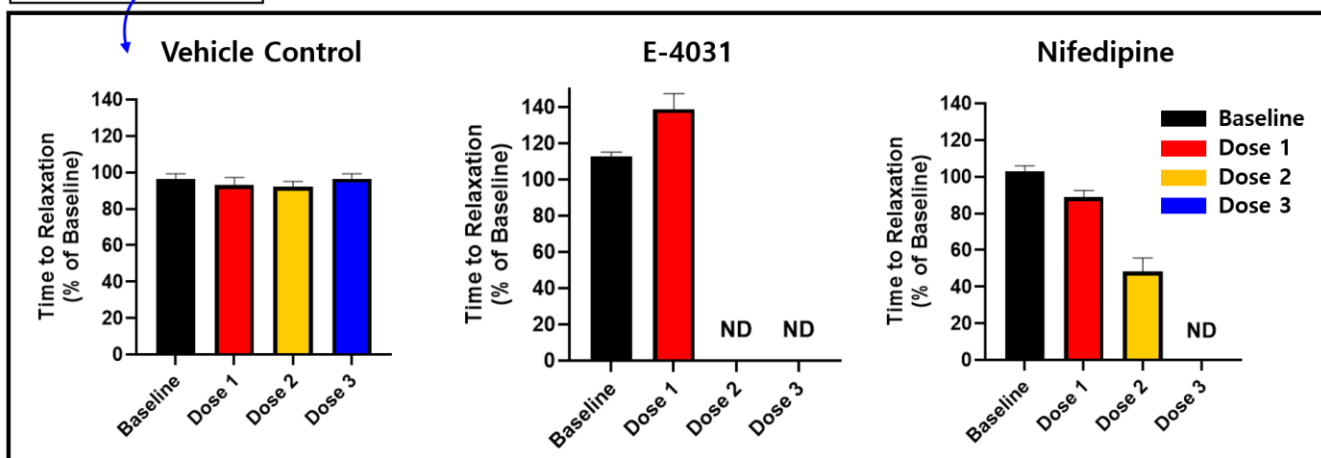
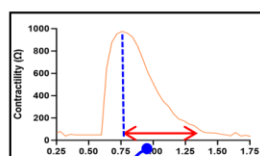


Figure 8. Quantitative Analysis of Time-to-Relaxation Following Vehicle, E-4031, and Nifedipine Treatment.

Time-to-relaxation (TTR) was quantified as the time interval from the peak impedance signal to the completion of relaxation and expressed as the percentage relative to the baseline. Compared with baseline, vehicle treatment decreased TTR by 7.02%, 7.89%, and 3.51% at Dose 1, Dose 2, and Dose 3, respectively. In contrast, E-4031 increased TTR by 38.89% at Dose 1, while TTR could not be quantified at Dose 2 and Dose 3 because contractile signals were not detected (ND). Nifedipine decreased TTR by 11.11% at Dose 1 and 51.85% at Dose 2. TTR could not be quantified at Dose 3 because contractile signals were not detected (ND).



Supplemental Data

- No supplementary data.

Keyword

CIMFS-96, Cardiac Organoid, Field Potential, MEA, Contractility

