



Neuroprotective Effects of *Cyclosorus terminans* Extract on Cognitive Decline and Brain Mitochondrial Dysfunction in Obese Rats

Wasana Pratchayasakul^{1,2}, Busarin Arunsak¹, Aphisek Kongkaew³, Sujinda Songtra⁴, Sireewan Kaewsuwan^{5,6},
Nipon Chattipakorn^{1,2}, Siriporn C Chattipakorn^{1,7}

¹ Neurophysiology Unit, Cardiac Electrophysiology Research and Training Center, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, ² Cardiac Electrophysiology Unit, Department of Physiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, ³ Research Administration Section, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, ⁴ Faculty of Medical Technology, Rangsit University, Pathumthani, Thailand, ⁵ Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Songkhla, Thailand, ⁶ Phytomedicine and Pharmaceutical Biotechnology Excellence Center, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Songkhla, Thailand, ⁷ Department of Oral Biology and Diagnostic Science, Faculty of Dentistry, Chiang Mai University, Chiang Mai, Thailand.

INTRODUCTION

Long-term consumption of a high-fat diet causes brain mitochondrial dysfunction, as indicated by mitochondrial swelling and changes in mitochondrial membrane potential; these alterations consequently lead to increased brain mitophagy, brain apoptosis, and cognitive decline.¹ We previously reported that treatment with *Cyclosorus terminans* extract alleviates neuroinflammation in obese rats,² however the preventive effects of *Cyclosorus terminans* extract on brain mitochondrial dysfunction and cognitive decline in obese condition have not been determined.

Objective

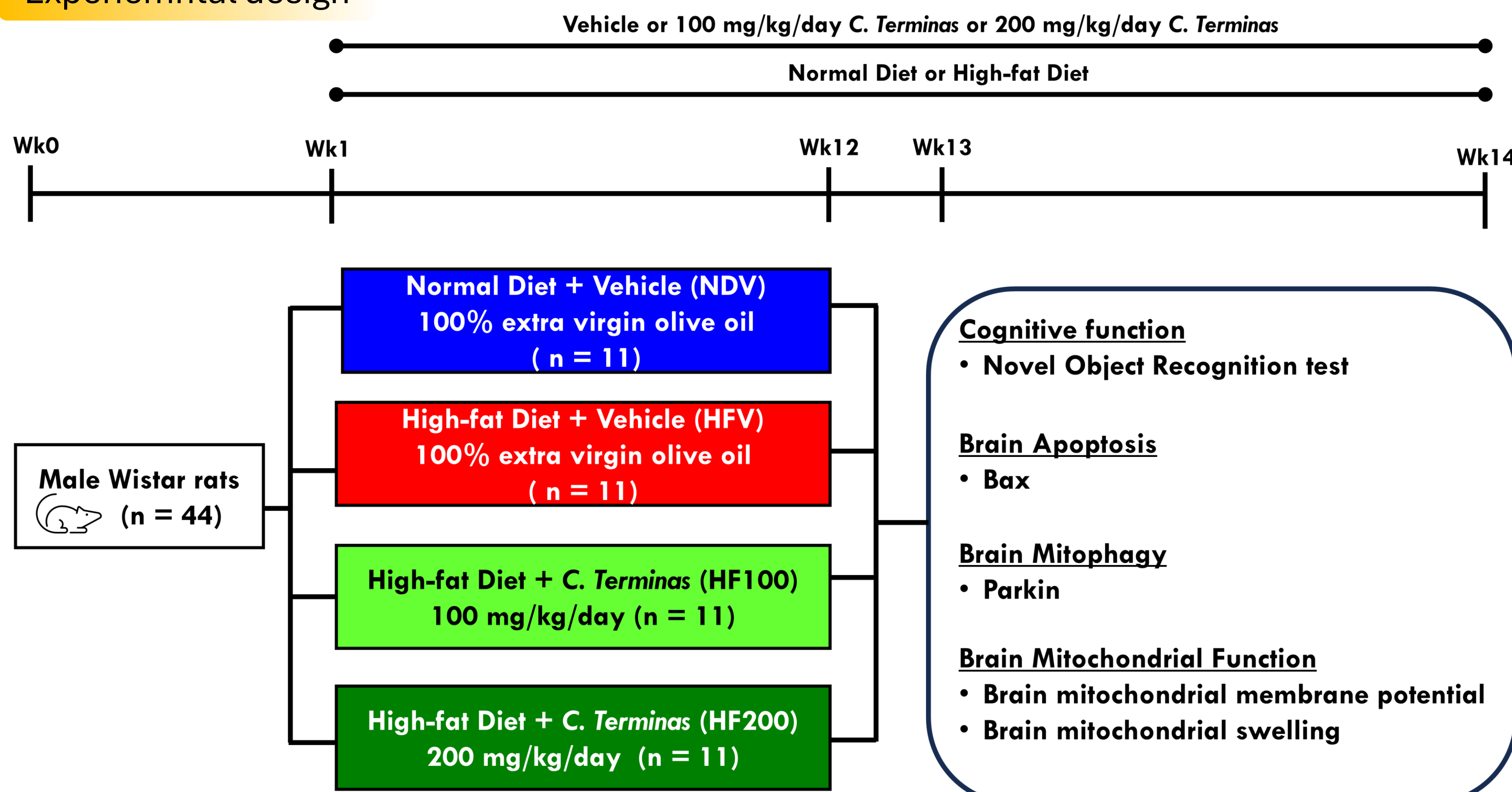
To investigate the preventive effect of *Cyclosorus terminans* extract on cognitive function and brain mitochondrial function in obese model

References

1. Sa-Nguanmoo P, Tanajak P, Kerdphoo S, Satjaritanun P, Wang X, Liang G, Li X, Jiang C, Pratchayasakul W, Chattipakorn N, Chattipakorn SC. FGF21 improves cognition by restored synaptic plasticity, dendritic spine density, brain mitochondrial function and cell apoptosis in obese-insulin resistant male rats. *Horm Behav*. 2016 Sep;85:86-95.
2. Oo TT, Pratchayasakul W, Chattipakorn K, Siri-Angkul N, Choovuthayakorn J, Charumporn T, Ongnok B, Arunsak B, Chunchai T, Kongkaew A, Songtra S, Kaewsuwan S, Chattipakorn N, Chattipakorn S. *Cyclosorus Terminans* Extract Alleviates Neuroinflammation in Insulin Resistant Rats. *Mol Neurobiol*. 2024 Jul;61(7):4879-4890.

METHODS

Experiemntal design



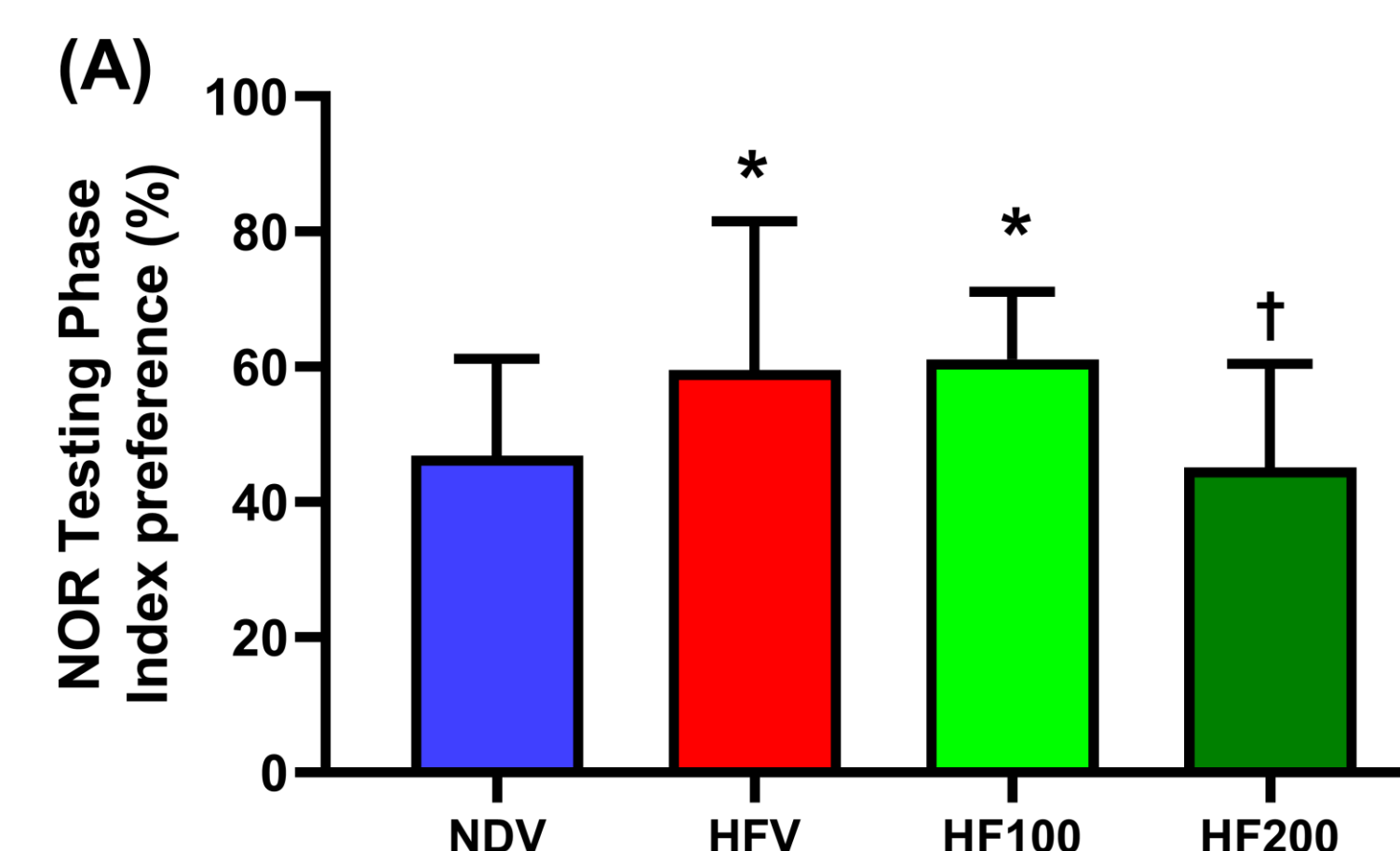
Male Wistar rats were divided into 4 groups as following: 1) normal-diet fed rats-treated with vehicle (NDV); 2) HFD-fed rats-treated with vehicle (HFV); 3) HFD-fed rats-treated with 100 mg/kg/day of *Cyclosorus terminans* extract (HF100); 4) HFD-fed rats-treated with 200 mg/kg/day of *Cyclosorus terminans* extract (HF200). Each group were given a diet along with vehicle or *Cyclosorus terminans* extract for 14-week. At week 13, the cognitive function of each group was assessed using the novel object recognition (NOR) test. After that, rats were sacrificed, and the brain was rapidly removed to determine mitochondria function (mitochondria membrane potential change and mitochondria swelling), mitophagy and apoptosis.

RESULTS

Cognitive Function

- Pretreatment with 200mg/kg/day of *Cyclosorus terminans* extract attenuated cognitive deficit in HFD-fed rats.

Novel objective recognition (NOR) test



Brain Apoptotic Level

- Pretreatment with 200mg/kg/day of *Cyclosorus terminans* extract attenuated brain apoptotic level in HFD-fed rats.

Brain Bax level

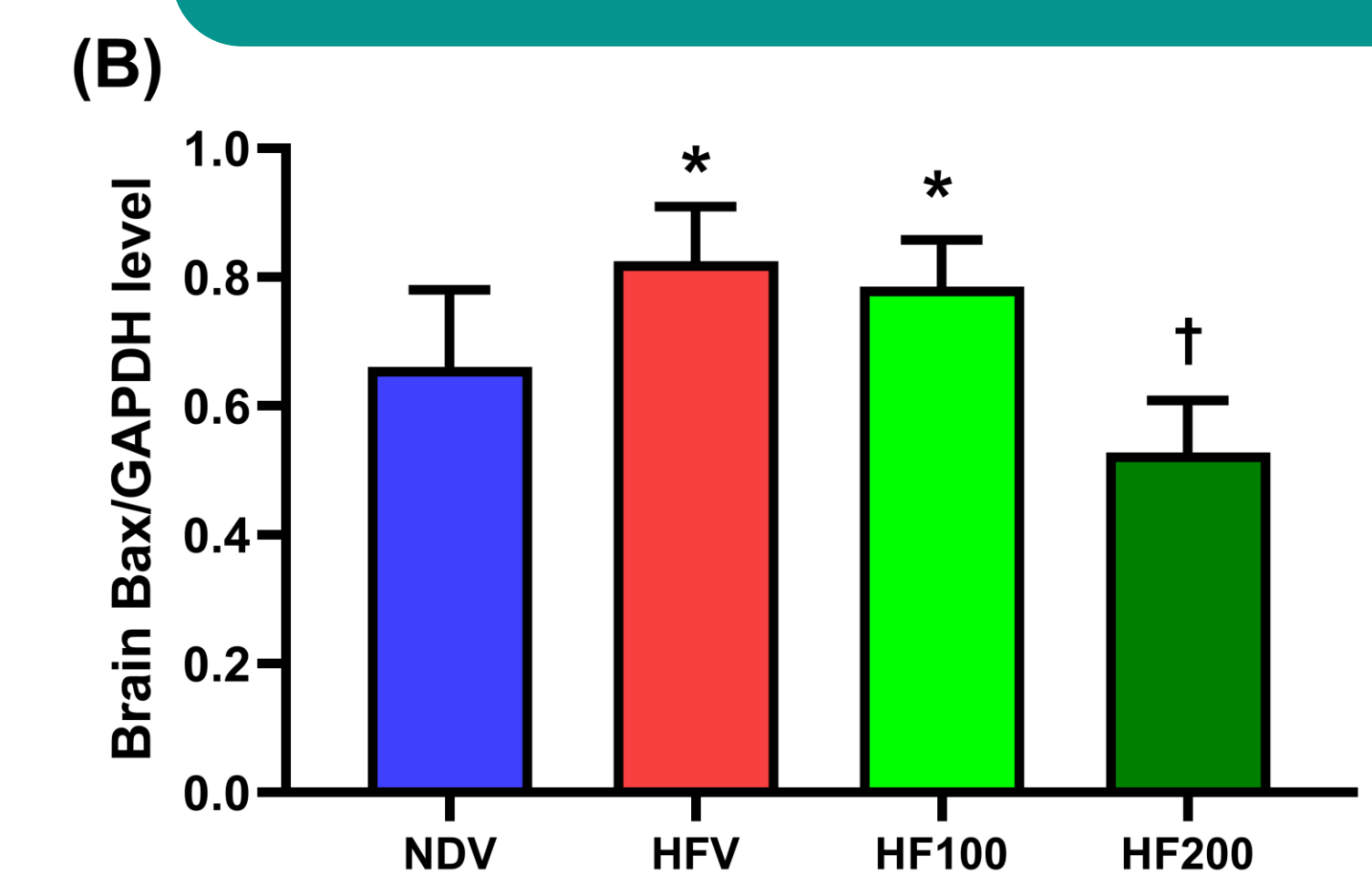


Figure 1. Prophylactic effects of *Cyclosorus terminans* extract on cognition, and brain apoptotic level in obese rats. (A) Cognitive function as indicated by preference index of novel objective recognition (NOR; %); (B) Brain apoptosis as indicated by Bax level; n= 6/ group; *p<0.05 vs NDV; †p<0.05 vs HFV; NDV, ND-fed rat treated with vehicle; HFV, HFD-fed rats treated with vehicle; HF100, HFD-fed rats treated with *Cyclosorus terminans* extracts (100 mg/kg/day); HF200, HFD-fed rats treated with *Cyclosorus terminans* extracts (200 mg/kg/day)

Brain Mitophagy & Brain Mitochondrial Function

- Pretreatment with 200mg/kg/day of *Cyclosorus terminans* extract attenuated brain mitophagy, brain mitochondrial dysfunction in HFD-fed rats.

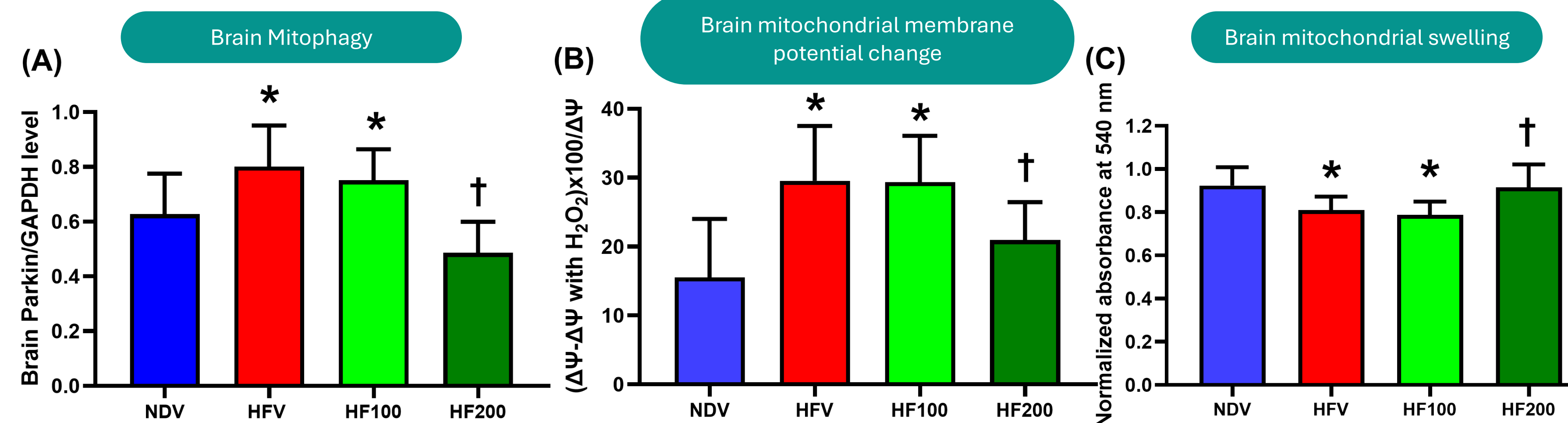


Figure 2. Prophylactic effects of *Cyclosorus terminans* extract on brain mitophagy and mitochondrial pathways in obese rats. (A) Brain mitophagy as indicated by Parkin level; (B) Brain mitochondrial membrane potential change as indicated by the % change JC-1 level after H_2O_2 stimulation; (C) Brain mitochondrial swelling as indicated by the normalized absorbance at wavelength of 540 nm; n= 6/ group; *p<0.05 vs NDV; †p<0.05 vs HFV; NDV, ND-fed rat treated with vehicle; HFV, HFD-fed rats treated with vehicle; HF100, HFD-fed rats treated with *Cyclosorus terminans* extracts (100 mg/kg/day); HF200, HFD-fed rats treated with *Cyclosorus terminans* extracts (200 mg/kg/day)

CONCLUSION

- Pretreatment with 200mg/kg/day of *Cyclosorus terminans* extract attenuated cognitive deficit, brain apoptosis, brain mitophagy, and brain mitochondrial dysfunction in HFD-fed rats
- Cyclosorus terminans* extract may serve as a prophylactic strategy to improve cognitive function in the case of obesity by enhancing brain mitochondrial pathways.

ACKNOWLEDGEMENTS



CONTACT



Wasana Pratchayasakul, PhD.
Neurophysiology Unit, Cardiac Electrophysiology Research and Training Center, Faculty of Medicine, Chiang Mai University, Thailand
Email: wasana.pratcha@cmu.ac.th