Introduction: Diabetes mellitus is characterized by elevated blood glucose levels. Ectopic fat accumulation is associated with insulin resistance and type 2 diabetes mellitus. In this case, triglycerides stored more in tissues which normally contain only small amounts of fat than adipose tissue, inducing metabolic processes disruption and organ function impairment. *Citrus Sudachi* is an evergreen tree that distributes mainly in Tokushima Prefecture of Japan. Previously, we have demonstrated that *Citrus Sudachi* could prevent the blood glucose and fatty acid elevation in human subjects. In this study, we illustrated the function of methanol extracts from *Citrus Sudachi* peel and investigated the mechanism of this effect.

Methods: We got the five kinds of methanol extracts by using diaion HP-20, and those were named by hydrophobicity from M-F1 to M-F5. C2C12 cells were stimulated by five kinds of Sudachi peel methanol extractions. After the treatment, intracellular triglyceride and non-essential fatty acid were assessed. PCR and Western blotting were used to determine the effect of M-F4 of key metabolism-regulating genes. Results: Among the 5 kinds of Sudachi methanol extracts, only M-F4 significantly decreased the intracellular triglyceride of C2C12 cells. It augmented the AMPK activity and increased the transcription of PPARα and its downstream target CPT-1b and UCP2.

Conclusion: M-F4 improved the lipid metabolism possibly through AMPK, PPARα and their downstream targets like CPT-1b and UCP2. Furthermore, this extract may be useful for preventing obesity and diabetes related diseases.