Integrated Metabolome-Microbiome Analyses to Evaluate the Alleviating Effects of Short-term Green Tea Supplementation for UVB-induced Erythema

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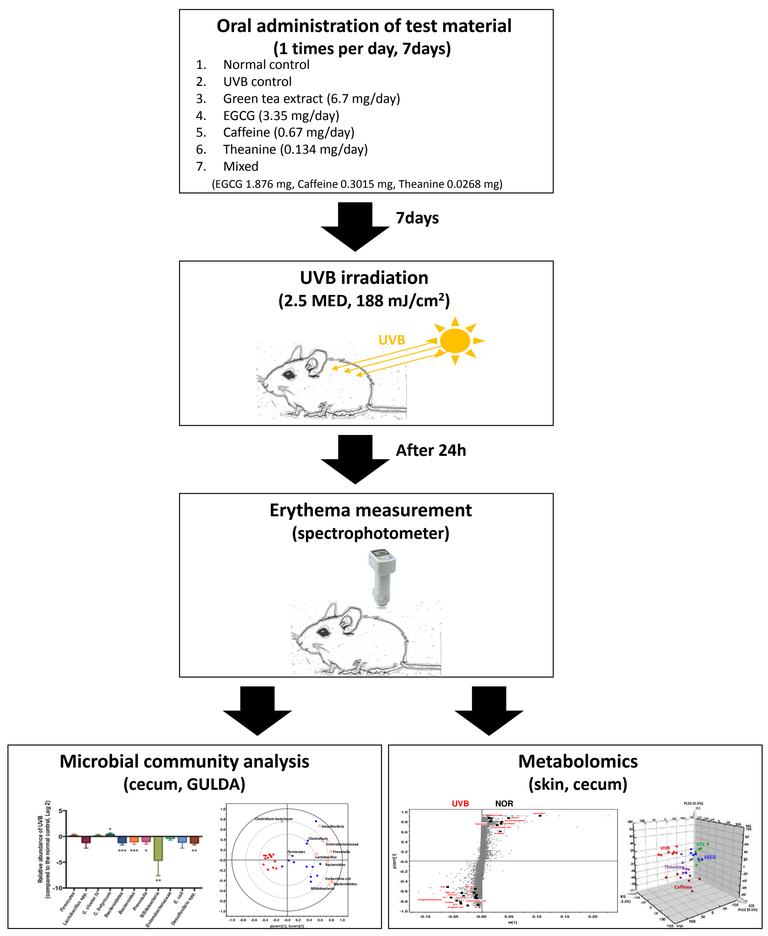
ABSTRACT

In this study, we aimed to establish an integrative skin and cecal metabolomics model for reveal preventing effects of erythema formation by short-term administration of green tea extracts (GTE) or its ingredients including epigallocatechin gallate (EGCG), caffeine, and theanine. Single ultraviolet (UV) B irradiation (188 mJ/cm^2) caused significant influences on both skin and cecum, i.e., erythema formation, alteration of skin and cecal metabolome, and cecal microbiome abundance (*Clostridium*, *Bifidobacteria*, *Bacteroidetes*, *Enterobacteriaceae*, *Prevotella*, *Bacteroides*, and *Desulfovibrio*). The oral administration of GTE for 7 days prior to UVB irradiation, significantly suppressed the erythema formation on dorsal skin in mice. However, significant suppression effects were observed on *Firmicutes* to *Bacteroidetes* ratio in each mice cecum of GTE, EGCG, caffeine, and theanine administrated. The mass spectrometry based metabolomics analysis showed an alteration in various skin and cecum metabolites including amino acids, organic compounds, fatty acids, lipids, saccharides, and nucleobases following administration of teat materials compared to UVB group. Especially, the relative levels of skin fatty acids, skin lysophospholipids, and cecal fatty acids were significantly altered through prior supplementation of GTE in UVB irradiated mice, compared to other supplements. Abundance of cecal microbiome including *Clostridium*, *Bifidobacteria*, *Bacteroidetes*, and *Bacteroides* were significantly modulated according to metabolome changes in GTE group. These results demonstrated that short-term supplementation of GTE or its ingredients highly modulated both skin and gut micro-environment, mitigating the changes induced through UVB irradiation. Particularly, GTE supplementation lead to preventing erythema on skin which might related to the alteration in endogenous metabolome and cecal microbiome in mice.

OBJECTIVE

To investigate, using integrative metabolome-microbiome analysis, the metabolic effects on skin and cecum associated with the preventing effects of erythema by short-term administration of green tea extracts as well as its ingredients including EGCG, caffeine, theanine.

METHODS



RESULTS

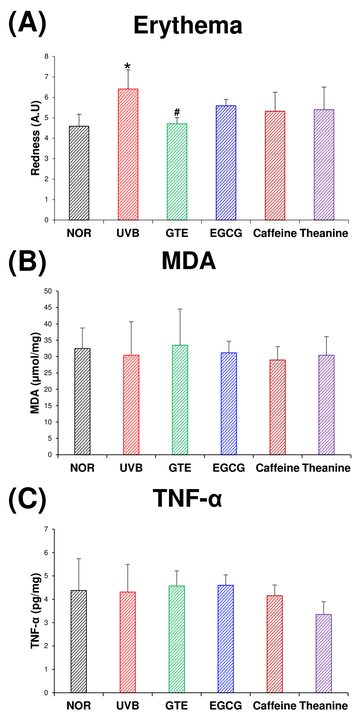


Figure 1. The clinical observation and biochemical parameters of skin tissue associated with the effects of short-term administration of GTE, EGCG, caffeine, and theanine on single UVB irradiation.

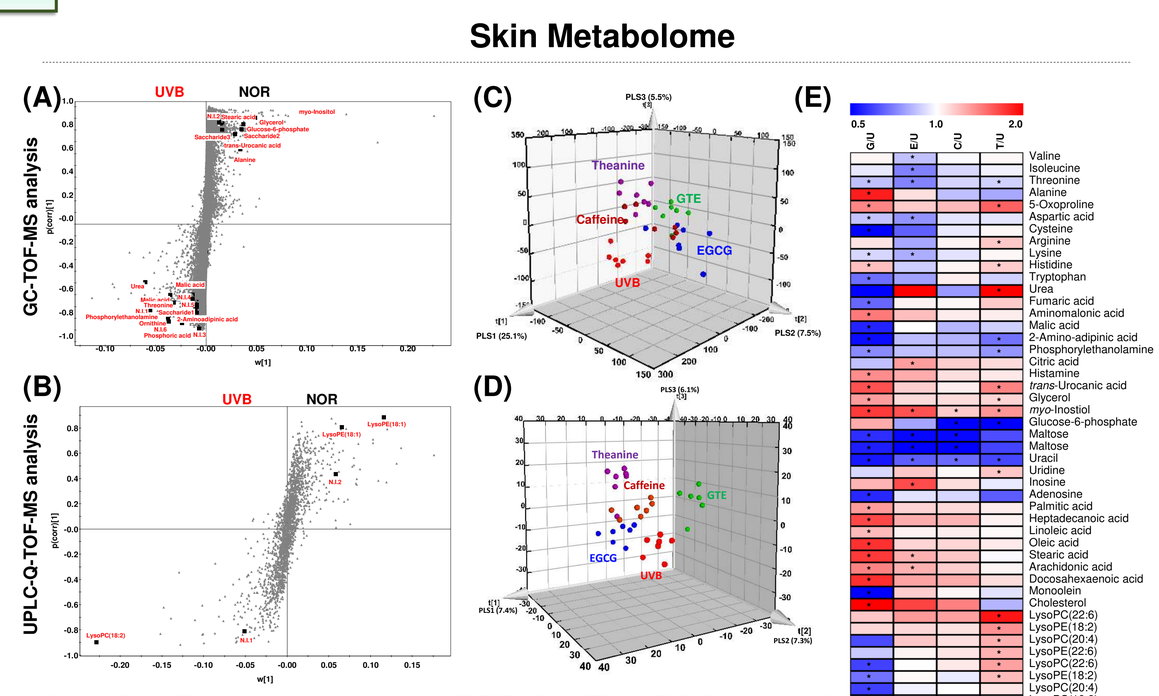


Figure 2. Metabolite profiling of skin tissue extracts based on GC-TOF-MS and UPLC-Q-TOF-MS analysis. (A, B) The loading S-plot for mice skin metabolite profiling of normal group (NOR) and single UVB-irradiated group (UVB). Each labeled marks (■) in the S-plot were statistically significantly different metabolites (VIP > 1, p-value < 0.05 in PLS-DA) between NOR and UVB. (C,D) Three-dimensional PLS-DA score plot for skin metabolite profiling of UVB group and groups that short-term (7 days) administration of GTE, EGCG, caffeine, theanine, respectively, before singly UVB irradiation. (E) The heatmap of significantly different metabolites (VIP > 1, p-value < 0.05) derived from PLS-DA (C, D). Each data point shown on the heatmap was normalized by the values of UVB group.

Cecal microbial community analysis

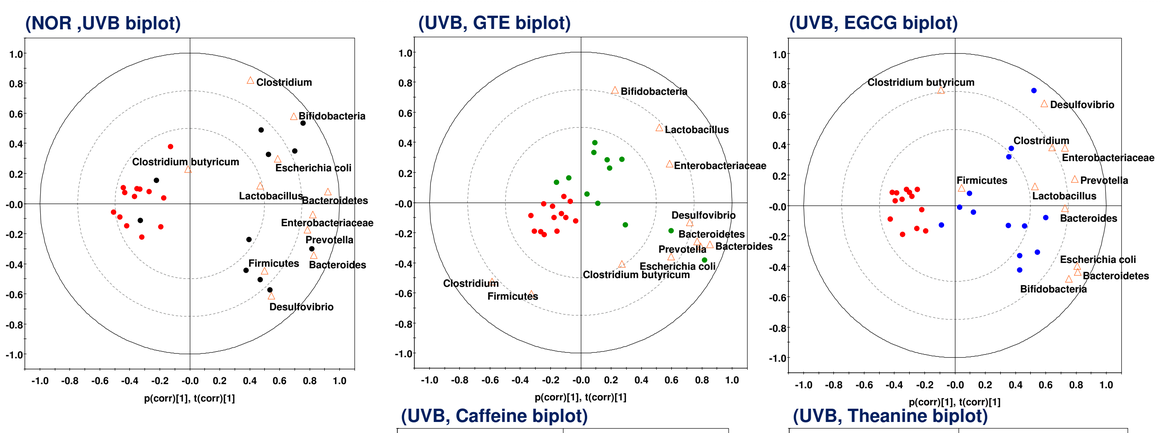


Figure 4. The principal component analysis (PCA) biplot analysis for the cecum microbiome analyzed by gut low-density array (GULDA). Each PCA biplot was generated by using two groups; NOR (●) and UVB (●) groups, UVB (●) and each short-term (7 days) oral administrated groups GTE (●), EGCG (●), caffeine (●), and theanine (●), respectively.

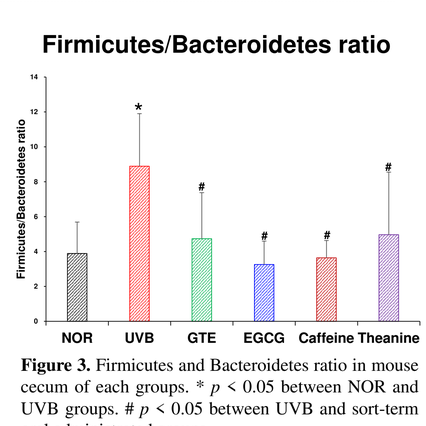
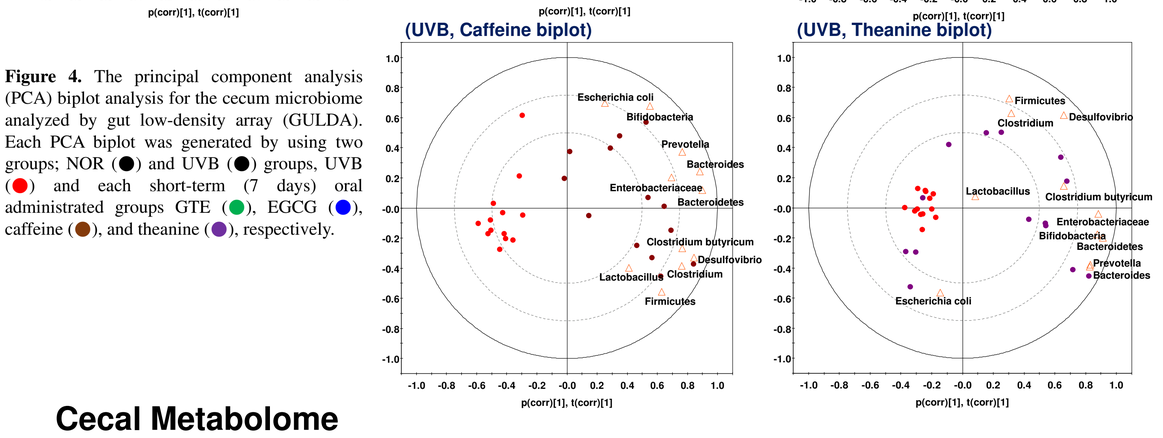


Figure 3. Firmicutes and Bacteroidetes ratio in mouse cecum of each groups. * p < 0.05 between NOR and UVB groups. # p < 0.05 between UVB and sort-term oral administrated groups.



Cecal Metabolome

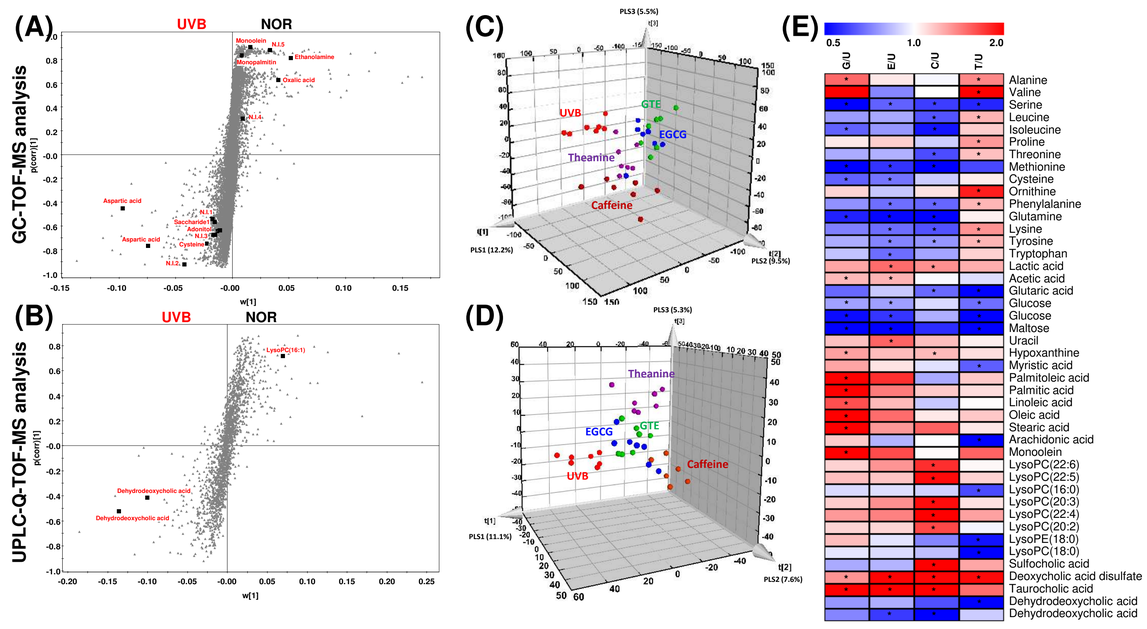


Figure 6. Metabolite profiling of cecum extracts based on GC-TOF-MS and UPLC-Q-TOF-MS analysis. (A, B) The loading S-plot for mice cecum metabolite profiling of normal group (NOR) and single UVB-irradiated group (UVB). Each labeled marks (■) in the S-plot were statistically significantly different metabolites (VIP > 1, p-value < 0.05 in PLS-DA) between NOR and UVB. (C,D) Three-dimensional PLS-DA score plot for cecum metabolite profiling of UVB group and groups that short-term (7 days) administration of GTE, EGCG, caffeine, theanine, respectively, before singly UVB irradiation. (E) The heatmap of significantly different metabolites (VIP > 1, p-value < 0.05) derived from PLS-DA (C, D). Each data point shown on the heatmap was normalized by the values of UVB group.

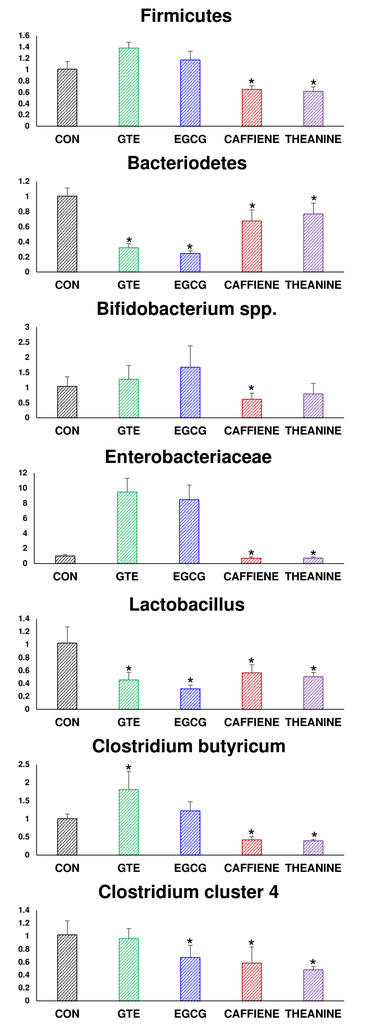


Figure 5. Microbial community analysis of in vitro fermentation of test materials with cecal contents 24 hour. * p < 0.05 between CON and other groups.

CONCLUSION

Single UVB irradiation induced significant influences on both skin and cecum metabolome and microbiome. The oral administration of GTE, EGCG, caffeine, and theanine for 7days prior to UVB irradiation highly modulated both skin and gut-micro-environment. Among them only GTE group significantly suppressed the erythema formation on dorsal skin of mice.