

## Documents

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**Evaluation of metabolomics behavior of human colon cancer HT29 cell lines treated with ionic liquid graviola fruit pulp extract**

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**Abstract**

Ethnopharmacological relevance: Medicinal plants have been used by indigenous people across the world for centuries to help individuals preserve their wellbeing and cure diseases. *Annona muricata* L. (Graviola) which is belonging to the Annonaceae family has been traditionally used due to its medicinal abilities including antimicrobial, anti-inflammatory, antioxidant and cancer cell growth inhibition. Graviola is claimed to be a potential antitumor due to its selective cytotoxicity against several cancer cell lines. However, the metabolic mechanism information underlying the anticancer activity remains limited. Aim of the study: This study aimed to investigate the effect of ionic liquid-Graviola fruit pulp extract (IL-GPE) on the metabolomics behavior of colon cancer (HT29) by using an untargeted GC-TOFMS-based metabolic profiling. Materials and methods: Multivariate data analysis was used to determine the metabolic profiling, and the ingenuity pathway analysis (IPA) was used to predict the altered canonical pathways after treating the HT29 cells with crude IL-GPE and Taxol (positive control). Results: The principal components analysis (PCA) identified 44 metabolites with the most reliable factor loading, and the cluster analysis (CA) separated three groups of metabolites: metabolites specific to the non-treated HT29 cells, metabolites specific to the treated HT29 cells with the crude IL-GPE and metabolites specific to Taxol treatment. Pathway analysis of metabolomic profiles revealed an alteration of many metabolic pathways, including amino acid metabolism, aerobic glycolysis, urea cycle and ketone bodies metabolism that contribute to energy metabolism and cancer cell proliferation. Conclusion: The crude IL-GPE can be one of the promising anticancer agents due to its selective inhibition of energy metabolism and cancer cell proliferation. © 2021 Elsevier B.V.

**Author Keywords**

Colon cancer (HT29); GC-TOFMS; Graviola (*Annona muricata*); Metabolomics; Principal components analysis

**Index Keywords**

17 octadecynoic acid, 4 aminobutyric acid, acetic acid, acetone, acetylglycine, acid, alanine, amine, *Annona muricata* extract, butane, butanol, butoxytrimethylsilane, butynol, carbamic acid, carbonylhydrazide, cyclooctasiloxane hexadecamethyl, decane, dichlorospiro hexan one, diethyl azodicarboxylate, diethylamino trimethylsilane, diethylene glycol, dimethoxybenzylamine, dioxolane heptyl, ethyl trifluoroacetate, glucopyranose pentakis, glycolic acid, hexadecane, hexafluoropropanone, hydrazide derivative, ionic liquid, ketone body, lactic acid, malonic acid, methoxyamphetamine, methyl chloride, octadecadiynoic acid, oxadiazole derivative, oxalic acid, oxopropanoate, paclitaxel, palmitelaidic acid, phosphoric acid, phosphorus acid derivative, propadiene dione, silane derivative, tetrafluorohydrazine, thiocyanic acid derivative, tricosadiynoic acid, trimethylsilylmethanol, unclassified drug, undecenoic acid; aerobic glycolysis, amino acid metabolism, *Annona muricata*, antineoplastic activity, Article, cancer growth, colon cancer, controlled study, data analysis software, drug mechanism, energy metabolism, fruit pulp, gas chromatography, HT-29 cell line, human, human cell, metabolic fingerprinting, metabolite, metabolomics, nonhuman, time of flight mass spectrometry, urea cycle

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