

***In silico* evaluation of coconut milk phenolic antioxidants and their metabolites by human gut bacteria**

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Coconut milk (CM) or the aqueous extract of grated coconut meat is used in culinary applications when preparing both vegetarian and non-vegetarian foods in many Asian countries. Despite CM is traditionally known to be beneficial for gut health, scientific evidence supporting such claims is extremely limited. The beneficial properties of phenolic antioxidants on gut microbiota suggest that phenolic-rich CM may also benefit gut health. Human intestinal gut microbiota plays a vital role in metabolizing dietary components that enter the intestinal tract. These metabolites possess molecular characteristics as well as biological activities, pharmacokinetic and toxicity properties that are different from their parent compounds. Due to a lack of experimental data to examine the gut microbial metabolism of phenolic compounds of CM, a computational study was designed to predict its phenolic metabolites. Our previous high-performance liquid chromatography (HPLC) study reported seven phenolic acids in the CM extract. BioTransformer 3.0 web-based tool was used to predict metabolic transformations of the seven phenolic acids by human gut bacteria. *In silico* studies were conducted to predict the antioxidant, intestinal anti-inflammatory, antibacterial activities and toxicity of the phenolic compounds and their metabolites using PASS and ProTox-II web servers respectively. The safety of the phenolic compounds of CM and their metabolites were also evaluated based on the endocrine-disrupting effect and the probability of interaction with multiple human receptors using Endocrine Disruptome web server. The *in silico* analysis of human gut microbial biotransformation predicted the formation of 41 metabolites from 7 parent phenolic compounds present in CM. Most of the parent phenolic acids and the predicted metabolites of CM were shown to have moderate to high antioxidant, intestinal anti-inflammatory activity and antibacterial activity with Probable activity (Pa) > Probable inactivity (Pi) values. Most of the metabolites had a low probability of binding to human nuclear receptors, causing small risks to the endocrine system and posing minimal risk to human health. Moreover, the results revealed that only a few compounds have a weak mutagenic and hepatotoxic potential, while all compounds were devoid of cytotoxicity. However, further *in vitro* and *in vivo* testing is required to confirm the impact of these parent phenolic acids and their metabolites on diverse gut microbes and human health and in promoting CM as a functional food as well as a vegan replacement for cow's milk.

Keywords: Coconut milk, Human gut microbiota, Gut microbial transformation, Endocrine disruption, Toxicity

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