



Impact of Citrus Polyphenols on Human Health

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Polyphenols are one of the crucial functional bioactive components found in citrus fruits such as oranges, grapefruits, lime, tangerine, bergamot and others. In general, we consume polyphenols more than 820 mg daily from several dietary sources including fruits and vegetables [1]. Multiple studies reported that consumption of citrus polyphenols in diet helps to prevent from heart diseases, cancers and several chronic diseases [2,3]. In fact, in citrus fruits natural polyphenols are classified into four major classes according to their chemical structures including flavonoids, lignans, stilbenes and phenolic acid [4]. The bioactivities of citrus polyphenols in humans depends on the enzymes related to absorption, digestion, and involvement of gut microbiota for their metabolism activities.

The *in vivo* studies of citrus polyphenols bioavailability is an important to conclude the role of citrus to promote human health. In this process, citrus polyphenols enters to small intestine where glycones form of polyphenols biotransformed to aglycones form for absorption in their host body. While, other complex structural forms which are not easily absorbed passes to the colon for the metabolism and biotransformation activities including cleaving of the conjugation moieties by the gut microbiota. Example- hydroxycinnamic acids (a subclass of polyphenols) are esterified to lipid, sugar and organic acid. Moreover, remaining aglycone form of polyphenols passes to the liver via portal vein system for phase II conjugation metabolism reactions such as methylation in the presence of catechol-O-methyl transferase, glucuronidation by UDP-glucosyltransferase and sulfation reaction in the presence of sulfotransferase. Further, these metabolites are circulated through blood stream and enters to the different organs and tissues until it excreted through urine, while some metabolites from liver as

bile components further passes to the small intestine and colon for enterohepatic recirculation and deconjugation and finally excreted through feces of the human body [5,6].

The mounting research evidence suggests that ample amount of citrus polyphenols consumption lowers the risk of cardiovascular disease, cancer and diabetes [7,8]. There is an emerging body of scientific literature showing the beneficial cognitive effects such as inhibit the proliferation of cancer cells and tumors cell invasion [9]. In addition, several studies confirmed that polyphenols such as flavonoids from sweet orange, grapefruits, lemon, berries, grapes, tea, pomegranate and wine reduces the risk of neurodegenerative disorders such as Alzheimer's, Parkinson's and dementia diseases [10,11]. Indeed, numerous *in vivo* and *in vitro* studies have reported that flavonoids such as hesperetin and naringenin metabolites are promising candidate to transverse blood brain barrier and provide protection to the neurons against oxidative stress, improves memory, and reduces depression [12,13].

It has been well acknowledged that citrus derived polyphenols and its corresponding metabolites bioavailability activities via gut microbiota interactions play a significant role on human health. However, more research studies are needed to understand how the same benefits from citrus polyphenols consumed in whole fruits can be derived from isolated metabolites forms showing more bioactivities than their parent compound. Therefore, more *in vivo* and clinical studies are required to understand the exact functional roles of individual citrus polyphenol metabolites and its effects on gut microbiota compositions and diversity in order to provide scientific diet and maintain human health.

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