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Biotransformation of Rutin to Quercetin by Human Gut Bacteria and Its Effect on Rutin Bioavailability

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Abstract *-Rutin is a flavonol glycoside containing quercetin and the rutinose. Rutin exert a wide range of biological benefits for human being. However, it is poorly absorbed by small intestine and most reaches the colon. Human gut bacteria play important role in biotransformation of rutin to quercetin. The biological activities of flavonoids and their metabolic roleafter consumption depends on their chemical structure and absorption. For instance, quercetin is the aglycone form of rutin with higher bioavailability,absorption in small intestine than rutin. The microbial biotransformation not only improves biological activities of plant glycosides but also improves their bioavailability. Gut microbiota was shown to improve rutin colonic absorption after its hydrolysis by β-glucosidase and α-l-rhamnosidase. The aim of the present review is to give updates on biological properties of rutin, biotransformation of rutin to quercetin by gut bacteria strains and its effect on rutinbioavailability.*

Keywords:*- Bioavailability, microbial biotransformation, rutin, quercetin*

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I. Introduction

Flavonoids are a group of bioactive compounds that are extensively found in foodstuffs of plant origin. The flavonoids are α or β glycoside such as flavonoid glucosides, galactosides, rhamnosides, arabinosides and rutinosides [1-5].One of these flavonoids, rutin (quercetin-3-O-rutinoside) is aflavonol glycoside composed of quercetin andrutinose [6, 7].The plant sources of rutin includesvegetables and fruits such as tea, green asparagus , ruta graveolens,onions,buckwheat,wine,eucalyptus spp., apples, and sophora japonica as well as berries[8-12].Rutin possess antioxidant properties, vasoprotective, anti-cancer, anti-hypercholesterolemia, anti-diabetic, anti-hypertensive ,exerts renal protective effects [13-16] as well as reducing the risk of atherosclerosis [16]. Quercetin is the aglycone form of flavonoid glycosides such as rutin and quercitrin[17]. Quercetin was reported to have so many biological properties[18]including anti- osteoporosis, anti-inflammatory[19], anti-carcinogenic, anti-pulmonary and cardiovascular diseases ,anti- aging[20], antiviral, antioxidant, and psychostimulant activities as well as immunological improvement[21].

However,the bioavailability of rutin is relatively low due to its low solubility which limits its practical applications [22-25].In addition, glycosylation by rutinose limits the absorption of flavonoids in the small intestine[26].Moreover, quercetin aglycone has a very high bioavailability[27], but rutin is absorbed comparatively slowly and most reaches the colon [28]. Therefore, biotransformation of polyphenols changes the structure of polyphenols to improve bioavailability and maintains their original bioactivity[29].In order to exert biological effects, gut microbiota contributes a lot in the bioavailability and health effects of poorly absorbed polyphenols [30-32].Glycosides reach microflora in colon where they are hydrolyzed by β-glycosidase from gut bacteria (Griffiths and Barrow 1972, Di Gioia, Bregola et al. 2010). Few studies have been focused on biotransformation of rutin to quercetin by gut bacteria. The aim of the present review is to give updates on biological properties of rutin, biotransformation of rutin to quercetin by gut bacteria strains and its effect on rutin bioavailability.

II. Biological Properties Of Quercetin And Rutin

The biological effectsare associated to the metabolites which succeed to reach the internal organs rather than their native compounds found in foods**Table 1**[33]. Moreover, microbial degradation of flavonoids in the human intestine beneficially affect human health.

For example, the antioxidant and antiproliferative potential of rutin deglycosylated with hesperidinase and naringinase were higher than that of rutin[34, 35].Moreover, antioxidant activity of flavonoid measured as DPPH radical scavenging activity was found to be 62.6% for rutin and 89.8% for quercetin [35] .Quercetin exerts hepatoprotective[36], anti-inflammatory activities [37],strongest antioxidant activities compared to other flavonoids [38, 39], anti- skin damages[40], neuroprotective effects on brain injury[41], anti-apoptotic[42, 43], anti-aging activities[44], anti -colorectal lung metastasis [45], anti -breast cancer ,prostate cancer activities [46].

Table 1.Biological properties of rutin

Biological properties	References
Anti -Cancer	[35, 47-49]
Antioxidant	[50, 51]
Antiallergic	[52]
Anti-inflammatory	[53-55]
Hypolipidaemic	[56, 57]
Neuroprotective	[58-61]
Antihyperglycaemic	[62, 63]
Gastro-protective activity	[64]

III. Biotransformation Of Rutin To Quercetin By Human Gut Bacteria

The microbial biotransformationof rutin to quercetin have been reported [65]. This results from hydrolysis of rutin by bacterial α-rhamnosidases and β-glucosidases in the colon as shown in **Fig.1** [11, 66].

Rutin require hydrolysis by intestinal or microbial enzymes for their absorption in vivo [67, 68]. Some colonic bacteria including Lactobacillus spp., Bacteroides spp. and Bifidobacterium spp. can cleave glycosides by their β-glucosidases [69].

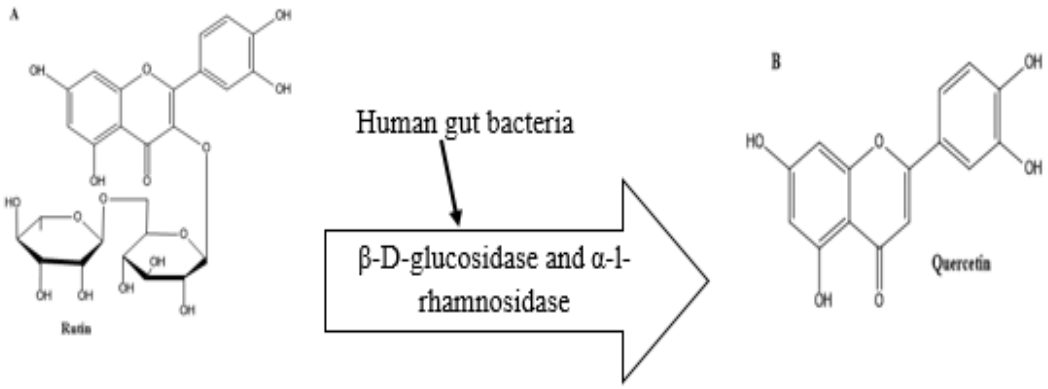

Figure 1. Human gut bacteria enzymes converting rutin to quercetin

Rutin is absorbed from the colon after deglycosylation[70].The colonic microbiota break down rutin to release quercetin[71, 72]. During fermentation, kaempferol and quercetin glycosides were found to be transformed in their corresponding aglycones [73, 74]. Biotransformation can produce new compounds with potential biological activity [75, 76]. In addition, metabolism of phenolic compounds by microbiota can only occur after deglycosylation or deconjugation [77, 78].

Researches has shown that metabolites from dietary polyphenols might have greater biological activities than their parent compounds [28, 79]. For example the deglycosylation of flavonoid glycosides to their aglycones have been reported to improve also their antioxidant activity[3].Microbial biotransformation, metabolic engineering andenzymeengineering have been reported for production of bioactive flavonoids[80, 81]. Furthermore, microbial fermentation ismostly used for biotransformation [82] due to its advantages asshown in **Table 2**[83, 84].

Table 2. General advantages of microbial biotransformation

Advantages	References
Improve the production yield	[83-85]
Microbial cells or enzymes can be immobilized and reused for many cycles	[29]
High specificity	[86-88]
Economic and environmental friendly	[89-91]

Plant metabolite deglycosylation was shown to improve the flavor and taste of fermented products [92] . Glycosidases from some microorganisms shown in **Table 3**(α-l-rhamnosidase and β-glucosidase) hydrolyze the bonds between quercetin and rutinose, and between glucose and rhamnose[93].

Table 3. Some microorganisms involved in biotransformation of rutin to quercetin

Microorganism	Product	References
*Enterococcus avium*EFEL009	Quercetin	[94]
Bacteroides uniformis ATCC 8492T	Quercetin	[95]
Lactobacillus plantarum ,*Lactobacillus acidophilus*	Quercetin -3-O-glucoside	[96]
Bacteroides sp. 22 *and Bacteroides sp.* 45	Quercetin -3-O-glucoside	[97]

Fusobacterium K-60 and *Bacteroides JY*-6 by could degrade rutin to lose sugars by β-glucosidase and α-rhamnosidase. Lactobacilli are probiotics and among the predominant members of the intestinal bacteria[98]. The presence of Lactobacillus plantarum in the gut microflora was reported to enhance flavonoid bioavailability [99] . Lactobacilli convert rutin and hesperidin into their aglycone forms and contribute to their bioavailability and absorption [100-102].*Lactobacillus buchneri* and *Lactobacillus acidophilus* were able to convert wheat flavonoid glycosides into aglyconic forms to increase their absorption [101]. Lactobacillus is estimated to constitute 6% of the total bacterial cell numbers in the human duodenum and approximately 0.3% of all bacteria in the colon[103]. The bacterial concentration in the small intestine is low. So Lactobacillus spp. should not be major contributor of rutin transformer in vivo. Due to long history of application as probiotic and in fermented food, it has the industrial potential to transform rutin in food production.

IV. Effect Of Biotransformation Rutin To Quercetinon Rutin Bioavailability

The bioavailability for intestinal absorption, interaction with target tissues and metabolism of bioactive polyphenols influence their health promoting effects[104]. Flavonoids need to be consumed in a form that can be absorbed in the small intestine before their potential degradation [99] . More complex flavonoid glycosides are not absorbed by the small intestine and reach the colon [105].

For example, rutin is poorly absorbed by small intestine but mostly degraded by the gut bacteria after consumption [11, 106]. The enzymatic de-glycosylation of flavonoids has been reported to increase their bioavailability[107]. For instance, rutin deglycosylation by β-glucosidase from gut microbiota (Kim, Jung et al. 1998) was shown to improve its colonic absorption [108] . In addition, removal of rhamnose group by rhamnosidases improves also the bioavailability of flavonoids. The microbial biotransformation not only improves bioavailability but also provides more selectivity and less toxicity compared to chemical synthesis [31, 109-111].

Many aglycones and some of the monoglycosides are absorbed in the ileum [112]. Moreover, the study showed that bioavailability of quercetin from rutin is higher that from quercetin aglycone in cows after oral application [113]. It has been reported that deglycosylation of quercetin glycosides by β-glucosidase, improves its absorption[114] .Therefore quercetin aglycone is easy for the small intestine uptake[115-117].

V. Conclusion

Rutin exerts so many biological effects including antioxidant, anti-cancer, anti-hypercholesterolemia, anti-diabetic, anti-hypertensive as well as renal protective effects. Unfortunately rutin absorption in small intestine is lower than that of quercetin poorly and a large amount reach the colon where it is degraded by human intestinal bacteria. Human gut bacteria hydrolyze rutin to quercetin by α-l-rhamnosidase and β-glucosidase. In summary, health-promoting effects of rutin, biotransformation of rutin to quercetin and rutin bioavailabilityare greatly influenced by human gut bacteria strains. In addition, there very few studies done on probiotic bacteria strains involved in the biotransformation of rutin to quercetin. Further studies are needed to isolate and identify more human gut bacteria and probiotic strains which contribute to biotransformation of rutin to quercetin.

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