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Editorial

New Insights of Probiotics for Obesity and its Metabolic Disorders: Big Hope from the Small Micro-organisms

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Editorial

Excessive caloric intake and less physical expenditure are contributing the obesity and its associated metabolic disorders. The calories which come through the diet, accumulated in the adipose tissue as Triglycerides (TGs) and stored in the form of lipid droplets. Further, these TGs are breakdown into the Free Fatty Acids (FFAs) and enter into the circulation during obesity, insulin resistance and diabetes [1]. Increased circulatory FFAs further stores in the non-adipose tissue *viz*., muscle, liver & kidney and may contribute obesity associated metabolic diseases [2]. Ample of storage of lipids in the adipose tissue increase its size and makes them vulnerable for the infiltration of macrophages and further leads to low grade inflammation [3]. Recent evidence suggested that the pharmacological and surgical interventions are not effective for treating obesity [4]. So, people are keen interest towards alternative therapies like probiotics, prebiotics and herbal supplementations as natural medications with little or no side effects. According to the FAO/WHO (2001), probiotics are "live micro-organisms which when administered in adequate amounts confer health benefits to the host" [5]. The healthy human gut microbiota comprises 10^{12} microbes with major phyla *Bacteroidetes* and fewer *Firmicutes*, however, dysbiosis of aforementioned phyla occurs in obesity [6,7]. Several studies are demonstrated that probiotics (lactobacilli and bifidobacteria species) play a significant role in animal and human studies.

Gut microbiota and its effects on human metabolism reported by the several researchers. Lactobacilli and bifidobacteria species are predominantly studied for their anti-obesity effects [8,9]. Reports suggesting that oral administration of *Lactobacillus rhamnosus* PL60/PL62 and GG into obese mice showed a significantly reduction of body weight, visceral fat and liver biomarker enzymes [10-12]. In our previous study, we demonstrated that probiotic dahi (traditional Indian fermented milk) containing *Lactobacillus casei* had a significant reduction in body weight, fasting blood glucose levels, epididymal fat tissue in high fat diet fed C57BL/6 mice [8]. In other recent studies, milk fermented by *Lactobacillus rhamnosus/plantarum* alone or in combination of herbal supplementation observed lowering of hyperglycemic and hyperlipidemic effects in diet induced obese mice. In addition, a significant decrease in the adipocyte cell size and pro-inflammatory cytokines [13,14].

The intestinal micro-organisms are utilized the indigestible carbohydrates for the synthesis of volatile fatty acids like acetate, propionate and butyrate [15]. These Short Chain Fatty Acids (SCFAs) are utilized by the intestinal cells as energy source and some other contributes to the activation of fatty acid oxidation pathways to decrease adiposity [16-18]. Administration of mixed culture of probiotics VSL#3 (*Streptococcus thermophillus, Bifidobacterium* and *Lactobacillus*) in obese mice (Lep ob/ob) had shown reduction in the body weight and feed intake through butyrate via stimulating the secretion of glucagon like peptide levels from intestinal cells [19].

Due to adequate storage of the lipids in the adipose tissue also increase the size and results in less vascularization (fewer blood vessels); hypoxia which contributes for recruiting immune cells (macrophages) [3]. Infiltration of macrophages responsible for the release of pro-inflammatory cytokines (tumor necrosis factor-alpha and interleukins) in the adipose tissue. Furthermore, low grade inflammation also occurs by the release of Lipopolysaccharides (LPS) from the Gram negative bacteria and referred as metabolic endotoxemia [20]. These LPS are initially damage to the intestinal tight junction proteins (eg: ZO-1, claudin-2 and occludin) and enters into the circulation where binds to its receptors located on the immune cells to promote inflammation [21,22]. The cocktail of VSL#3 probiotics, *Lactobacillus plantarum* MB452 and *Akkermansia mucinphila* were reported to be an improvement in the intestinal permeability damage by adhering to its membrane in obese and diabetic animals [23,24]. In addition, *bifidobacterium* selectively showed a positive effect on intestinal tight junction proteins in the presence of prebiotic oligofructose by the production of SCFAs [25]. In case of clinical studies very few reports are available in this regard. Studies on milk fermented by *Lactobacillus gasseri* SBT2055 (200g/day, 10^8 cfu/day) had shown a decrease in the body weight gain, visceral fat mass and serum TGs levels in obesity tendency human subjects [26,27,28]. A combination of several probiotic species (*Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W51 *Enterococcus faecium* W54, *Lactobacillus acidophilus* W22, *Lactobacillus brevis* W63 and *Lactococcus lactis* W58) were also improves tight junction proteins in endurance trained humans [29].

However, some of the contradictory results are also reported with the lactobacilli and other organisms. These results indicated that these micro-organisms are mainly strain dependent, type of diet and animal model used. In near future, more studies are required in the field of probiotics in clinical applications to cure obesity and its associated metabolic disorders.

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