Journal of Advanced Zoology

ISSN: 0253-7214
*Volume **44** Issue **S-5 Year 2023** Page **1770:1776***

Using Gut Microbiome as A Tool in Dietary Intervention for Prevention and Management of Obesity

Ms. Janani Tamilvanan[1]*, Chinnappan. A. Kalpana[2]

*[1]*Research Scholar and Avinashilingam Institute for Home Science and Higher Education for Women Bharati Park Road, Forest College Campus, Saibaba Colony Tamil Nadu 641043*
[2]Professor, Department of Food Science and Nutrition Avinashilingam Institute for Home Science and Higher Education for Women Bharati Park Road, Forest College Campus, Saibaba Colony Tamil Nadu 641043

**Corresponding author's E-mail: janu084@gmail.com & kalpana_fsn@avinuty.ac.in*

Article History

Received: 06 June 2023
Revised: 05 Sept 2023
Accepted: 02 Nov 2023

Abstract

The gut microbiome has trillions of bacteria which play an important role in human health and disease. Several animal and human studies have shown that dysbiosis, microbial imbalance as the causative factor in obesity and metabolic syndrome. Significant research evidence demonstrates that changes in the proportion of Bacteroidetes and Firmicutes has been associated with obesity, but this has been recently challenged. Similar studies were carried out in several populations, however, there are no such studies, to date, among Asian Indians. We aimed to examine the usefulness of gut microbiome testing in developing personalized diet for managing obesity. In this study, we selected individuals, generally healthy, free- living adults, both men and women with BMI 25- 40 kg/m2 and with previous history of failures at weight loss who visited a Weight Loss Clinic, based in Coimbatore, India & were offered a gut microbiome test. We included 54 individuals in the intervention group who received personalized dietary advice for weight loss based on the gut microbiome test and another set of 52 individuals visiting the same clinic were included in the comparison group based on their age, height, weight and BMI who received generic diet. A statistically significant increase in the Bacteroidetes genus was observed in the personalized nutrition group (p = .04). The change (delta) values in gut microbiome composition in personalized nutrition group were significantly higher at the end of 120 days. Gut microbiome-based personalized microbiome modulation through diet significantly improves gut microbiome profiles among obese individuals. We would further need studies with larger sample size to validate these study findings and long-term follow-up are needed.

Keywords: *Gut Microbiome Testing, Personalized Nutrition, Obesity Management*

1. Introduction

Exponential increase in obesity rates cause concern about health risks associated with rising obesity has become nearly universal. During the previous three decades, the mean body mass index (BMI) and the prevalence of obese and overweight individuals increasing worldwide. Unfortunately, prevention and treatment of obesity and related complications have proven complex, and successful strategies to tackle this pathology remain limited. Epidemiological studies have highlighted potential environmental exposures, including - diet, energy expenditure, early life influences, sleep deprivation, endocrine disruptors, chronic inflammation, and gut microbiome status, is contributing to higher risk of obesity *(Franks & McCarthy, 2016).* Among these, the microbiome has received extensive attention during the previous decade.

Variation in gut microorganisms might play an important role in the pathogenesis of obesity. Although the composition of intestinal microbiota is highly diverse in healthy individuals, those exhibiting overall adiposity, insulin resistance and dyslipidemia are characterized by low bacterial richness *(Le Chatelier et al., 2013*). Moreover, composition of gut microbiota in obesity individuals differs from that in lean individuals, although inconsistent changes have been reported. *Bacteroidetes* prevalence is lower in obese people, with this proportion increasing along with weight loss based on a low-calorie diet *(Ley et*

al., 2006a). *Lactobacillus* and *Clostridium* species are associated with insulin resistance, with *Lactobacillus* positively correlated with fasting glucose and HbA1c levels, whereas *Clostridium* showed a negative correlation with these parameters (Karlsson et al., 2013). These data suggest that specific bacterial phyla, class, or species or bacterial metabolic activities could be beneficial or detrimental to the onset of obesity.

Impact of gut microbiota on local and distant organs contributes to obesity development and progression. In local tissues, obesity-associated gut microbiota has an increased capacity to harvest energy from the diet, stimulate gene reprogramming in the colon, change polypeptide hormones and other bioactive molecules released by EC cells, decrease the intestinal barrier, and disturb immune homeostasis. Gut microbiota also communicate with host adipose tissue and the liver and brain. Microbiota-fat-signaling axis. Gut microbiota participates in the regulation of adipogenesis through distinct mechanisms. LPS triggers an immune response along with inflammation and immune-cell infiltration. SCFAs also participate in insulin-mediated fat accumulation in adipocytes via activation their receptors GPR43 and GPR41, which inhibits lipolysis and encourages adipocyte differentiation *(Sun et al., 2018).* Some mechanisms have been proposed to explain the role of gut microbiota in obesity development.

Short Chain Fatty Acids

The gut microbiota metabolizes energy from the diet, e.g., indigestible dietary fibers, which are chemically polysaccharides and oligosaccharides. They are converted into short chain fatty acids (SCFA), such as acetate, propionate, and butyrate. After absorption, SCFAs can induce lipogenesis and increase triglyceride stores through molecular pathways. They activate the carbohydrate-responsive element-binding protein and the sterol regulatory element-binding transcription factor 1, both involved in the process of lipogenesis. The rate of SCFA metabolism can establish the direction of host energy balance by increasing the effectivity of calorie uptake. Moreover, SCFAs suppress the fasting-induced adipocyte factor, which inhibits lipoprotein lipase, inducing triglycerides accumulation in adipocytes (Rosenbaum et al., 2015). Dietary fibers, which are the main source of SCFAs, are suggested to have a protective effect for maintaining a healthy body weight. Several mechanisms have been suggested for how SCFAs may participate in the development of obesity. SCFAs provide an extra energy source (approximately 10% of daily energy requirement) and contribute to extra fat deposition in the body; SCFAs are ligands for G protein-coupled receptor GPR 41 and GPR43, which are expressed in the intestinal epithelium, immune cells, and adipocytes and are responsible for regulating energy expenditure; regulation of fasting-induced adipose factor; de novo lipogenesis; regulation of glucose homeostasis; Regulation of leptin secretion via free fatty acid receptor; and modulation of satiety response *(Cuevas-Sierra et al., 2019).*

Adenosine monophosphate kinase (AMPK) and fasting-induced adipose factor (Fiaf)

Adenosine monophosphate kinase (AMPK) and fasting-induced adipose factor (Fiaf) are circulating lipoprotein lipase inhibitors. Gut microbiota can decrease liver fatty acid oxidation by suppressing AMPK and Fiaf, which causes increased fat accumulation. The bacterial suppression of the expression of Fiaf and AMPK in the liver and skeletal muscle, leads to weight gain from a carbohydrate and fat rich diet. Fiaf is produced by the intestine, liver, and adipose tissue. Inhibition of Fiaf results in increased activity of LPL, which mediates cellular uptake of triglycerides and accumulation of triglycerides in adipocytes.

Bile Acids

A reduced bile acid concentration in the gut has been associated with bacterial overgrowth and inflammation *(Cerdó et al., 2019).* Recent studies suggest farnesoid X receptor (FXR) signalling as an important pathway for the interaction between the gut microbiota and bile acids. The FXR pathway through which bile acids and gut microbiota contribute to host metabolism is by metabolizing bile acids into primary and secondary bile acids, which then bind to the FXR receptor and stimulate secretion of gut-derived hormones, such as fibroblast growth factor FGF19. In turn, FGF-19 regulates bile acid synthesis as well as lipid and glucose metabolism. Increased bile acid synthesis contributes to increased energy expenditure in the host by stimulating the brown adipose tissue and skeletal muscle *(Lee et al., 2020).*

LPS Lipopolysaccharides (LPS)

LPS contain lipid A, which can cross the intestinal mucosa through tight junctions or with the aid of chylomicrons. LPS are responsible for the absorption and transport of dietary triglycerides and initiate an inflammatory process that result in the insulin resistance often observed in obesity. LPS

concentrations are low in healthy people but may reach high concentrations in obese individuals and cause metabolic endotoxemia. Metabolic endotoxemia increases adipocyte hyperplasia and recruitment of macrophages into adipose tissue in a CD14-dependent pathway and increases the production of activin A, which activated the proliferation of adipocyte precursor cells (Gomes et al., 2018). Gut microbiota also may contribute to metabolic disturbances observed in obese patients by triggering systemic inflammation.

Overall, currently available evidence suggests that changes in the gut microbiota could contribute to the pathogenesis of obesity and to the development of obesity-related metabolic disorders, including type 2 diabetes, NAFLD, metabolic syndrome, and cardiovascular disease. Obesity treatments such as calorie reduced diets and/or bariatric surgery modify the gut microbiota in ways that are associated with health benefits, supporting the hypothesis that changing gut microbiota composition has the potential to provide an additional mechanism for achieving stable weight loss *(Muscogiuri et al., 2019).* The present study aimed to examine the usefulness of gut microbiome testing among obese individuals.

2. Materials And Methods

A comparative analysis was done to examine the usefulness of gut microbiome testing among the obese individuals. Participants were divided into two groups, personalised nutrition group receiving dietary recommendations based on gut microbiome testing and non-personalised nutrition group receiving a standardised diet of 1500 kcal for losing weight. BMI and waist circumference were measured among the two groups. Changes in the gut microbiome composition and abundance of species in the personalised nutrition group was measured at 30 days, 60 days, 90 days and 120 days to evaluate the usefulness of gut microbiome testing.

Selection of Criteria for assessment of gut microbiome markers

Direct sequencing of the bacterial 16S rRNA gene has become the most widely adopted method to obtain information with respect to microbiota composition of any given ecosystem, including that of the human gut. This type of microbiota profiling has provided a phylogenetic framework of the gut microbiota. Typical ecosystem features that can be obtained from such analyses include microbial community typing, determining microbial diversity, as well as identifying microbes that are differently abundant between groups of subjects, all of which can be used as targets for microbiome-based classification. Microbial community typing based on 16S rRNA genes includes identifying the presence of community types and the existence of alternative stable compositional states.

Diversity of a microbiota includes the number of different taxa (richness) as well as their (relative) abundance distribution (evenness) within an ecosystem. A high microbial diversity is considered to be beneficial as it is suggested to contribute to resilience after disturbance of the microbiome (Liu, *et al*., 2020). Indeed, the microbiota diversity is generally higher in healthy subjects than compromised subjects. The gut microbiome profile of an individual is basically characterised by the following three parameters:

(i) Composition (ii) Abundance (iii) Diversity

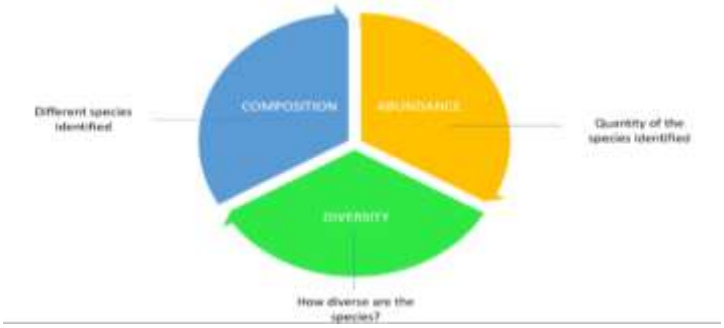

Figure.1 Determinants of Gut Microbiome Profile

Composition: The composition of any gut microbiome belongs to 4 major groups of microorganisms called - Bacteria, Archaea, Virus and Eukaryota. For the present study these bacterial sub-groups – actinobacteria, bacteroidetes, firmicutes, proteobacteria were chosen to study the gut composition.

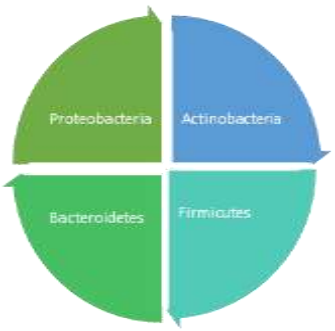

Figure.2 Major Bacterial Sub- groups selected for the study

It is well established that firmicutes were more effective in energy harvest than bacteroidetes, subsequently leading to weight gain. Studies also suggest that altered bacterial composition/ diversity are usually associated with the changes in the gut microbiome composition that influences host health status. The firmicutes/ bacteroidetes ratio has been considered as a possible hallmark for obesity (Bandt, *et al.*, 2007) (Zou, *et al.*, 2020).

The phylum Firmicutes includes bacterial species that are predominantly from the genera Bacillus, Clostridium, Enterococcus, Lactobacillus, and Ruminicoccus, whilst the phylum Bacteroidetes includes bacterial species that are predominantly from the genera Bacteroides, Alistipes, Parabacteroides, and Prevotella (Gibiino, *et al.*, 2018). Probiotics are usually administered to regulate the firmicutes: Bacteroidetes ratio. Table.I provides the list of probiotics used in the present study that was appropriately chosen based on the gut microbiome profile of the individual.

Table I List of Probiotics and their food sources and its influence on the Firmicutes: Bacteroidetes Ratio

	Microbes	Food sources	Firmicutes: Bacteroidetes Ratio
1.	Bifidobacterium breve, Lactobacillus Johnsonii,	Fermented vegetables	Increased Firmicutes and decreased Bacteroidetes.
2.	Bifidobacterium infantis,	Yoghurt	Increased Firmicutes and Bacteroidetes.
3.	Lactobacillus reuteri	kefir	Increased Firmicutes and Bacteroidetes.
4.	Lactobacillus casei	Fermented milk	Increased Firmicutes and Bacteroidetes.
5.	Lactobacillus rhamnosus	Buttermilk	Increased Bacteroidetes and decreased Firmicutes.
6.	Lactobacillus brevis, Lactobacillus gasseri,	Kimchi	Increased Bacteroidetes and decreased Firmicutes.
7.	Leuconostoc mesenteroides	Sauerkraut	Increased Firmicutes and Bacteroidetes.

Ways to increase the abundance and diversity of the gut microbiome:

According to several studies, these bacterial genus and species have been associated with beneficial health marker, performs important functional roles and have been negatively associated with various diseases including obesity. The following bacterial species were considered for the study, Akkermansia muciniphila sp, bifidobacterium sp., Eubacterium sp., Roseburia sp. and Faecalibacterium prausnitzii sp.

Development of gut microbiome specific dietary recommendations

The gut microbiome specific dietary recommendations were formulated taking into consideration to maintain gut microbiome composition, increase diversity and abundance of species. According to several studies, these bacterial genus and species have been associated with beneficial health marker, obtain important functional roles and have been negatively associated with various diseases including obesity. The following bacterial species were considered for the study, Akkermansia muciniphila sp, Bifidobacterium sp., Eubacterium sp., Roseburia sp. and Faecalibacterium prausnitzii sp. The rationale for choosing these species are research evidences that have established the role of these species with respect to health and in obesity. Personalised recommendations specific to these organisms are provided in Table II.

Table II List of Gut Microbes and their Functions

	Microbes	Functional Role	Recommendations
1.	Akkermansia muciniphila sp	Akkermansia muciniphila are positively associated with greater microbial gene richness and with a healthier metabolic status. Moreover, A. muciniphila are associated with greater improvement in glucose homoeostasis, blood lipids and waist circumference after calorie restriction.	Include polyphenol containing foods such as walnuts, cranberries, grapes, black tea and FOS (fructose oligosaccharides), a natural prebiotic found in natural foods such as banana, garlic, asparagus, onions.
2.	Faecalibacterium prausnitzii sp.	Are highly abundant species in the human gut microbiome. In healthy adults, F. prausnitzii represents more than 5% of the bacteria in the intestine, making it one of the most common gut bacteria and It is known to boosts our immune system and reduce inflammation. Lower than normal levels of F. prausnitzii in the intestines have been associated with obesity.	Include Prebiotics such as inulin-type fructans and arabinoxylans. Inulin is found in fruits and vegetables such as chicory roots, wheat, onion, banana, garlic, and leek. Arabinoxylans are found in wheat, rye, rice, barley, oat, and sorghum.
3.	Roseburia sp.	Are part of the commensal bacterial community that that resides in human gut. They are known to produce short-chain fatty acids, especially butyrate, which possibly affects colonic motility, immunity, maintenance and anti-inflammatory properties. This genus was observed to be positively associated with Mediterranean diet, and negatively associated with metabolic disease, especially obesity.	Include plant-based foods (e.g. fruit and vegetables), whole grains, legumes and nuts. Include walnuts, chilli peppers (capsaicin), prebiotic long chain arabinoxylans and prebiotic inulin containing foods.
4.	Eubacterium sp.	Play an important role in the gut microbiome and are known as a core bacteria in the human gut (Appears in more than 95% of the population). Important in digestion of complex carbohydrates originated from beans, legumes and whole grains.	Include foods such as zucchini, spinach, and tomato — fruit, nuts, fish and seafood, full-fat yogurt, and eggs.
5.	Bifidobacterium sp	Its main role is to digest fiber and other complex carbs. It also produces other important chemicals too, including B vitamins and healthy fatty acids	Include foods rich in fibre such apples, plaintain stem, almonds and pistachios, probiotics and prebiotics. (probiotic list is also provided separately)

3. Results and Discussion

Evaluation of personalised nutrition group and non- personalised nutrition group

Firmicutes family were observed in higher abundance in the obese individuals (p-value 0.014, Mann-Whitney u-test) in non-personalised nutrition group at the end of 120 days, whereas bacteriodetes family were higher in personalised nutrition group (p-value 0.022, Mann-Whitney u-test).

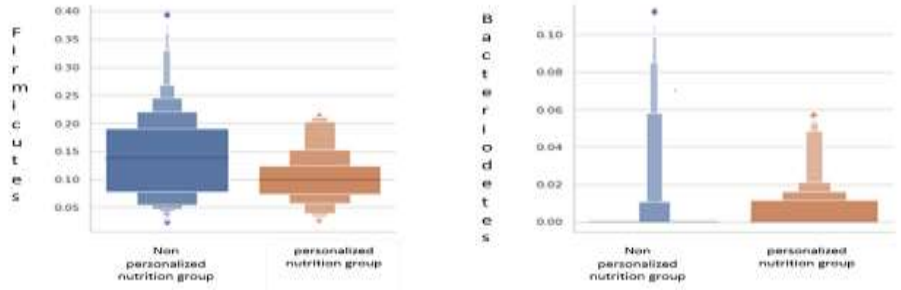

Figure 3. Relative abundance of firmicutes and bacteriodetes in personalised and non-personalised nutrition group at 120 days.

Similarly, the relative abundances of Bacteroidetes at the beginning (1st day) and at the end of 120 days in personalised nutrition group is represented in Figure 4 as pre and post intervention.

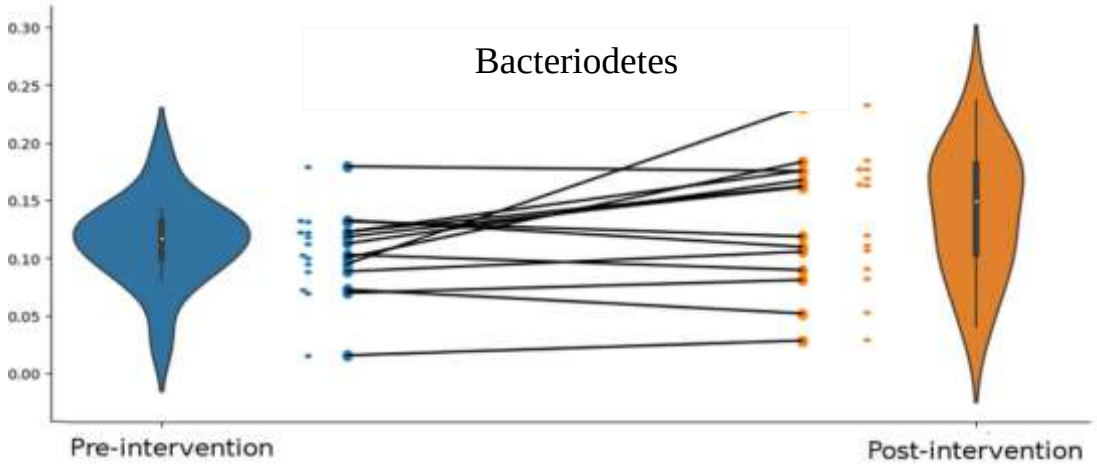

Figure 4. Bacteroidetes relative abundances for the personalized nutrition group pre and post-intervention

Post Interventional Changes in Gut Microbiota Profiles

After 120 days of intervention, a significant shift in microbiota profiles in terms of alfa- or beta-diversity was observed in both groups. A trend of decrease in the firmicutes family for the personalized nutrition intervention group was observed; and was found to be statistically significant (p= .05, paired t-test). A statistically significant increase in the bacteriodetes genus was observed in the personalized nutrition group (p= .04). The percentage distribution of gut microbiome profiles with different bacterial groups are presented in figure.5

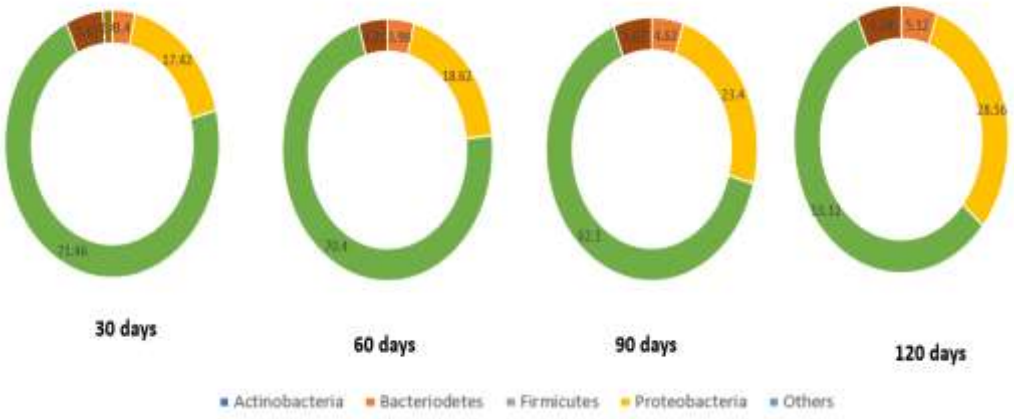

Figure 5. Changes in gut microbiome compositions in the personalised nutrition group.

4. Conclusion

Currently, the optimal diet for managing individuals with obesity is lacking. The ideal diet should be effective to maintain a healthy state of the gut microbiome. It should be sustainable and personalized. Our study is first of its kind to develop a personalized diet based on gut microbiome profile and to

determine whether it modulates the obese individual microbiota. The gut microbiota of obese individuals showed significant differences in beta diversity calculated at genus level. When we look at the bacterial taxonomy, the most notable differences were observed in bacteriodetes and firmicutes families. Bacteriodetes was increased and firmicutes were decreased in the personalized nutrition group, firmicutes was increased and bacteriodetes remained the same in the non personalized nutrition group. Some of the limitations of our study are the sample size was small and the intervention period was for 6 months (180 days). We would need more randomized controlled trials to validate our study findings.

Acknowledgements

We would like to acknowledge the individuals who consented to take part in the study and provided their support with the necessary data.

Author Contributions

Janani Tamilvanan conceived this manuscript, carried out the search of literature, edited the article writing and tables/ figures preparation. Kalpana CA is the corresponding author of this article and was involved in writing, reviewing and editing.

Conflict of Interest

The author(s) declare(s) that there is no conflict of interest.

References:

1. Cerdó, T.; García-Santos, J.A.; Bermúdez, M.G.; Campoy, C. The Role of Probiotics and Prebiotics in the Prevention and Treatment of Obesity. Nutrients 2019, 11, 635.
2. Cuevas-Sierra, A.; Ramos-Lopez, O.; Riezu-Boj, J.I.; Milagro, F.I.; Martinez, J.A. Diet, Gut Microbiota, and Obesity: Links with Host Genetics and Epigenetics and Potential Applications. Adv. Nutr. 2019, 10 (Suppl. S1), S17–S30.
3. Franks PW, McCarthy MI. Exposing the exposures responsible for type 2 diabetes and obesity. Science. 2016 Oct 7;354(6308):69-73. doi: 10.1126/science.aaf5094. PMID: 27846494.
4. Gomes, A.C.; Hoffmann, C.; Mota, J.F. The human gut microbiota: Metabolism and perspective in obesity. Gut Microbes 2018, 9, 308–325.
5. Karlsson, F., Tremaroli, V., Nookaew, I. et al. Gut metagenome in European women with normal, impaired and diabetic glucose control. Nature 498, 99–103 (2013). https://doi.org/10.1038/nature12198.
6. Le Chatelier, E., Nielsen, T., Qin, J. et al. Richness of human gut microbiome correlates with metabolic markers. Nature 500, 541–546 (2013). https://doi.org/10.1038/nature12506.
7. Lee, C.J.; Sears, C.L.; Maruthur, N. Gut microbiome and its role in obesity and insulin resistance. Ann. N. Y. Acad. Sci. 2020, 1461, 37–52.
8. Muscogiuri, G.; Cantone, E.; Cassarano, S.; Tuccinardi, D.; Barrea, L.; Savastano, S.;
9. Colao, A. Gut microbiota: A new path to treat obesity. Int. J. Obes. Suppl. 2019, 9, 10–19.
10. Rosenbaum, M.; Knight, R.; Leibel, R.L. The gut microbiota in human energy homeostasis and obesity. Trends Endocrinol. Metab. 2015, 26, 493–501.
11. Sun, L., Ma, L., Ma, Y. et al. Insights into the role of gut microbiota in obesity: pathogenesis, mechanisms, and therapeutic perspectives. Protein Cell 9, 397–403 (2018). https://doi.org/ 10.1007/ s13238-018-0546-3.