Pharmacophore

ISSN-2229-5402

Journal home page: http://www.pharmacophorejournal.com

Pharmacophore
an International Journal
ISSN 2229-5402

THE INTERDEPENDENCE BETWEEN DIET, MICROBIOME, AND HUMAN BODY HEALTH - A SYSTEMIC REVIEW

Miere (Groza) Florina[1], Ganea Mariana[1]*, Nagy Csaba[2], Vicas Laura Gratiela[1]

1. ***Faculty of Medicine and Pharmacy, University of Oradea, 410087 Oradea, Romania.***
2. ***Faculty of Management and Rural Development, University of Agronomic Sciences and Veterinary Medicine Bucharest, 011464, Bucharest, Romania.***

ARTICLE INFO

Received:
18 Jan 2022
Received in revised form:
27 Mar 2022
Accepted:
02 Apr 2022
Available online:
28 Apr 2022

Keywords: Microbiome, Bacteria, Health, Pathology

ABSTRACT

Recent studies from the literature show more and more the interdependence between diet and intestinal microbiome and the health of the human body and the health of the intestinal microbiome. It has been shown so far that the intestinal microbiome is itself an “organ” that has its metabolic activity influencing the entire metabolism of the body host. In this paper, the main roles of the intestinal microbiome, its composition, and implications in maintaining the health of the organism and the changes in case of existing pathology were pointed out. Our study combines recent in vivo or in vitro tests that have shown a direct link between microbiota imbalances and certain pathologies. Changes in the composition of the microbiome in pathologies such as Alzheimer disease, intestinal or skin pathologies have been described. However, this paper summarizes the main notions and interdependencies between the health of the bacterial intestinal microflora and the health of the human body.

To Cite This Article: Florina M, Mariana G, Csaba N, Gratiela VL. The Interdependence Between Diet, Microbiome, And Human Body Health - A Systemic Review. Pharmacophore. 2022;13(2):1-6. https://doi.org/10.51847/1e4vd1jlS4

Introduction

The totality of microorganisms distributed throughout the small intestine forms the intestinal microbiome. It has multiple roles but the most important role is to maintain the normal parameters of the human body. To date, it has been shown in numerous studies that there is a very close link between the health of the gut microbiome and the health of the host organism, and this is influenced by lifestyle [1-3].

Thus, it can be stated that lifestyle changes lead to changes in the bacterial composition of the gut microbiome.

In other words, improving lifestyle and diet will lead to a change in the microbiome (in a positive sense) and improved health, or it may prevent the development of various pathologies [1].

It is therefore very important to know the interaction between food and intestinal bacteria in order to be able to say what is the interaction between them. Many pieces of research prove that a restructuring of the gut microbiome composition can have positive or negative effects on health [4, 5].

Multiple factors such as temperature, pH, presence of bacteriophages, the bioavailability of nutrients, and percentage of anaerobiosis are strongly involved in the type of composition and function of the total intestinal bacterial population, which is directly influenced [6, 7].

The activity of gut microorganisms is so intense and present in the host organism that nowadays the microbiome is considered to function as a "real organ" [8].

The variation of the human intestinal microbiome can reflect the lifestyle and behaviors of the host and it can influence the levels of biomarkers in the blood [9].

Recent findings advance the concept of precise nutrition and they have the potential to present more effective and accurate dietary approaches to disease prevention through changes in the gut microbiome [10].

Therefore, this paper aims to highlight several recent studies on the interrelationship between the health of the microbiome and the health of the human body and to allow an overall assessment of the importance of nutrition in the prevention or treatment of various diseases.

The Human Colon and Fermentation

Corresponding Author: Ganea Mariana; Faculty of Medicine and Pharmacy, University of Oradea, 410087 Oradea, Romania. E-mail: mganea@uoradea.ro.

The number of bacteria in the colon is impressive, on the order of trillions, and all of them are involved in the processes of digestion, absorption, and metabolism of food, acting in the first phase through the fermentation process [11-13].

Carbohydrates throughout the digestive tract are not fully hydrolyzed by digestive enzymes (especially complex, indigestible ones such as pectin, gums, cellulose, etc.) but through the microbiota they are fermented, this process resulting in energy and production of SCFA (propionate, acetate, and butyrate) and gases [14-17].

Following the fermentation process of carbohydrates and proteins under physiological conditions, in addition to those mentioned above, branched-chain fatty acids (BCFA), lactic acid, amines, etc. are produced, all these reaction products having an important role in maintaining the metabolic balance of the host organism. More recently it has also been shown to play a role in increasing the body's immunity [18, 19].

It is however worth mentioning that protein fermentation occurs only after carbohydrates have been fermented and for this reason, it takes place in the distal colon [20-22].

Protein fermentation can become harmful to the body (considered an important factor in colorectal cancer) but there are also situations in which it is beneficial, namely when it intervenes in regulating the nitrogen balance of the host by releasing ammonia that can be absorbed into cells [23, 24].

The impact of the gut microbiome on lipids is more complex as it generates a variety of fatty acids that in increased amounts can affect the health of the host. For example, the metabolism of linolenic acid has a direct connection with species of *Roseburia* bacteria which play a role in promoting the health of the host organism by forming vaccenic acid (a precursor for conjugated linoleic acid) [18].

An *in vivo* study shows that the metabolism of unsaturated fatty acids is also influenced by the presence of bacteria such as Lactobacillus sp. Reaction intermediates (especially hydroxylated compounds) were monitored and it was shown that depending on the composition of the microbial flora, their level is different. In other words, the lipid profile of the host can be modified depending on the health of the intestinal microbial flora [18, 25, 26].

The bacteria most often involved in fermentation processes are of the genera *Bifidobacterium*, *Ruminococcus*, *Lactobacillus*, and *Clostridium*. Also of major importance are *Eubacteriumrectale*, *Roseburia spp*., and *Faecalibacterium prausnitzii* [8, 20, 27, 28].

The Interrelationship of the Microbiome and the Appearance of Multiple Diseases

To date, numerous studies have been performed on the influence of the microbiome on the health of the body and the direct connection with various pathologies. An overview of the intestinal bacterial genera and species commonly affected by diet is presented in **Table 1**.

Table 1. Overview of intestinal bacterial genera and species commonly affected by diet.

Bacteria	Characteristics	Associated physiological changes	Associated disease states	Ref.
Bifidobacterium spp.	○ gram-positive ○ branched-chain anaerobic;	○ low SCFA production; ○ improve the intestinal mucosa barrier; ○ lower intestinal LPS levels	○ low amount of obesity	[29, 30]
Lactobacillus spp.	○ optional anaerobic ○ rod-shaped ○ gram-positive	○ regulates SCFA production; ○ anti-inflammatory activity ○ anti-cancer activity	○ low amount in IBD	[31]
Alistipes spp.	○ gram-negative ○ rod-shaped anaerobic ○ resistant to bile acids and pigments	-	○ Reported in the tissues of acute appendicitis and perirectal and cerebral abscesses	[32]
Bilophila spp.	○ gram-negative ○ anaerobic ○ resistant to bile acids and pigments	○ Promotes TH1 pro-inflammatory immunity	○ observed in colitis, perforated appendicitis and gangrene, liver and soft tissue abscesses, cholecystitis	[33, 34]
Eubacterium spp.	○ gram-positive ○ rod-shaped aerobic	○ involved in SCFA production ○ forms beneficial phenolic acids	○ low amount in IBD	[35, 36]
Escherichia coli	○ gram-negative ○ rod-shaped anaerobic	-	○ increased in gastroenteritis, IBD, and meningitis	[37, 38]
Akkermansia muciniphila	○ gram-negative ○ anaerobic ○ oval shape	○ Anti-inflammatory effects	○ Low amount of IBD, obesity, and psoriasis	[39]

Alzheimer Disease

Alzheimer's disease (AD) is a progressive neurodegenerative disorder for which there is currently no treatment to stop or cannot be prevented [40]. Theoretically, AD is characterized by extracellular accumulations of peptides and intracellular deposits of hyperphosphorylated proteins [41, 42].

It has recently been shown that there is a close link between the intestinal microbiome and the maintenance of cognitive health, with an imaginary bowel-brain axis that is due to immune, endocrine, and neural signaling pathways.

Thus, in patients with mild cognitive impairment and dementia, there is an imbalance in the intestinal flora that has been shown to be responsible for the accumulation of a pro-inflammatory lipopolysaccharide at the neuronal level [43-46].

The ketogenic and low-calorie diet is considered to be beneficial in this category of patients because it has a neuroprotective effect and does not allow the accumulation of extracellular peptides at the neuronal level. also, this type of diet modulates positively and balances the important bacterial species in the intestine [17, 47].

Inflammatory Bowel Disease

Genetic factors and lifestyle are some of the factors that can have an important contribution to the occurrence of intestinal pathology such as inflammatory bowel disease (IBD) [48]. The unbalanced microbiome seems to have an extremely high contribution to these pathologies because the imbalance of the microbial population produces by fermentation proinflammatory components that will become precursors of this pathological sphere which includes Crohn's disease and ulcerative colitis [38, 49].

Crohn's disease (CD) affects the mucous and submucosal tissues, leading to regional ileitis. It is shown that the microbial changes that occur in this condition are characterized by an increase in the abundance of the bacterial species *Enterobacteriaceae,* including *Escherichia coli, Fusobacterium, Serratia marcescens* and *Candida tropicalis*, something not found in patients without this condition [50]. The impact of this imbalance is major, modifying the host's metabolism and thus causing oxidative stress. The basal metabolic rate decreases in these patients a lot, which also leads to a decrease in the production of intermediates that benefit the human body, such as short-chain fatty acids, which are easily absorbed [51-53].

The imbalance of the intestinal bacterial flora in the sense of the increase of the population of *Enterobacteriaceae sp*. and *Bacteroides fragilis* is the main feature of ulcerative colitis pathology [3, 54, 55].

Inflammatory Skin Diseases

Atopic dermatitis (AD) affects 15% -20% of children and 1% -3% of adults worldwide [56]. As for the balance of the intestinal microbiome in this condition, it is disturbed, and unbalanced. However, studies are showing that the use of probiotics leads to the remission of inflammatory dermatological conditions, thus confirming the existence of the intestinal-skin axis. For this reason, future treatments for these conditions will consider rebalancing the microbial flora and then topical treatment [56-60].

Type 2 Diabetes and Obesity

Increased consumption of high-fat and high-sugar diets has been shown to alter the microbial flora, which leads up to the idea that gut microbiota may function as an "environmental" factor that results in increased energy production and obesity [61, 62].

Obesity pathology is conceded to be associated with changes in the diversity and composition of the intestinal microbiota.

There is an increased concentration of *Firmicut* and a decreased one of *Bacteroids*, which are the 2 dominant types of intestinal microbiota. *In vivo*, it has been illustrated that a high-fat diet is associated with a decreased level of bacteria associated with Firmicutes (*Eubacterium rectale* and *Blautia coccoides*), bifidobacteria, and intestinal bacteria [17, 63].

The pathology of obesity and type 2 diabetes is associated with changes in the abundance of the main bacteria and the increase of the *Firmicutes* / *Bacteroidetes* ratio [30, 64-66].

In humans, the abundance of *Bifidobacterium* appears to be lower in overweight, obese, or type 2 diabetic patients than in healthy subjects.

Another species with a low concentration in type 2 diabetes is *Faecalibacterium prausnitzii*. *Bifidobacterium* and *Faecalibacterium prausnitzii* are associated with anti-inflammatory effects. Furthermore, another study indicated that the microbial composition during childhood may predict overweight [30].

In other studies, was identified a higher level of *Staphylococcus aureus* and a lower level of bifidobacteria in the faecal samples of children who became overweight. In a recent study, intestinal microbiota infusion from a healthy donor has been shown to temporarily improve insulin sensitivity in people with metabolic syndrome [2, 67, 68].

Conclusion

Based on clinical, epidemiological, and immunological evidence, changes in the gut microbiota may be a key factor in the incidence of many inflammatory disorders. The recent identification of symbiotic bacteria with strong anti-inflammatory properties and their correlative absence during the disease suggests that certain aspects of human health may depend on the condition of the microbiota. The medical and social reconsideration of microbial flora can generate profound consequences for the health of our future generations. Therefore, it is important to understand the complexity of gut microbial flora and how colonization patterns based on potential disorders can have both immediate and long-term consequences.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: None

References

1. Tamang JP. Health Benefits of Fermented Foods and Beverages. Routledge & CRC Press; 2015.
2. Arboleya S, Watkins C, Stanton C, Ross RP. Gut Bifidobacteria Populations in Human Health and Aging. Front Microbiol. 2016;7:1204.
3. Guo XY, Liu XJ, Hao JY. Gut microbiota in ulcerative colitis: insights on pathogenesis and treatment. J Dig Dis. 2020;21(3):147-59.
4. Nicholson JK, Holmes E, Kinross J, Burcelin R, Gibson G, Jia W, et al. Host-gut microbiota metabolic interactions. Science. 2012;336(6086):1262-7.
5. Holmes E, Kinross J, Gibson GR, Burcelin R, Jia W, Pettersson S, et al. Therapeutic modulation of microbiota-host metabolic interactions. Sci Transl Med. 2012;4(137):137rv6.
6. Kleszken E, Timar AV, Memete AR, Miere F, Vicas SI. On overview of bioactive compounds, biological and pharmacological effects of mistletoe (Viscum Album L). Pharmacophore. 2022;13(1):10-26.
7. Memete AR, Timar AV, Vuscan AN, Miere (Groza) F, Venter AC, Vicas SI. Phytochemical Composition of Different Botanical Parts of Morus Species, Health Benefits and Application in Food Industry. Plants. 2022;11(2):152.
8. Jones RM, Neish AS. Gut Microbiota in Intestinal and Liver Disease. Annu Rev Pathol. 2021;16:251-75.
9. Fu Y, Wang Y, Gao H, Li D, Jiang R, Ge L, et al. Associations among Dietary Omega-3 Polyunsaturated Fatty Acids, the Gut Microbiota, and Intestinal Immunity. Mediators Inflamm. 2021;2021:8879227.
10. Nathan NN, Philpott DJ, Girardin SE. The intestinal microbiota: from health to disease, and back. Microbes Infect. 2021;23(6-7):104849.
11. Scott KP, Gratz SW, Sheridan PO, Flint HJ, Duncan SH. The influence of diet on the gut microbiota. Pharmacol Res. 2013;69(1):52-60.
12. Bruci A, Tuccinardi D, Tozzi R, Balena A, Santucci S, Frontani R, et al. Very Low-Calorie Ketogenic Diet: A Safe and Effective Tool for Weight Loss in Patients With Obesity and Mild Kidney Failure. Nutrients. 2020;12(2):E333.
13. Walker AW, Ince J, Duncan SH, Webster LM, Holtrop G, Ze X, et al. Dominant and diet-responsive groups of bacteria within the human colonic microbiota. ISME J. 2011;5(2):220-30.
14. Petrof EO, Khoruts A. From stool transplants to next-generation microbiota therapeutics. Gastroenterology. 2014;146(6):1573-82.
15. Martinez-Medina JN, Flores-Lopez R, López-Contreras BE, Villamil-Ramirez H, Guzman-Muñoz D, Macias-Kauffer LR, et al. Effect of Gut Microbial Enterotypes on the Association between Habitual Dietary Fiber Intake and Insulin Resistance Markers in Mexican Children and Adults. Nutrients. 2021;13(11):3892.
16. Sharma R, Gupta D, Mehrotra R, Mago P. Psychobiotics: The Next-Generation Probiotics for the Brain. Curr Microbiol. 2021;78(2):449-63.
17. Meslier V, Laiola M, Roager HM, De Filippis F, Roume H, Quinquis B, et al. Mediterranean diet intervention in overweight and obese subjects lowers plasma cholesterol and causes changes in the gut microbiome and metabolome independently of energy intake. Gut. 2020;69(7):1258-68.
18. Claesson MJ, Cusack S, O'Sullivan O, Greene-Diniz R, de Weerd H, Flannery E, et al. Composition, variability, and temporal stability of the intestinal microbiota of the elderly. Proc Natl Acad Sci U S A. 2011;108 Suppl 1:4586–91.
19. Chopyk DM, Grakoui A. Contribution of the Intestinal Microbiome and Gut Barrier to Hepatic Disorders. Gastroenterology. 2020;159(3):849-63.
20. Elamin EE, Masclee AA, Dekker J, Pieters HJ, Jonkers DM. Short-chain fatty acids activate AMP-activated protein kinase and ameliorate ethanol-induced intestinal barrier dysfunction in Caco-2 cell monolayers. J Nutr. 2013;143(12):1872-81.
21. Feng Y, Wang Y, Wang P, Huang Y, Wang F. Short-Chain Fatty Acids Manifest Stimulative and Protective Effects on Intestinal Barrier Function Through the Inhibition of NLRP3 Inflammasome and Autophagy. Cell Physiol Biochem. 2018;49(1):190-205.
22. Sivaprakasam S, Bhutia YD, Yang S, Ganapathy V. Short-Chain Fatty Acid Transporters: Role in Colonic Homeostasis. Compr Physiol. 2017;8(1):299-314.
23. D'Amelio P, Sassi F. Gut Microbiota, Immune System, and Bone. Calcif Tissue Int. 2018;102(4):415-25.

24. Dimidi E, Cox SR, Rossi M, Whelan K. Fermented Foods: Definitions and Characteristics, Impact on the Gut Microbiota and Effects on Gastrointestinal Health and Disease. Nutrients. 2019;11(8):E1806.
25. Gomaa EZ. Human gut microbiota/microbiome in health and diseases: a review. Antonie Van Leeuwenhoek. 2020;113(12):2019-40.
26. Gagliardi A, Totino V, Cacciotti F, Iebba V, Neroni B, Bonfiglio G, et al. Rebuilding the Gut Microbiota Ecosystem. Int J Environ Res Public Health. 2018;15(8):E1679.
27. Wu GD, Chen J, Hoffmann C, Bittinger K, Chen YY, Keilbaugh SA, et al. Linking long-term dietary patterns with gut microbial enterotypes. Science. 2011;334(6052):105-8.
28. de Oliveira GLV, Leite AZ, Higuchi BS, Gonzaga MI, Mariano VS. Intestinal dysbiosis and probiotic applications in autoimmune diseases. Immunology. 2017;152(1):1-12.
29. Cukrowska B, Bierła JB, Zakrzewska M, Klukowski M, Maciorkowska E. The Relationship between the Infant Gut Microbiota and Allergy. The Role of Bifidobacterium breve and Prebiotic Oligosaccharides in the Activation of Anti-Allergic Mechanisms in Early Life. Nutrients. 2020;12(4): E946.
30. Singer-Englar T, Barlow G, Mathur R. Obesity, diabetes, and the gut microbiome: an updated review. Expert Rev Gastroenterol Hepatol. 2019;13(1):3-15.
31. Li SC, Hsu WF, Chang JS, Shih CK. Combination of Lactobacillus acidophilus and Bifidobacterium animalis subsp. lactis Shows a Stronger Anti-Inflammatory Effect than Individual Strains in HT-29 Cells. Nutrients. 2019;11(5):E969.
32. Parker BJ, Wearsch PA, Veloo ACM, Rodriguez-Palacios A. The genus Alistipes: gut bacteria with emerging implications to inflammation, cancer, and mental health. Front Immunol. 2020;11:906.
33. Dahl WJ, Rivero Mendoza D, Lambert JM. Diet, nutrients, and the microbiome. Prog Mol Biol Transl Sci. 2020;171:237-63.
34. Verhaar BJH, Hendriksen HMA, de Leeuw FA, Doorduijn AS, van Leeuwenstijn M, Teunissen CE, et al. Gut Microbiota Composition Is Related to AD Pathology. Front Immunol. 2021;12:794519.
35. Kummen M, Thingholm LB, Rühlemann MC, Holm K, Hansen SH, Moitinho-Silva L, et al. Altered Gut Microbial Metabolism of Essential Nutrients in Primary Sclerosing Cholangitis. Gastroenterology. 2021;160(5):1784-98.
36. Chung WSF, Walker AW, Louis P, Parkhill J, Vermeiren J, Bosscher D, et al. Modulation of the human gut microbiota by dietary fibers occurs at the species level. BMC Biol. 2016;14(1):1-13.
37. Palmela C, Chevarin C, Xu Z, Torres J, Sevrin G, Hirten R, et al. Adherent-invasive Escherichia coli in inflammatory bowel disease. Gut. 2018;67(3):574-87.
38. Santana PT, Rosas SLB, Ribeiro BE, Marinho Y, de Souza HSP. Dysbiosis in Inflammatory Bowel Disease: Pathogenic Role and Potential Therapeutic Targets. Int J Mol Sci. 2022;23(7):3464.
39. Zhai Q, Feng S, Arjan N, Chen W. A next-generation probiotic, Akkermansia muciniphila. Crit Rev Food Sci Nutr. 2019;59(19):3227-36.
40. Soria Lopez JA, González HM, Léger GC. Alzheimer's disease. Handb Clin Neurol. 2019;167:231-55.
41. GBD 2016 Dementia Collaborators. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(1):88-106.
42. Vogt NM, Kerby RL, Dill-McFarland KA, Harding SJ, Merluzzi AP, Johnson SC, et al. Gut microbiome alterations in Alzheimer's disease. Sci Rep. 2017;7(1):13537.
43. Liu CC, Liu CC, Kanekiyo T, Xu H, Bu G. Apolipoprotein E, and Alzheimer disease: risk, mechanisms, and therapy. Nat Rev Neurol. 2013;9(2):106-18.
44. Penke B, Bogár F, Fülöp L. β-Amyloid and the Pathomechanisms of Alzheimer's Disease: A Comprehensive View. Molecules. 2017;22(10):E1692.
45. Le Page A, Dupuis G, Frost EH, Larbi A, Pawelec G, Witkowski JM, et al. Role of the peripheral innate immune system in the development of Alzheimer's disease. Exp Gerontol. 2018;107:59-66.
46. Pașc P, Dobjanschi L, Zdrîncă M, Zdrîncă M, Ștefan L, Huniadi CA, et al. Safety and Efficacy of Modern Stents in Patients with Metabolic Syndrome. Appl Sci. 2022;12(7):3277.
47. Kowalski K, Mulak A. Brain-Gut-Microbiota Axis in Alzheimer's Disease. J Neurogastroenterol Motil. 2019;25(1):48-60.
48. Mansour SR, Moustafa MA, Saad BM, Hamed R, Moustafa ARA. Impact of diet on the human gut microbiome and disease risk. New Microbes New Infect. 2021;41:100845.
49. Ni J, Wu GD, Albenberg L, Tomov VT. Gut microbiota and IBD: causation or correlation? Nat Rev Gastroenterol Hepatol. 2017;14(10):573-84.
50. Elias AE, McBain AJ, O'Neill CA. The role of the skin microbiota in the modulation of cutaneous inflammation—Lessons from the gut. Exp Dermatol. 2021;30(10):1509-16.
51. Chiodini RJ, Dowd SE, Chamberlin WM, Galandiuk S, Davis B, Glassing A. Microbial Population Differentials between Mucosal and Submucosal Intestinal Tissues in Advanced Crohn's Disease of the Ileum. PLoS One. 2015;10(7):e0134382.
52. Schwermer M, Fetz K, Längler A, Ostermann T, Zuzak TJ. Complementary, alternative, integrative and dietary therapies for children with Crohn's disease - A systematic review. Complement Ther Med. 2020;52:102493.
53. Ganea M, Miere F, Vicaș LG, Moisa CF. In Vitro Studies of the Stability of Ketoprofen Tablets based on the European Pharmacopoeia Guideline (ICHQ1A). Pharmacophore. 2021;12(5):1-6.

54. Wang KY, Li SN, Liu CS, Perng DS, Su YC, Wu DC, et al. Effects of ingesting Lactobacillus- and Bifidobacterium-containing yogurt in subjects with colonized Helicobacter pylori. Am J Clin Nutr. 2004;80(3):737-41.
55. Cardos AI, Maghiar A, Zaha DC, Pop O, Fritea L, Miere (Groza) F, et al. Evolution of Diagnostic Methods for Helicobacter pylori Infections: From Traditional Tests to High Technology, Advanced Sensitivity and Discrimination Tools. Diagnostics. 2022;12(2):508.
56. Sinha S, Lin G, Ferenczi K. The skin microbiome and the gut-skin axis. Clin Dermatol. 2021;39(5):829-39.
57. Gupta J, Grube E, Ericksen MB, Stevenson MD, Lucky AW, Sheth AP, et al. Intrinsically defective skin barrier function in children with atopic dermatitis correlates with disease severity. J Allergy Clin Immunol. 2008;121(3):725-30.
58. Miere (Groza) F, Teușdea AC, Laslo V, Cavalu S, Fritea L, Dobjanschi L, et al. Evaluation of in vitro wound-healing potential, antioxidant capacity, and antimicrobial activity of Stellaria media (L.) Vill. Appl Sci. 2021;11(23):11526.
59. Antonescu (Mintaș) IA, Antonescu A, Miere (Groza) F, Fritea L, Teușdea AC, Vicaș L, et al. Evaluation of Wound Healing Potential of Novel Hydrogel Based on Ocimum basilicum and Trifolium pratense Extracts. Processes. 2021;9(11):2096.
60. Jeziorkowska R, Sysa-Jędrzejowska A, Samochocki Z. Topical steroid therapy in atopic dermatitis in theory and practice. Postepy Dermatol Alergol. 2015;32(3):162-6.
61. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature. 2006;444(7122):1027-31.
62. Gupta A, Osadchiy V, Mayer EA. Brain-gut-microbiome interactions in obesity and food addiction. Nat Rev Gastroenterol Hepatol. 2020;17(11):655-72.
63. Furet JP, Kong LC, Tap J, Poitou C, Basdevant A, Bouillot JL, et al. Differential adaptation of human gut microbiota to bariatric surgery-induced weight loss: links with metabolic and low-grade inflammation markers. Diabetes. 2010;59(12):3049-57.
64. Goldsmith JR, Sartor RB. The role of diet on intestinal microbiota metabolism: downstream impacts on host immune function and health, and therapeutic implications. J Gastroenterol. 2014;49(5):785-98.
65. Bazzocco S, Mattila I, Guyot S, Renard CMGC, Aura AM. Factors affecting the conversion of apple polyphenols to phenolic acids and fruit matrix to short-chain fatty acids by human faecal microbiota in vitro. Eur J Nutr. 2008;47(8):442-52.
66. Clarke SF, Murphy EF, O'Sullivan O, Lucey AJ, Humphreys M, Hogan A, et al. Exercise and associated dietary extremes impact on gut microbial diversity. Gut. 2014;63(12):1913-20.
67. Zhao L, Zhang F, Ding X, Wu G, Lam YY, Wang X, et al. Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes. Science. 2018;359(6380):1151-6.
68. Zhang PP, Li LL, Han X, Li QW, Zhang XH, Liu JJ, et al. Fecal microbiota transplantation improves metabolism and gut microbiome composition in db/db mice. Acta Pharmacol Sin. 2020;41(5):678-85.