Review Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2024.57.009069

Gut Microbiota Modulation in Veterinary Medicine: Faecal Microbiota Transplantation as a New Frontier

Umra Rasool[1]*, Peter Thomson[2] and Luigi Bertolotti[1]

[1]*University of Turin, Italy*

[2]*The university of Sydney, Australia*

***Corresponding author:** Umra Rasool, University of Turin, Italy

ARTICLE INFO

Received: July 05, 2024

Published: July 26, 2024

Citation: Umra Rasool, Peter Thomson and Luigi Bertolotti. Gut Microbiota Modulation in Veterinary Medicine: Faecal Microbiota Transplantation as a New Frontier. Biomed J Sci & Tech Res 57(5)-2024. BJSTR. MS.ID.009069.

ABSTRACT

Dysbiosis, or changes in the composition of the gut microbiome, can be brought on by a variety of things, including illnesses, antibiotics, stress, and food. Currently, there are a number of methods for modifying the gut microbiome, including dietary modifications and the use of probiotics, prebiotics, synbiotics, postbiotics, and antibiotics. One novel approach to regulating gut microbiota in animals with the goal of reestablishing the recipient's intestinal microbiome is fecal microbiota transplantation (FMT). This type of bacteriotherapy is successfully applied in human medicine to treat recurrent Clostridium difficile infections (CDI). For a number of years, large animal medicine has been aware of FMT. The application of FMT is not a standard procedure in small animal medicine.

Keywords: Dogs; Faecal Microbiota Transplantation; Gut; Probiotics; Microbiome; Modulation

Abbreviations: FMT: Fecal Microbiota Transplantation; CDI: Clostridium Difficile Infections; CFU: Colony-Forming Units; GIT: Gastrointestinal Tract; SCFAs: Short-Chain Fatty Acids; DI: Dysbiosis Index, AD: Acute Diarrhea; FDA: Food and Drug Administration; ESBL: Extended-Spectrum Beta-Lactamase

Introduction

The term "faecal microbiota transplantation" refers to an approach whereby feces are transferred from a healthy donor to the gut of an unhealthy recipient through multiple methods. For instance, an endoscopy, enema, nasogastric tube, colonoscopy or in the form of capsules [1-3]. The purpose of treatment is to adjust and reconstruct the recipient's gut composition. Currently, the primary indication for this type of bacteriotherapy in people is recurrent CDI that is not improved by antibiotics [4]. FMT is helpful in treating a number of different gastrointestinal and non-gastrointestinal disorders that are closely linked to dysbiosis. Transfaunation, or the therapeutic transfer of rumen content, was first documented in large animal therapy in the 17th century [5,6]. To put FMT into practice, more study is needed as there aren't many publications currently available that outline its positive effects in both chronic and acute disorders in small animals. In addition to highlighting its advantages, alternatives, and potential application in small animal gastroenterology in the future, the primary goal of this review is to provide a summary of well-known information regarding transplanting feces in small animal medicine.

Gut Miccrobiome

A diverse range of microorganisms, including bacteria, viruses, fungus, and protozoa, inhabit the gastrointestinal system of every individual. The term "microbiome" refers to the collective genome of all intestinal microbiome [7].

Microbial Diversity in Health

In any organism that hosts the gastrointestinal system, bacteria are the predominant population. From the stomach to the colon, their abundance increases [8]. The concentration of bacteria in a healthy dog stomach varies from 101 to 106 colony-forming units (CFU) per gram [9]. Aerobic and facultative anaerobes comprise the intestinal microbiota of the small intestine, where the microbial concentration ranges from 102 to 106 CFU per gram. In the colon, anaerobes prevail with a bacterial density of about 1011 CFU per gram [9,10]. Each individual, however, has a unique microbial composition; in the gastrointestinal tract (GIT) of healthy dogs and cats, Firmicutes, Actinobacteria, Fusobacteria, and *Bacteriodetes* are the most common phyla [10,11]. Within this core bacterial ecosystem, the phylum Fir-

micutes has a large number of important species. Three Clostridium clusters-IV, XI, and XIV-dominate, making Clostridium the most common bacterial class. Within the phylum Firmicutes, Bacilli and *Erysipelotrichi* are important classes in addition to Clostridium [12-15]. In human beings, the occurrence of phylum Fusobacteria is linked to gastrointestinal disorders, however in dogs, Fusobacteria is linked to a healthy microbiome. This finding suggests that the function of Fusobacterium in animals differs from that in humans [12,13]. It has been observed that Fusobacterium is more prevalent in outdoor dogs as well as other carnivorous species [12,16-19]. The variety of gut microbiota in healthy dogs is shown in Figure 1.

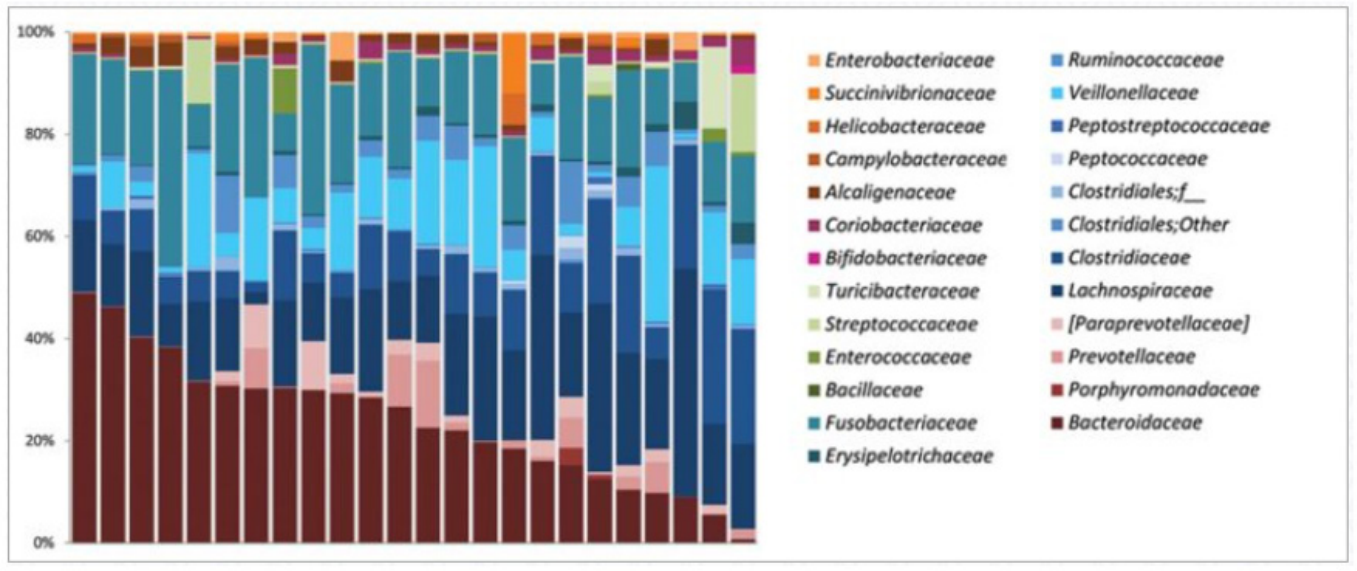

Figure 1: In healthy dogs, the diversity of the gut microbiota [14,20]. The microbiota composition of a single healthy dog is shown by each column. Reprinted by consent from Suchodolski J [14].

The Function of the Gut Microbiome

In addition to being involved in the pathophysiology of numerous diseases, the gut microbiome has a wide range of functions in maintaining health. Protection of host from infectious agents, improving the function of the intestinal barrier by forming tight junctions, supplying nutrients, and modifying the immune system through interactions between cells (Toll-like receptors, dendritic cells) and the generation of microbial metabolites, such as vitamins, bile acids (Bas), short-chain fatty acids (SCFAs), and tryptophan metabolites, are among its most significant roles [20,21]. Additionally, several bacteria release antimicrobial compounds that directly destroy enteropathogens [22]. Positive effects of the gut microbiota can be observed locally as well as in the surrounding organs because of the systemic transfer of these products and cells produced in the intestine. The gut-organ axis, which encompasses the gut-brain, gut-lung axes and gut-skin, is the term used to describe this phenomenon [23]. As a distinct organ, the gut microbiota participates in numerous processes [24]. Table 1 outlines these gut bacteria metabolic pathways and how they affect the host. A microbiome that is in equilibrium benefits the health of the host. Unbalances within a few of these routes can be detrimental. The indole route, SCFAs, and BAs are the three most significant pathways [24].

Table 1: The gut microbiota's advantageous and detrimental metabolic pathways and how they affect the host.

		Consequence for Host		
Source	**Bacterial Group Involved**	**Derived Metabolites**	**Beneficial**	**Harmful**
Dietary carbohydrates	*Faecalibacterium*, *Bacteriodes*, *Ruminococcus*, *Blautia* [24].	Fermentation to SCFAs (acetate, butyrate, propionate) [30].	• Anti-inflammatory effect. • Maintenance of intestinal • barrier function. • Motility regulation. • Source of energy for epithelial cells [30,31].	Virulence factors of enteropathogen activation (e.g., Salmonella type III secretion system) [24].
Dietary fat	*C. perfringens*, *Bifidobacterium bifidum*, *Propiobacterium*) [24].	Conversion to hydroxystearic acids [24].	None [24].	Fatty acid diarrhoea [24].
Primary bile acids	In small animals, mainly *C. hiranonis* [26].	Transformation to secondary BAs in colon [26].	_ Anti-inflammatory effect. _ Growth inhibition (C. difficile, Clostridium perfringens, Escherichia coli). _ Modulation of glucose/insulin secretion [27].	• Secretory diarrhoea caused by lack of C. hiranonis (e.g., chronic enteropathies). • In humans, a diet rich in fat, due to increased secondary BAs,represents a high risk of colon cancer [26,28,29].
Dietary amino acid tryptophan _	Various [24].	Indole metabolites [33].	• Anti-inflammatory effect. • Maintenance of intestinal function [33].	• Cytotoxic and putrefactive, but only in high concentrations. • Indoxyl sulfate acts as a uremic toxin [24].
Dietary amino acids tyrosine and phenylalanine	Various [24].	P-cresol [24].	None [24].	Progression of chronic kidney disease similar to uremic toxin [24].
Drug mycophenolate mofetil	Various [24].	MPA (mycophenil acids) and acylglucuronide [24].	None [24].	Production of proinflammatory cytokines causing diarrhoea [24].

The primary species of bacteria that converts BA in dogs is *Clostridium hiranonis* [25,26]. In the canine colon, these bacteria change basic amino acids (BAs) into secondary BAs, such as deoxycholic and lithocholic acids. Secondary Bas in the colon serve a variety of purposes. via attaching to the natural receptors G protein-coupled bile acid receptor 1 (GPBAR-1), they function as signaling molecules. They help preserve a normal glucose concentration via connecting to the farnesoid X receptor [27]. Furthermore, they prevent Clostridium difficile spores from germinating, while an increase in primary bile acids-a consequence of dysbiosis-allows bacterial spores to germinate [24]. In dogs with chronic enteropathies or following antibiotic treatment, there is a reduction in secondary BAs in the colon [26,28,29]. The fundamental cause of secretory diarrhea, a rise in the concentration of primary BA, is brought on by a decrease in C. hiranonis [24]. Under such circumstances, C. hiranonis can be reinstated by FMT, resulting in the proper conversion of primary to secondary Bas [26]. Bacteria including *Turicibacter*, *Ruminoccocus*, and *Faecalibacterium* ferment dietary carbohydrates to produce butyrate, acetate, and propionate, or SCFAs [30].

These SCFAs serve as nutrients that control intestinal motility, give intestinal epithelial cells a significant source of energy and growth factors, and create an environment that is sensitive to pH-sensitive enteropathogens [31,32]. Additionally, SCFAs modulate immunity. For instance, acetate efficiently improves intestinal permeability, while butyrate stimulates immunoregulatory T-cells [24]. Tryptophane is metabolized to produce indole, a chemical that enhances intestinal permeability and boosts the formation of mucin [31]. Additionally, it has been demonstrated that indole improves intestinal barrier integrity, reduces the expression of interleukin 8, and improves enteropathy brought on by nonsteroidal anti-inflammatory medications in rats [32].

Dysbiosis

Gut dysbiosis is defined as an imbalance in the composition of the gut microbiota that may result in modifications to the transcriptome, metabolome, or proteome of microorganisms [33]. Dysbiosis is observed in the gastrointestinal tract in a range of diseases, both locally and systemically [34]. The quality and kind of the mother's diet, the

makeup of the mother's gut microbiota, stress, and use of antibiotics are some of the elements that affect the microbiota's composition from the time of birth [35]. Apart from these variables, a number of systemic or localized illnesses are linked to dysbiosis and affect the gut microbiome [35]. When compared to healthy individuals, those with intestinal dysbiosis have alterations in the variety, abundance, and function of bacterial species [24]. These alterations in the microbiota cause the intestinal barrier to be destroyed, which raises the risk of pathogen translocation and the emergence of diseases. Inflammatory responses can be encouraged by immune system activation. Variations in the concentration of bacterial metabolites are additional consequences of dysbiosis [36].

Impact of Dysbiosis on Canine Health

Intestinal dysbiosis is most clearly associated with digestive disorders. Intestinal dysbiosis occurs together with gastrointestinal diseases in the majority of dogs and cats [36,37]. Both acute and chronic diseases tend to modify the gut flora. Acute digestive disorders, such as acute uncomplicated diarrhea (AD) and acute hemorrhagic diarrhoea (AHDS), cause significant changes in the microbial compositions of dogs. Actinobacteria and Firmicutes, which produce SCFA, are less common than E. coli, *C. perfringen* and *Sutterella* [38,39]. Since C. perfringens is a commensal of the intestines, it can be found in healthy individuals [40]. Intestinal dysbiosis is linked to several chronic GIT illnesses, including inflammatory bowel disease (IBD). Mucosa-adherent Proteobacteria genera (E. coli) have been observed to grow in this chronic situation, while *Bacteriodaceae*, *Prevotellaceae*, *Fusobacteria*, and *Clostridiales* have declined [41]. The number of Bacteriodetes and Firmicutes was found to be declining in the study that characterized canine luminal dysbiosis in IBD, whereas *Actinobabacteria* and Proteobacteria were shown to be more abundant [42].

Dysbiosis Index

The dysbiosis index (DI), a unique method, has been developed to evaluate the canine faecal microbiota [32]. Together with the overall bacterial count, the qPCR assay measures the abundances of seven different bacterial groups: *Faecalibacterium* spp., E. coli, *Fusobacterium* spp., *Turibacter* spp., Streptococcus spp., *Blatitia* spp., and *C. hiranonis* [43]. It then summarizes these data into a single number (DI) [32]. *AlShawaqfeh* et al. have provided a description of a mathematical model for calculating DI [32]. Table 2 describes the reference ranges for various bacterial groupings. It is imperative to understand the DI in conjunction with the abundance of specific taxa wherever possible. A normal microbiome is indicated by a DI of less than 0. An ambiguous DI falls between 0 and 2, signifying a slight alteration in the microbiota. In these situations, the examination of the subsequent samples may be carried out a few weeks afterward. An indicator of microbial dysbiosis is a DI > 2. There is a decreased quantity of healthy *C. hiranoni* bacteria in most of these canines because of an abnormal conversion of primary to secondary bile acids. One important factor contributing to the development of dysbiosis in dogs is the loss of secondary bile acids [37].

Table 2: Final DI and reference intervals for the abundances of seven bacterial groupings.

	Normal Abundance	Changes Seen in Dogs with Dysbiosis
Turicibacter	4.6–8.1	decreased
Faecalibacterium	3.4–8.0	decreased
Streptococcus	1.9–8.0	increased
E. coli	0.9–8.0	increased
C. hiranonis	5.1–7.1	decreased
Blautia	9.5–11.0	decreased
Fusobacterium	7.0–10.3	decreased
Dysbiosis index	<0 normal 0–2 equivocal >2 dysbiosis	[32,54]

Note: Data were presented as logDNA per gram of faeces.

Dogs receiving antibiotic treatment (metronidazole, tylosine) showed an increase in DI along with a decrease in *C. hiranonis*, as did dogs with EPI and chronic enteropathies [25,26,37]. Conversely, dogs on raw food diets (BARF) or proton-pump inhibitors (omeprazole) showed an increase in DI along with a normal abundance of *C. hiranonis* [44,45]. Apart from identifying healthy and unhealthy microbiota, DI can evaluate changes in microbial composition over time or in response to therapies such as FMT (Figure 2).

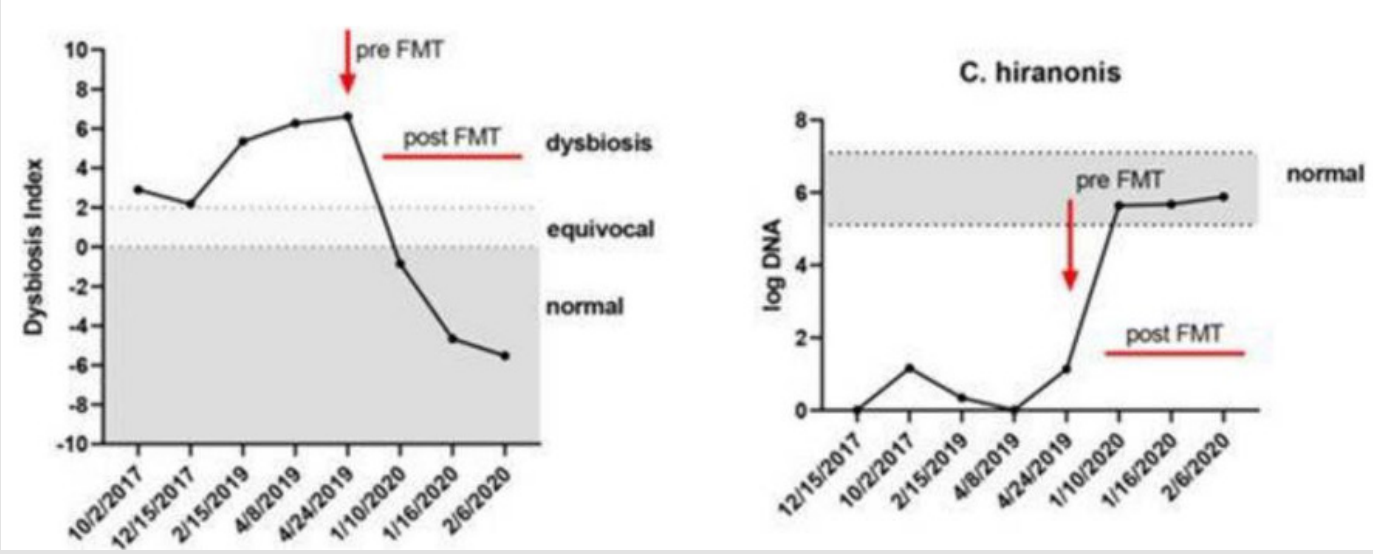

Figure 2: A dog that has recurring *C. difficile* infections and chronic dysbiosis. Following FMT, the abundance of *C. hiranonis* rose and the dysbiosis index returned to normal. After that, the dog tested negative for *C. difficile* [24]. No modifications were made to the article licensed under the CC BY-NC-ND license

Modulation of the Microbiome by FMT

While the pathophysiology of many gastrointestinal and systemic disorders is largely dependent on dysbiosis, a critical therapeutic goal is the restoration of the composition of the gut microbiota. FMT can currently alter the gut microbiota [24].

- **FMT**

"Faecal microbiota transplantation" is one of the innovative techniques for modifying the gut microbiota. The term "FMT" refers to the process of introducing a donor's fecal matter solution into a recipient's digestive tract with the primary goal of altering the recipient's microbiological nature [46,47]. A duodenoscopy, nasogastric/nasojejunal tube, enema, colonoscopy or peroral capsule can all be used to carry out this treatment [1,2].

History

In veterinary medicine, the transfer of gastrointestinal materials is not a novel technique. Numerous animal species have been documented to consume their own excrement, a practice known as coprophagy [48-50]. This process improves nutrition absorption, strengthens the gastrointestinal tract, and promotes resistance to pathogen colonization [4]. In Europe, the 17th century marked the first descriptions of transfaunation, or the therapeutic transfer of rumen content [5,6]. Ruminal acidosis in sheep and cattle as well as chronic diarrhea in horses were the indications for this treatment experiment. Additionally, it was utilized to strengthen the chicks' defenses against intestinal infections [51-53]. China has been using the FMT method on humans since the fourth century CE [3]. FMT is utilized in Chinese medicine for a variety of gastrointestinal ailments. It can be found in fresh, dried, fermented, and infant-derived products [37]. Faecal ingestion in people and animals has been frequent in Europe since manure had been employed as fertilizer, according to German physician Franz Christian Paullini.

He also wrote about the healing use of human and animal excrement in his book Hailsame Dreck Apotheke (Salutary Filth-Pharmacy), which was published in 1696 [54]. The Ben Eiseman team published a study in 1958 detailing the effective use of faecal enemas in the treatment of four patients with C. difficile-caused pseudomembranous colitis. According to this study, the usage of antibiotics caused the local microbial community that offers defense against infections to be suppressed [55]. They anticipated that the process would undergo standardization and clinical trial testing. Nevertheless, vancomycin's efficacy in treating pseudomembranous colitis was quickly established [55,56]. There is no question that treating patients with CDI has a positive impact in human health, but what is known about its effects and possible applications in canine?

Mechanism of Action of FMT

It's still unclear exactly how the gut microbiome functions. The important advantages of FMT for CDI patients include a shift in the microbial profiles toward those of healthy donors and an increase in the diversity of bacterial species [54,57]. Higher concentrations of Proteobacteria species and lower concentrations of Firmicutes and *Bacteriodetes* species are known signs of gut dysbiosis in CDI pa-

tients. Giving FMT may result in a decrease in Proteobacteria and an increase in communities of *Firmicutes* and *Bacteriodetes* [58]. Faecal matter administration not only provides antibiotics to make the environment less conducive to the growth of *C. difficile*, but it also initiates a process termed as competitive exclusion of pathogens [54]. The reestablishment of secondary bile acid preponderance over primary bile acid prevalence in faeces is one aspect of this mechanism [54,57]. It has been demonstrated that secondary bile acids are strong spore germination inhibitors, primary bile acids have been proven to promote spore germination [20]. A high concentration of secondary bile acids causes *C difficile* to outcompete it for nutrition and creates an environment that is not conducive to its growth [54].

It is important to note that transplanted feces alter the gut microbiota, which increases the amount of sialic acid that commensal bacteria use. *C. difficile* has a shortage of the carbohydrate energy supply as a result of this use [59]. The transplanted faecal material helps to restore the integrity of the intestinal barrier by secreting mucin [57]. Additionally, because butyrate-producing bacteria are produced when feces are administered, it helps to modulate the mucosal immune response and reduce the inflammatory response [57,60,61]. Additionally, bacteriophages discovered in the donor's feces probably contribute to the positive effects [61].

Forms of Application

FMT can be administered via a variety of methods, including colonoscopy, nasogastric duodenum, jejunal infusion, enema, and oral capsule intake [62-64]. Each of these techniques has certain drawbacks, such as the risk for nausea and aspiration pneumonia when the naso-gastric tube is being provided, the inability to properly hold the given suspension for the enema, or the possibility of tissue perforation during the colonoscopy and jejunal infusion [65]. In order to solve shortcomings and gaps found in earlier FMT delivery systems, oral capsules were developed. They are the least expensive, most non-invasive, and easiest to store means of administration. There are various procedural concerns associated with conventional FMT treatment methods that are eliminated when using this version of FMT. Oral capsules have been demonstrated by Kao et al. to be a successful treatment for rCDI (refractory Clostridium difficile infection), similar to colonoscopy [2]. The administration of these capsules has been linked to adverse events such as aspiration, vomiting, and inability to reach the intended digestive location [64,66]. There are two categories for FMT. The first involves using the patient's own feces for autologous transplantation, which is done before any kind of treatment. Through the use of antibiotics during allogeneic hematopoietic stem cell transplantation, this type of feces transfer is successfully employed to restore the composition of the damaged microbiota [66,67]. The second category consists of allogenic FMT, which uses a faecal sample from a related or unrelated healthy donor [68]. It seems that allogenic transplantation is highly successful when used for rCDI [69].

Recommendations for the Use of Faecal Microbiota Transplantation in and Dogs

As FMT proves more effective in treating a range of diseases there is an increasing need to standardize faecal material preparation and administration, adhering to recognized guidelines to protect both the donor and the recipient.

Donor Selection in Dogs: There aren't many research in canine medicine that focus on canine donor screening procedures. In order to guarantee that the feces used for FMT are safe and of the highest quality for the receiver, Chaitman and Gaschen proposed broad screening criteria [70]. A summary of these selection criteria can be seen in Table 3.

Table 3: Recommended selection criteria for canine faecal donors.

History and Physical Examination
• Age between 1 and 10 years; • No travel history outside the local area; • No history of chronic GI disease, cancer, allergies, or autoimmune diseases; • Healthy state in the last 6–12 months; • No antibiotics in the last 12 months; • Optimal weight (not overweight or underweight); • Fed a balanced diet; • Normal faecal consistency; • Feeding canine donors with a hydrolyzed diet for several weeks before and during collection is recommended [85,86].
Laboratory Screening
• No significant changes in the hematology and biochemistry profile; • Normal value of pancreatic enzymes, pancreatic immunoreactivity, and trypsin-like immunoreactivity); • Optimal serum concentration of cobalamin and folate (= tests of intestinal functions); • No presence of endocrinopathy (serum cortisol, thyroxine, TSH concentrations); • Negative for faecal parasites; • Negative for faecal pathogens (Salmonella spp., Campylobacter spp., etc.) [85,86].
Evaluation of the Faecal Microbiota
• Faecal dysbiosis index less than 0 [32].

Preparation and Administration of the Faecal Solution: To make a faecal solution, very identical methods are followed in veterinary medicine. Usually, six to twelve hours after defecation, twenty to one hundred grams of donor feces are used for the FMT treatment. After that, 4 volumes of 0.9% NaCl are combined with 1 volume of feces and filtered. After that, 10% final concentration of glycerol is added, and it is kept at 80°C for storage [1,2].

Recent Uses of FMT in Small Animals specifically in canines: Reports detailing the impact of FMT in small animal medicine are very few [70]. Burton et al. attempted to prevent postweaning diarrhea in puppies by giving the faecal inoculum orally. There was no discernible clinical improvement in this instance [71]. In a different study, the researchers combined normal treatment with FMT in an attempt to improve the survival rate of puppies infected with parvovirus. Although the duration of hospitalization was shortened and the duration of diarrhea was reduced to two days, this experiment did not significantly increase survival [72]. In dogs with simple, non-infectious diarrhea, Chaitman et al. conducted a trial comparing the administration of faecal material via enema versus a 7-day oral treatment of metronidazole (15 mg/kg q 12 h). Even though both groups' stools became more consistent after a week of treatment, only those receiving FMT showed firmer faeces by day 28. In most dogs treated with FMT, the faecal dysbiosis index returned to normal within one week, whereas it did not improve in the majority of patients receiving metronidazole [26,32]. Only dogs receiving FMT treatment showed a decrease in E. coli and an increase in beneficial bacteria such as *Faecalibacterium* and *C. hiranonis* in their feces [37]. A case study involving a toy poodle with refractory IBD proved to the beneficial effects of FMT even in cases of chronic illnesses. Nine FMTs were given to this dog via enema. The dog's stool consistency and Clinical IBD Activity Index both improved after six months [73]. An 8-month-old French bulldog with chronic colitis and a positive C difficile faecal culture was the subject of another study. FMT was given to this dog orally just once. By the end of two or three days, there was a noticeable improvement in both the frequency and consistency of feces. At least six months passed without any signs of relapse [72].

A single FMT seems to be quite effective when given to dogs suffering from acute diarrhea (AD), per Chaitman et al. [26]. Negative effects including decreased microbial diversity, alterations in particular bacterial taxa, abundance, and metabolic shift are avoided when an FMT is used in place of antibiotics [26,70]. Additionally, FMT appears to be a potential treatment for dogs suffering from long-term illnesses such exocrine pancreatic insufficiency or chronic enteropathies. Regrettably, relapses frequently occur after a few days of recovery following faecal transplant application. For this reason, in the majority of cases, multiple FMTs may be necessary [26]. These days, an FMT may help with acute and chronic dysbiosis-related disorders in small animal practice. Few studies have been conducted on its use, thus further study is needed to standardize it.

Safety of an FMT and Future Perspectives

One of the cutting-edge techniques for modifying the genetic make-up of the human gut microbiota is an FMT. Although FMT is the most well-established treatment for recurrent CDI, it may also be useful in the treatment of a variety of additional diseases linked to intestinal dysbiosis. Research indicates that the effects of FMT on IBD and other diseases are not as significant as those on CDI. While alterations in the microbiome are a common feature of both CDI and IBD, IBD is a more intricate disease that involves complex interactions between the host and its surroundings [74]. Even for individuals who are at high risk, this type of bacteriotherapy is usually regarded as safe and well-tolerated. On the other hand, others believe that the safety of a fecal microbiota test (FMT) is still debatable because of the unknown pathogenicity and composition of faecal bacteria [75]. The majority of short-term dangers are associated mostly to delivery techniques. These consist of brief fevers, diarrhoea, gas, bloating, elevated inflammatory markers, and vomiting (after duodenal infusions) [76].

The Food and Drug Administration (FDA) has released a safety alert that has sparked controversy. It warns of the possible hazards of spreading multi-drug resistance germs and contracting future illnesses that could be fatal. Extended-spectrum beta-lactamase (ESBL)-producing E. coli has been linked to CMV infection, norovirus gastroenteritis, E. coli bacteremia, and FMT in a number of cases [77-80]. Spreading disease-causing genes is another option, in addition to the spread of viruses. There is a chance that, in the process of transferring feces, some unidentified elements of the donor's stool will be transferred to the recipient and cause chronic illnesses (such as obesity, cardiovascular, autism, autoimmune, or gastrointestinal disorders) [77-99]. In order to guarantee patient safety and the appropriate administration of an FMT, standardized protocols for donor screening, stool preparation, delivery methods, and recipient reasons for therapy are expected to develop [65].

Conclusion

Transplanting fecal microbiota offers an additional therapeutic option in the event that traditional therapy is not successful or as a complement to it. We are just beginning to look into how an FMT might be used in veterinary medicine to modify the gut flora. Even yet, there is still plenty of information required in this field as we don't know about the precise mechanism of action. In the upcoming years, it is anticipated that an FMT will become more widely recognized and standardized. The area of gut microbiota targeted modification and personalized medicine are currently gaining popularity in human medicine; therefore, its advancement and application to veterinary medicine may be crucial to the future treatment of numerous gastrointestinal and extra gastrointestinal disorders.

References

1. Cammarota G, Ianiro G, Tilg H, Mirjana Rajilić-Stojanović, Patrizia Kump, et al. (2017) European consensus conference on faecal microbiota transplantation in clinical practice. Gut 66(4): 569-580.
2. Kao D, Roach B, Silva M, Beck P, Rioux K, et al. (2017) Effect of oral capsule-vs colonoscopy-delivered faecal microbiota transplantation on recurrent Clostridium difficile infection: A randomized clinical trial. JAMA 318(20): 1985-1993.
3. Zhang F, Cui B, He X, Nie Y, Wu K, et al. (2018) Microbiota transplantation: Concept, methodology and strategy for its modernization. Protein Cell 9(5): 462-473.
4. Petrof E, Khoruts A (2014) From Stool Transplants to Next-Generation Microbiota Therapeutics. Gastroenterology 146(4): 1573-1582.
5. DePeters EJ, George LW (2014) Rumen transfaunation. Immunol Lett 162(2 Pt A): 69-76.
6. Klein W, Müller R (2010) Das Eiweißminimum, die zymogene Symbiose und die Erzeugung von Mikrobeneiweiß im Pansen aus Stickstoff-verbindungen nicht eiweißartiger Natur. J Anim Breed Genet 48: 255-276.
7. (2012) Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. Nature 486: 207-214.
8. Swanson KS, Dowd SE, Suchodolski JS, Middelbos IS, Vester BM, et al. (2011) Phylogenetic and gene-centric metagenomics of the canine intestinal microbiome reveals similarities with humans and mice. ISME J 5(4): 639-649.
9. Mentula S, Harmoinen J, Heikkilä M, Westermarck E, Rautio M, et al. (2005) Comparison between cultured smallintestinal and faecal microbiotas in beagle dogs. Appl Environ Microbiol 71(8): 4169-4175.
10. Honneffer J, Steiner J, Lidbury JA, Suchodolski JS (2017) Variation of the microbiota and metabolome along the canine gastrointestinal tract. Metabolomics 13: 26.
11. Marsilio S, Pilla R, Sarawichitr B, Chow B, Hill SL, et al. (2019) Characterization of the faecal microbiome in cats with inflammatory bowel disease or alimentary small cell lymphoma. Sci Rep 9(1): 19208.
12. Pilla R, Suchodolski J (2020) The Role of the Canine Gut Microbiome and Metabolome in Health and Gastrointestinal Disease. Front. Vet Sci 6: 498.
13. Vazquez-Baeza Y, Hyde ER, Suchodolski JS, Knight R (2016) Dog and human inflammatory bowel disease rely on overlapping yet distinct dysbiosis networks. Nat Microbiol 1: 16177.
14. Suchodolski JS (2017) Intestinal Microbes and Digestive Disease in Dogs. Today's Vet Pract 7: 59-64.
15. Garcia Mazcorro JF, Dowd SE, Poulsen J, Steiner JM, Suchodolski JS (2012) Abundance and short-term temporal variability of faecal microbiota in healthy dogs. Microbiologyopen 1(3): 340-347.
16. Song SJ, Lauber C, Costello EK, Lozupone CA, Humphrey G, et al. (2013) Cohabiting family members share microbiota with one another and with their dogs. Elife 2: e00458.
17. Vital M, Gao J, Rizzo M, Harrison T, Tiedje JM (2015) Diet is a major factor governing the faecal 615 butyrate-producing community structure across Mammalia, Aves and Reptilia. ISME J 9(4): 832-843.
18. Bermingham EN, Young W, Kittelmann S, Kerr KR, Swanson KS, et al. (2013) Dietary format alters faecal bacterial populations in the domestic cat (*Felis catus*). Microbiologyopen 2(1): 173-181.
19. Bermingham EN, Maclean P, Thomas DG, Cave NJ, Young W (2017) Key bacterial families (Clostridiaceae, Erysipelotrichaceae and Bacteroidaceae) are related to the digestion of protein and energy in dogs. PeerJ 5: e3019.
20. Gasbarrini G, Montalto M (1999) Structure and function of tight junctions. Role in intestinal barrier. Ital J Gastroenterol Hepatol 31(6): 481-488.
21. Hooper LV, Gordon JI (2001) Commensal host-bacterial relationships in the gut. Science 292(5519): 1115-1118.
22. Dobson A, Cotter PD, Ross RP, Hill C (2012) Bacteriocin production: A probiotic trait? Appl. Environ. Microbiol 78(1): 1-6.
23. Zółkiewicz J, Marzec A, Ruszczynski M, Feleszko W (2020) Postbiotics- A Step Beyond Pre-and Probiotics. Nutrients 12(8): 2189.
24. Ziese AL, Suchodolski JS (2021) Impact of changes in gastrointestinal microbiota in canine and feline digestive diseases. Vet Clin N Am Small Anim Pract 51(1): 155-169.
25. Giaretta PR, Rech RR, Guard BC, Blake AB, Blick AK, et al. (2018) Comparison of intestinal expression of the apical sodium-dependent bile acid transporter between dogs with and without chronic inflammatory enteropathy. J Vet Intern Med 32(6): 1918-1926.
26. Chaitman J, Ziese AL, Pilla R, Minamoto Y, Blake AB, et al. (2020) Faecal microbial and metabolic profiles in dogs with acute diarrhoea receiving either faecal microbiota transplantation or oral metronidazole. Front Vet Sci 7: 192.
27. Pavlidis P, Powell N, Vincent RP, Ehrlich D, Bjarnason I, et al. (2015) Systematic review: Bile acids and intestinal inflammationluminal aggressors or regulators of mucosal defence? Aliment Pharm Ther 42(7): 802.
28. Blake AB, Guard BC, Honneffer JB, Lidbury JA, Steiner JM, et al. (2019) Altered microbiota, faecal lactate, and faecal bile acids in dogs with gastrointestinal disease. PLoS ONE 14(10): e0224454.
29. Manchester AC, Webb CB, Blake AB, Sarwar F, Lidbury JA, et al. (2019) Long-term impact of tylosin on faecal microbiota and faecal bile acids of healthy dogs. J Vet Intern Med 33(6): 2605-2617.
30. Arpaia N, Campbell C, Fan X, Dikiy S, van der Veeken, et al. (2013) Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation. Nature 504(7480): 451-455.
31. Rowland I, Gibson G, Heinken A, Scott K, Swann J, et al. (2018) Gut microbiota functions: Metabolism of nutrients and other food components. Eur J Nutr 57(1): 1-24.
32. Cherrington CA, Hinton M, Pearson GR, Chopra I (1991) Short-chain organic acids at ph 5.0 kill Escherichia coli and Salmonella spp. without causing membrane perturbation. J Appl Bacteriol 70(2): 161-165.
33. AlShawaqfeh MK, Wajid B, Minamoto Y, Markel M, Lidbury JA, et al. (2017) A dysbiosis index to assess microbial changes in faecal samples of dogs with chronic inflammatory enteropathy. FEMS Microbiol Ecol 93(11): fix136.
34. Whitfield Cargile CM, Cohen ND, Chapkin RS, Weeks BR, Davidson RA, et al. (2016) The microbiota-derived metabolite indole decreases mucosal inflammation and injury in a murine model of NSAID enteropathy. Gut Microbe 7(3): 246-261.
35. Zeng MY, Inohara N, Nunez G (2017) Mechanisms of inflammation-driven bacterial dysbiosis in the gut. Mucosal Immunol 10(1): 18-26.
36. Zapata HJ, Quagliarello VJ (2015) The microbiota and microbiome in aging: Potential implications in health and age-related diseases. J Am Geriatr Soc 63(4): 776-781.
37. Saari A, Virta LJ, Sankilampi U, Dunkel L, Saxen H (2015) Antibiotic exposure in infancy and risk of being overweight in the first 24 months of life. Pediatrics 135(4): 617-626.

38. Cox LM, Blaser MJ (2015) Antibiotics in early life and obesity. Nat Rev Endocrinol 11(3): 182-290.

39. Duboc H, Rajca S, Rainteau D, Benarous D, Maubert MA, et al. (2013) Connecting dysbiosis, bile-acid dysmetabolism and gut inflammation. Gut 62(4): 531-539.

40. Pilla R, Gaschen FP, Barr JW, Olson E, Honneffer J, et al. (2020) Effects of metronidazole on the faecal microbiome and metabolome in healthy dogs. J Vet Intern Med 34(5): 1853-1866.

41. Guard BC, Honneffer JB, Jergens AE, Jonika MM, Toresson L, et al. (2019) Longitudinal assessment of microbial dysbiosis, faecal unconjugated bile acid concentrations, and disease activity in dogs with steroid-responsive chronic inflammatory enteropathy. J Vet Intern Med 33(3): 1295-1305.

42. Suchodolski JS, Markel ME, Garcia Mazcorro JF, Unterer S, Heilmann RM, et al. (2012) The faecal microbiome in dogs with acute diarrhoea and idiopathic inflammatory bowel disease. PLoS ONE 7(12): e51907.

43. Zitvogel L, Daillere D, Roberti MP, Routy B, Kroemer G (2017) Anticancer effects of the microbiome and its products. Nat Rev Microbiol 15(8): 465-478.

44. Minamoto Y, Dhanani N, Markel ME, Steiner JM, Suchodolski JS (2014) Prevalence of Clostridium perfringens, Clostridium perfringens enterotoxin and dysbiosis in faecal samples of dogs with diarrhoea. Vet Microbiol 174(3-4): 463-473.

45. Suchodolski JS, Dowd SE, Wilke V, Steiner JM, Jergens AE (2012) 16S rRNA gene pyrosequencing reveals bacterial dysbiosis in the duodenum of dogs with idiopathic inflammatory bowel disease. PLoS ONE 7(6): e39333.

46. Jergens AE, Simpson KW (2012) Inflammatory bowel disease in veterinary medicine. Front Biosci (Elite Edn.)., 4(4): 1404-1419.

47. Patra AK (2011) Responses of feeding prebiotics on nutrient digestibility, faecal microbiota composition and short-chain fatty acid concentrations in dogs: A meta-analysis. Animal 5(11): 1743-1745.

48. Garcia Mazcorro F, Suchodolski JS, Jones KR, Clark-Price SC, Dowd SE, et al. (2012) Effect of the proton pump inhibitor omeprazole on the gastrointestinal bacterial microbiota of healthy dogs. FEMS Microbiol Ecol 80(3): 624-636.

49. Bakken J, Borody T, Brandt L, Brill J, Demarco D, et al. (2011) Treating Clostridium difficile infection with faecal microbiota transplantation. Clin. Gastroenterol. Hepatol 9(12): 1044-1049.

50. Smits L, Bouter K, De Vos W, Borody T, Nieuwdorp M (2013) Therapeutic potential of faecal microbiota transplantation. Gastroenterology 145(5): 946-953.

51. Ley RE, Lozupone CA, Hamady M, Knight R, Gordon JI (2008) Worlds within worlds: Evolution of the vertebrate gut microbiota. Nat Rev Microbiol 6(10): 776-788.

52. Hopkins DW, Chudek JA, Bignell DE, Frouz J, Webster EA, et al. (1998) Application of 13C NMR to investigate the transformations and biodegradation of organic materials by wood- and soilfeeding termites, and a coprophagous litter-dwelling dipteran larva. Biodegradation 9(6): 423-431.

53. Guy PR (1977) Coprophagy in the African elephant (Loxadonta africana Blumenbach). Afr J Ecol 15: 174.

54. Jasmin BH, Boston RC, Modesto RB, Schaer TP (2011) Perioperative ruminal pH changes in domestic sheep (Ovis aries) housed in a biomedical research setting. J Am Assoc Lab Anim Sci 50(1): 27-32.

55. McGovern K (2013) Approach to the adult horse with chronic diarrhoea. Livestock 18(5): 189-194.

56. Nurmi E, Rantala M (1973) New aspects of Salmonella infection in broiler production. Nature 241(5386): 210-211.

57. Kelly CR, Kahn S, Kashyap P, Laine L, Rubin D, et al. (2015) Update on faecal microbiota transplantation 2015: Indications, methodologies, mechanisms, and outlook. Gastroenterology 149(1): 223-227.

58. Eiseman B, Silen W, Bascom GS, Kauvar AJ (1958) Faecal enema as an adjunct in the treatment of pseudomembranous enterocolitis. Surgery 44(5): 854-859.

59. Levine DP (2006) Vancomycin: A history. Clin. Infect. Dis 42: S5-S12.

60. Khoruts A, Sadowsky MJ (2016) Understanding the mechanisms of faecal microbiota transplantation. Nat Rev Gastroenterol Hepatol 13(9): 508-516.

61. Shahinas D, Silverman M, Sittler T, Chiu C, Kim P, et al. (2012) Toward an understanding of changes in diversity associated with faecal microbiome transplantation based on 16S rRNA gene deep sequencing. mBio 3(5): e00338-12.

62. Ng KM, Ferreyra JA, Higginbottom SK, Lynch JB, Kashyap PC, et al. (2013) Microbiota-liberated host sugars facilitate post-antibiotic expansion of enteric pathogens. Nature 502(7469): 96-99.

63. Quraishi MN, Shaheen W, Oo YH, Iqbal TH (2020) Immunological mechanisms underpinning faecal microbiota transplantation for the treatment of inflammatory bowel disease. Clin Exp Immunol 199(1): 24-38.

64. Zuo T, Wong SH, Lam K, Lui R, Cheung K, et al. (2018) Bacteriophage transfer during faecal microbiota transplantation in Clostridium difficile infection is associated with treatment outcome. Gut 67(4): 634-643.

65. Bibbò S, Ianiro G, Gasbarrini A, Cammarota G (2017) Fecal microbiota transplantation: Past, present and future perspectives. Minerva Gastroenterol Dietol 63(4): 420-430.

66. Wang JW, Kuo CH, Kuo FC, Wang YK, Hsu WH, et al. (2019) Faecal Microbiota Transplantation: Review and Update. J Formos Med Assoc 118: S23-S31.

67. Heath RD, Cockerell C, Mankoo R, Ibdah JA, Tahan V (2018) Faecal Microbiota Transplantation and Its Potential Therapeutic Uses in Gastrointestinal Disorders. North Clin Istanb 5(1): 79-88.

68. Kim KO, Gluck M (2019) Faecal Microbiota Transplantation: An Update on Clinical Practice. Clin Endosc 52(2): 137-143.

69. Ramai D, Zakhia K, Ofosu A, Ofori E, Reddy M (2019) Faecal Microbiota Transplantation: Donor Relation, Fresh or Frozen, Delivery Methods, Cost-Effectiveness. Ann Gastroenterol 32(1): 30-38.

70. DeFilipp Z, Hohmann E, Jenq RR, Chen YB, Faecal (2019) Microbiota Transplantation: Restoring the Injured Microbiome after Allogeneic Hematopoietic Cell Transplantation. Biol Blood Marrow Transplant 25(1): 17-22.

71. Kelly CR, Khoruts A, Staley C, Sadowsky MJ, Abd M, et al. (2016) Effect of Faecal Microbiota Transplantation on Recurrence in Multiply Recurrent Clostridium Difficile Infection: A Randomized Trial. Ann Intern Med 165(9): 609-616.

72. Chaitman J, Gaschen F (2021) Faecal transplantation in dogs. Vet Clin N Am Small Anim Pract 51(1): 219-233.

73. Chaitman J, Jergens A, Gaschen FP, Garcia Mazcorro JF, Markrs SL, et al. (2016) Commentary on key aspects of faecal microbiota transplantation in small animal practice. Vet Med Res Rep 7: 71-74.

74. Burton NB, O' Connor E, Ericsson AE, Franklin CL (2016) Evaluation of Faecal Microbiota Transfer as Treatment for Postweaning Diarrhoea in Research- Colony Puppies. J Am Assoc Lab Anim Sci 55(5): 582-587.

75. Pereira GQ, Gomes LA, Santos IS, Alfieri AF, Weese JS, et al. (2018) Faecal microbiota transplantation in puppies with canine parvovirus infection. J Vet Intern Med 32(2): 707-711.

76. Niina A, Kibe R, Suzuki R, Yuchi Y, Teshima T, et al. (2019) Improvement in clinical symptoms and faecal microbiome after faecal microbiota transplantation in a dog with inflammatory bowel disease. Vet Med (Auckl) 10: 197-201.

77. Lopez J, Grinspan A (2016) Faecal Microbiota Transplantation for Inflammatory Bowel Diseases. Gastroenterol Hepatol 12(6): 374-379.

78. Olesen SW, Leier MM, Alm EJ, Kahn SA (2018) Searching for superstool: Maximizing the therapeutic potential of FMT. Nat Rev Gastroenterol Hepatol 15(7): 387-388

79. Merrick B, Allen L, Masirah MZN, Forbes B, Shawcross D, et al. (2020) Regulation, risk and safety of Faecal Microbiota Transplant. Infect Prev Pract 2(3): 100069.

80. Fong W, Li Q, Yu J (2020) Gut microbiota modulation: A novel strategy for prevention and treatment of colorectal cancer. Oncogene 39(26): 4925-4943.

81. Jalanka Tuovinen J, Salonen A, Nikkila J, Immonen O, Kekkonen R, et al. (2011) Intestinal microbiota in healthy adults: Temporal analysis reveals individual and common core and relation to intestinal symptoms. PLoS ONE 6(7): e23035.

82. Edwards SM, Cunningham SA, Dunlop AL, Corwin EJ (2017) The Maternal Gut Microbiome during Pregnancy. MCN Am J Matern Child Nurs 42(6): 310-317.

83. Levy M, Kolodziejczyk AA, Thaiss CA, Elinav E (2017) Dysbiosis and the immune system. Nat Rev Immunol 17(4): 219-232.

84. Xu M (2015) Faecal microbiota transplantation broadening its application beyond intestinal disorders. World J Gastroenterol 21(1): 102-111.

85. Murphy EF, Cotter PD, Healy S, Marques TM, O'Sullivan, et al. (2010) Composition and energy harvesting capacity of the gut microbiota: Relationship to diet, obesity and time in mouse models. Gut 59(12): 1635-1642.

86. Parks BW, Nam E, Org E, Kostem E, Norheim F, et al. (2013) Genetic control of obesity and gut microbiota composition in response to high-fat, high-sucrose diet in mice. Cell Metab 17(1): 141-152.

87. Greenblum S, Turnbaugh PJ, Borenstein E (2012) Metagenomic systems biology of the human gut microbiome reveals topological shifts associated with obesity and inflammatory bowel disease. Proc Nat Acad Sci USA 109(2): 594-599.

88. Turnbaugh PJ, Hamady M, Yatsunenko T, Cantarel BL, Duncan A, et al. (2009) A core gut microbiome in obese and lean twins. Nature 457(7228): 480-484.

89. Schwiertz A, Taras D, Schäfer K, Beijer S, Bos NA, et al. (2010) Microbiota and SCFA in lean and overweight healthy subjects. Obesity 18(1): 190-195.

90. Teixeira TF, Collado MC, Ferreira CL, Bressan J, Peluzio MC (2012) Potential mechanisms for the emerging link between obesity and increased intestinal permeability. Nutr Res 32(9): 637-647.

91. Kootte RS, Vrieze A, Holleman F, Dallinga Thie GM, Zoetendal EG, et al. (2012) The therapeutic potential of manipulating gut microbiota in obesity and type 2 diabetes mellitus. Diabetes Obes Metab 14(2): 112-120.

92. Udayappan SD, Hartstra AV, Dallinga Thie GM, Nieuwdorp M (2014) Intestinal microbiota and faecal transplantation as treatment modality for insulin resistance and type 2 diabetes mellitus. Clin Exp Immunol 177(1): 24-29.

93. Kieler IN, Kamal SS, Vitger AD, Nielsen DS, Lauridsen C, et al. (2017) Gut microbiota composition may relate to weight loss rate in obese pet dogs. Vet Med Sci 3(4): 252-262.

94. Montoya Alonso JA, Bautista Castano I, Pena C, Suarez L, Juste MC (2017) Tvarijonaviciute, A. Prevalence of Canine Obesity, Obesity-Related Metabolic Dysfunction, and Relationship with Owner Obesity in an Obesogenic Region of Spain. Front Vet Sci 4: 59.

95. Wu J, Zhang Y, Yang H, Rao Y, Miao J, et al. (2016) Intestinal Microbiota as an Alternative Therapeutic Target for Epilepsy. Can J Infect Dis Med Microbiol, pp. 9032809.

96. Taur Y, Coyte K, Schluter J, Robilotti E, Figueroa C, et al. (2018) Reconstitution of the Gut Microbiota of Antibiotic-Treated Patients by Autologous Faecal Microbiota Transplant. Sci Transl Med 10(460): eaap9489.

97. Schwartz M, Gluck M, Koon S (2013) Norovirus gastroenteritis after faecal microbiota transplantation for treatment of Clostridium difficile infection despite asymptomatic donors and lack of sick contacts. Am J Gastroenterol 108(8): 1367.

98. Quera R, Espinoza R, Estay C, Rivera D (2014) Bacteremia as an adverse event of faecal microbiota transplantation in a patient with Crohn's disease and recurrent Clostridium difficile infection. J Crohns Colitis 8(3): 252-253.

99. Hohmann EL, Ananthakrishnan AN, Deshpande V (2014) Case Record of the Massachusetts General Hospital. Case 25-2014. A 37-year-old man with ulcerative colitis and bloody diarrhoea. N Engl J Med 371(7): 668-675.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2024.57.009069

Umra Rasool. Biomed J Sci & Tech Res