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Impact of Probiotics on microbiota in the gut of antibiotic treated Vertebrates

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Abstract

The gut microbiota (moreover alluded to as gut flora) is the populace of microscopic organisms that colonizes the human intestine. As the significance of the gut microbiota is getting to be progressively apparent, considers have been carried out with the point of picking up a more comprehensive understanding of the possibly destructive impacts of antibiotics on this fundamental biological system. Clearly antibiotics have bactericidal and bacteriostatic properties against pathogenic organisms. But agreeing to later examinations antibiotics moreover do have a tremendous effect on our gut microbiota particularly on the health advancing good microbes. They halt microscopic organisms within the intestine from making proteins, partitioning, makingcell walls and transporting nutrients and also can make gaps within their cell wall or membranes.A few pathogenic microscopic organisms too create antibiotic resistance which may be a genuineissue these days. Hence human intend to intake probiotics after an antibiotic course to maintain their gut microbiota. In this paper I have reviewed about the microflora in vertebrates and the various probiotics that have positive action on them after antibiotic effect.

Keywords: Gut microbiota, antibiotic, probiotic

Introduction

During birth, the gastrointestinal tract is a aseptic area and microbial establishment starts amid the maternal fecal or vaginal flora and/or environmental transmission method [1]. The 'gut microbiota' is called the bacteria, archaea and eukarya group colonizing the gastrointestinal area and has developed over thousands of years with the host to create a perplexing and symbiotic relationship [2]. The intestinal microbiota has numerous essential capacities in the body, including promoting pathogen resistance, influencing the immune structure, playing a role in the assimilation and digestion mechanism, regulating the expansion and separation of epithelial cells, altering resistance to insulin and disturbing its secretion and affecting the host's behavior and its neural capacities. [3]. The host uses specific mechanisms to shape its own intestinal microbiota and preserve its balance [4]. Taxonomically, bacteria are categorized by phyla,

groups, orders, families, genera, and species and mainly few phyla are represented, representing more than 160 species. [5]. Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria, and Verrucomicrobia are the dominant gut microbial phyla, with the 2 phyla Firmicutes and Bacteroidetes comprising 90% of the gut microbiota [6]. The phylum Firmicutes consists of 200 separate genera such as *Lactobacillus, Bacillus, Clostridium, Enterococcus,* and *Ruminicoccus*[6]. 95% of the Firmicutes phyla are of Clostridium genera and the prevalent genera, such as *Bacteroides and Prevotella*, are Bacteroidetes [5]. Proportionally less common and primarily represented by the genus *Bifidobacterium* [6] is the Actinobacteria phylum.[6] Gut microbiota switch concurring to the digestive tract anatomic regions, which alter in terms of pH, physiology and O_2 level stress, digestive stream speeds (quick inside the mouth to the caecum, slower a short time later), substrate accessibility, and host secretions [7].

1. Types of Microflora in different species of vertebrates

1.1. Microflora in Fishes

Acinetobacter johnsonii[8], aeromonads (notably *Aeromonas hydrophila, A. bestiarum, A. caviae, A. jandaei,A. schubertii, and A. veronii biovar sobria*[9]), *Alcaligenes piechaudii, Enterobacter aerogenes, Escherichia coli, Flavobacterium*[10], *Flexibacter* spp., *Micrococcus luteus, Moraxella* spp., *Pseudomonas fluorescens, Psychrobacter* [11], and *Vibrio fluvialis* have been reported to be bacteria from the surface of fresh water fish. Yellow-pigmented Gram- negative rods dominate the gills, in particular *Cytophaga* spp. [12]. The digestive tract of adult freshwater fish has been associated with a comparatively wide variety of taxa, including Acinetobacter, Enterobacter, Escherichia, Klebsiella, Proteus, Serratia, Aeromonas[12] -isolates

were classified by microplate hybridization as *A. caviae, A. Hydrophila, A. jandaei,A. sobria, and A. veronii -Alcaligenes, Eikenella, Bacteroides , Citrobacter freundii, Hafnia alvei, Cytophaga/Flexibacter, Bacillus, Listeria, Propionibacterium, Staphylococcus, Moraxella,* and *Pseudomonas*[13][14][15]. Stable turbot's liver and kidney were found to be inhabited by mainly Pseudomonas and Vibrio, including V. fischeri, V. harveyi, V. pelagius, and V. splendidus [16].

1.2. Microflora in Amphibians

Amphibians live in wet or marine habitats and are thus exposed to a large number of microorganisms by contact with water, soil, plants, invertebrates, and vertebrates, and it is possible that the skin of amphibians has a subset of microbiota from these territories because of the high levels of variations within the bacterial populations in these diverse environments. [17]. Five major taxonomic classes of bacteria that includes Alpha-, Beta-, and Gamma-Proteobacteria(68.3 percent), Bacteroidetes/Chlorobi (20 percent), and Actinobacteria (11.7 percent), are present in the skin of amphibians primarily frogs [18]. The 12 classes of bacteria present in the gut of frogs are *Pseudomonas, Vibrio-Aeromonas group, Enterobacteriaceae, Moraxella, Acinetobacter, Flavobacterium, Bacillus, coryneforms, Micrococcus, Staphylococcus, Streptococcus* and pin-hole colony formers [19].

1.3. Microflora in Reptiles

In turtles *Mycobacterium* spp., *Leptospira* spp. and aquatic bacteria are found [20]. Presence of Bifidobacteria was found in geckos and also Vietnamese box turtles[21].*Staphylococcus, Gordonia, Bacillus, Streptomyces, Serratia, Pantoe, Chryseobacterium* are also some of the bacterial communities present in reptiles[22]. Most species of the wild crocodile lizard gut microbiota were categorized as Proteobacteria (56.4%), Bacteroidetes (19.1%) and Firmicutes at the phylum level (2.6 percent) [23]. The alligator gut microbiota, dominated by Fusobacteria, is an exception. [24]. Commonly isolated from reptiles, gram-negative bacteria include *Aeromonas hydrophila, Klebsiella oxytoca, and K. Pneumoniae, Morganella morganii, Pseudomonas aeruginosa, Salmonella arizonaee* and *Providencia rettgeri* [25].

1.4. Microflora in Birds

Unicellular microorganisms housed in the digestive tract, i.e. bacteria, fungi and protozoa [26], are included in the digestive flora of birds. Large proportions of these bacteria are Gram positive and primarily include optional anaerobes from the crop to the terminal ileum, while caeca also include strict, dominant anaerobes. [27]. The crop flora consists mainly of lactobacilli attached to the epithelium and forming a nearly continuous layer, as well as enterococci,

coliforms and yeast. [26]. Also microorganisms isolated from postmortem samples obtained from parrots, falcons, quails, peacocks, ostriches, pigeons, turkeys, guineafowls and ducks included *Escherichia coli* , *Staphylococcus aureus* , *Proteus* spp., *Pseudomonas aeruginosa* , *Pasteurella multocida* , *Mycoplasma gallisepticum, Corynebacterium pyogenes, Klebsiella* spp., *Bacillus* spp., *Salmonella gallinarum* , *Streptococcus* spp., *Aeromonas* spp., *Micrococcus* spp., *Pasteurellahaemolytica Aspergillus fumigatus* and *Candida albicans* [28].

1.5. Microflora in Mammals

It is estimated that the human body comprises 10^{14} cells, 10 percent of which belong to the proper body and the remaining 90 percent constitute the population of organisms living in or on the host and are collectively referred to as microbiota [29]. The predominant species types in humans differ according to the niche of the body, such as in the oral cavity, skin, respiratory tract,vagina, stomach, ileum, colon or urinary tract [30]. In mammals, the growth of commensal bacteria protecting the host from pathogenic bacteria is primarily assisted by human skin and the resident gram-positive bacteria include Staphylococcus, Micrococcus and Corynebacterium sp. Staphylococcus aureus and Streptococcus pyogenes in the skin are notoriously pathogenic [31]. In the skin ecosystem, gram-positive species of bacteria predominate. Gram-positive cocci such as *S. auricularis, S. capitis, S. cohnii, Staphylococcus aureus S. saprophyticus, S. simulans, S. warneri,*

*S. xylosus, Micrococcus luteus, M.lylae, , S. epidermidis, S. haemolyticus, S. hominis ,S. saccharolyticus, M. nishinomiyaensis, M. kristinae, M. roseus, M. varians M. sedentarius,;*Gram- positive bacilli such as, *C. minutissimum, Propionibacterium acnes, Corynebacterium jeikeium,*

C. urealyticum, P. avidum, P. granulosum, Brevibacterium epidermidis; Gram-negative bacilli such as

Acinetobacter johnsonii; Yeasts such as *Malassezia furfur*; Moulds such as *Trichophyton mentagrophytes var;* Mite such as *Demodex folliculorum* are the commonly detected human skin microbes[32]. *Actinomyces israelii, A. viscosus, A. naeslundii, Eubacterium alactolyticum, E. saburreum,Lactobacillus casei, Bifidobacterium dentiu interdigitale* are gram-positive bacilli and filamentous bacteria commonly detected in the human oral cavity.; *Prevotella melaninogenica, Fusobacterium nucleatum, P. intermedia, P. loescheii,P. denticola,Porphyromonas gingivalis, P. assacharolytica, P. endodontalis* are the gram-negative bacteria commonly detected in the oral cavity of humans [32].Commonly detected microbial groups in vaginal washings obtained from humans are Anaerobic Gram-positive cocci, *Bacteroides, , Mycoplasma, Propionibacterium, Staphylococcus, Eubacterium, Gardnerella, Lactobacillus Streptococcus, Ureaplasma,Candida, Corynebacterium,* [32]. In the upper respiratory tract of humans, the commonly seen bacteria are,,*S. mutans, S. cricetus, S. rattus ,S. sobrinus ,S. crista, Staphylococcus epidermidis, S. aureus. salivary, S. uteri's, S. pneumoniae, S. gordonii* [33]. Bacteria in stomach include Gram positive aerobes,*lactobacilli,streptococci* and *H.pylori*; in colon includes *Bacteroides, Eubacteria, Bifidobacteria, Fusobacteria, Petostreptococci* and in small intestine include aerobic gram positive and gram negative anaerobes[30].

2.Factors that affect the intestinal microbiota

The composition of the microbiota is subject to host and environmental shaping, so the GI tract restricts the exposure of the host safe system to the microbiota through the authentication of a multifactorial and energetic intestinal barrier that includes a few integrated components such as physical (epithelial and body fluid layers), biochemical (chemicals and antimicrobial proteins)and immunological (IgA and epithelia-associated safe cells) components [34].

3.1 .Age

At first, the digestive tracts of newborn children born vaginally are colonized by life forms from the maternal vagina, which is best demonstrated by the life forms of the genera *Lactobacillus* and *Prevotella* [35]. On the contrary, the maternal skin flora typically colonizes the digestive system of the infant in cesarean delivery, as exemplified by the dominance of *Streptococcus, Corynebacterium,* and *Propionibacterium* [35]. Despite the fact that the initially evolving microbiota is to a large extent affected after primary inoculation by the type of feed (breast drain or equation nourishes), the transient shift is affected by dietary designs, way of life, life occasions, and natural variables counting anti-microbial use [36]. Unusual colonization of microbiota in the intestine may lead to pediatric infections due to poor resistance. [37].

3.2.Diet

Also in adulthood, diet is the most significant determinant in the formation of the structure, variety and abundance of the intestinal microbiota [38]. Individuals that consume diets abundant in fruits, vegetables and fibers have a greater abundance of the Firmicutes phylum's insoluble carbohydrate metabolizing species such as *Ruminicoccus bromii, Roseburia* and *Eubacterium rectale* [39]. There were

variations associated with dietary habits, as it was seen that rural African children had a higher abundance of *Prevotella*, whereas children from Europe had higher proportions of *Bacteroides* [40].The higher abundance of Prevotella is taxonomically and functionally similar, suggesting an agrarian diet eaten by African children.[38]. On the contrary, the children of Europe consumed a Western diet high in animal protein, sugar and starch and low in fibers, which is characterized by a greater abundance of *Bacteroides*.[38] Meat-based diet

consumption shows relative abundance of Actinobacteria phylum [41].

3.3. Antibiotics

Despite the fact that antibiotic studies have generally focused on their bactericidal and bacteriostatic pathogens exercises, recent years have seen a few holistic studies on their impact on the bacterial environment of the intestine. [38]. The use of antibiotics can therefore be a two- edged weapon: it aimlessly devastates both pathological and useful organisms, allowing intestinal microbiota or so-called dysbiosis to misfortune and the development of undesirable microbes. [42]. Clindamycin [43], clarithromycin and metronidazole, and ciproflaxin [44] have all been shown to influence the structure of microbiota over different lengths of time and have found that both short- and long-term microbial adjustments are drastically disturbed, including a decrease in the abundance and diversity of the community. It has been shown that the impact of indeed short- term use (7 d) of broad-spectrum antibiotics with predominant anaerobic coverage (e.g. Clindamycin) could last up to 2 years, with a determined non-recovery of differences in *Bacteroides* [43].

3.4. Genes

The number of particular microbes found within the intestinal microbiota is affected by the genetic makeup of the host in ways that influence the digestive system and may ultimately affect health [45].Family individuals have more similar microbiota communities than unrelated individuals, and the intestinal microbiota is more similar in monozygotic than in dizygotic twins. [45].

3.5. Probiotics

Probiotics can be characterized as a living microorganism with a beneficial effect on the host by adjusting the balance of its intestinal microbiota [46]. When consumed in satisfactory amounts, they can provide the well-being of the host. [46]. Probiotics produce antimicrobial agents or metabolic compounds that suppress the development of other microorganisms or compete with other intestinal mucosa receptors and binding sites [47]. Moreover, probiotics can modulate intestinal immunity and alter the responsiveness of intestinal epithelia and immune cells to microbes in the intestinal lumen [48]. The effects of probiotics on the composition, diversity and function of intestinal microbiota have been studied using a variety of tools and techniques, ranging from targeted, culture-dependent methods to metagenomic sequencing [49]. However, not many studies have shown associations of modified microbiota following treatment with probiotics. [49].

3. Effect of probiotics on the Gut Microbiota

The word probiotic was first used by Lilly and Stillwell in 1965, as opposed to the word antibiotic, to qualify as "a microbial substance capable of stimulating the development of another micro-organism"[46]. Probiotics are live micro-organisms that, when taken in appropriate doses, ensure human health [50]. Nobel laureate Elie Metchnikoff presented the concept of probiotics to the logical community and published a seminal report linking the life span of Bulgarians to the use of fermented milk products containing viable *Lactobacillus* [51]. Probiotics have been widely shown and consumed, generally as dietary supplements or useful food products, since they have been found to be beneficial to human well-being.[51] The most commonly used probiotic species are *Lactobacillus*, *Bifidobacteria* and yeasts, such as *Saccharomyces boulardii*. [52]. Probiotic mechanisms include manipulation of intestinal microbial communities, suppression of pathogens, immunomodulation, stimulation of epidermal and dermal cell multiplication, and separation and fortification of the intestinal barrier [48]. The mode of activity of the probiotics may be related, first, to the modulation of the host microbiota, and one of the primary modes of activity proposed is the "barrier" impact, also known as resistance to colonization, applied against pathogenic microscopic organisms that prevent or restrict their colonization. [46]. The enhancement of the barrier function of the intestinal mucosa is the second mode of operation, and this barrier functionis linked to the quality of tight junctions between intestinal epithelial cells [46]. The third mode of action is the immune system balance, as more than 70% of resistant cells are found at the level of the intestine, especially in the small intestine, which makes up the lymphoid tissue associated with the intestine (GALT) [46]. Subsequently, their behavior can be direct, related to colonizationrelated to their stomach, or indirect, as these strains can modulate the microbiota by extending the microbe inoculum with beneficial results [46].

4.Types of probiotic and their effect

For probiotic strains, one of the desirable properties often mentioned is that they should be resistant to antibiotics [53]. The reason for this strategy is that probiotic products can be used to reconstitute the intestinal microflora of patients with antibiotic-associated colitis or to feed farm animals with antibiotic 'growth-promoting' levels in their food [54]. Since antibiotic residues could be found in patients' or farm animals' intestines, only antibiotic resistant probiotic strains would be able to colonize the ecosystem [54]. A probiotic culture must be consumed in adequate amounts to benefit the health of the host, and the proposed concentration for probiotic bacteria is within the product range of 10^6-10^7 cfu/g. [55].

4.1.*Saccharomyces boulardii* - a probiotic

Saccharomyces boulardii is a live, non-pathogenic yeast commonly used as a probiotic and often sold as a dietary supplement. It was first isolated in Indochina from lychee fruit and was used in France in the 1950s to treat diarrhea. Such yeasts are common in nature and can be found on trees, fruit, plants and soil, and are also used in the baking and brewing industry. [58]. *S.boulardii* also has many properties that make it a potential probiotic agent, i.e. it survives transit through the food channel, its optimum temperature is 37 deg C, it inhibits the growth of a number of microbial pathogens both in vitro and in vivo. [59]. In the past 30

years, this probiotic yeast *S. boulardii* has been prescribed for prophylaxis and treatment of diarrheal diseases caused by bacteria or antibiotics [60].

Some of the factors that classify as a successful probiotic for *S.boulardii* are:-

[1] Survives passage to its target organ (mostly the colon): while most of the oral dose is lost (usually stool levels are 100-1000 times lower than the oral dose), surviving oral doses (usuallyat levels above 10^8 organisms/gram of stool) are found to be effective [61].

[2] Survives at body temperature (37 ° C): the special benefit of being one of the few yeastvarieties that perform best at human body temperature [62].

[3] *S. boulardii* in its lyophilized forms can live in gastric acid and bile [62].

[4] *S. boulardii* is immune to antibiotic compared to other yeasts [62].

[5] *S. boulardii* is proteolysis immune [63].

[6] *S. boulardii* develops within the competitive environment of the intestinal tract [63].

[7] In patients with disturbed intestinal microbiota (due to antibiotic use), levels of *S. boulardii* arehigher than in patients without antibiotic exposure. [64].

[8] It reaches steady-state amounts within three days when administered orally and is clearedwithin 3-5 days after it is discontinued. [61].

[9] *S. boulardii* concentration by 22% was increased by certain kinds of fiber (psyllium), whileother fiber types (pectin) showed no effect. [61].

Amoxicillin-clavulanic acid is commonly used in human therapeutic care and is well known for the disturbance and destruction of intestinal microbiota and has been shown to be successful in treating and preventing these disorders through the use of probiotics such as S. boulardii, non-pathogenic yeast associated with *S. cerevisiae* [65].

4.2. Lactic acid bacteria- a probiotic

Lactic acid bacteria (LAB) such as *Lactobacillus* sp, *Bifidobacterium* sp and *Enterococcus* sp [66] belong to the majority of probiotic microorganisms. *Lactobacillus acidophilus, Lactobacillus casei Shirota* strain, *Lactobacillus delbrueckii subspecies bulgaricus, Lactobacillus johnsonii, Lactobacillus plantarum, Lactobacillus reuteri, Lactobacillus rhamnosus,* is some of the *Lactobacillus* species used as probiotic. [54]. In general, LABs with probiotic activity are enteric flora, which are thought to play a beneficial role in the human gastrointestinal tract ecosystem [67]. Possible adjuvants are also LAB, and their oral administration induces both mucosal and systemic immune responses [68].

The following are the different nutritional and therapeutic results attributed to LAB.:

- Improvement of the food and feed nutritional consistency
- Metabolic stimuli of vitamin synthesis and development of enzymes
- Intestinal microflora stabilization and competitive removal of enteric pathogens
- Boost innate host defenses through producing antimicrobial substances

- Reduction by assimilation processes of serum cholesterol
- Decreased risk of colon cancer by carcinogen detoxification
- Tumor suppression through regulation of immunity mediated by cells [67].

Because of the historical assumption that these bacteria are desirable members of the intestinal microflora, they are common choices, emerging from the very fact that lactic acid bacteria have long been used in the production of dairy foods and are thus 'generally considered healthy,' and since the resulting large-scale cultivation and preservation methods for lactic acid bacteria in a viable state already have been developed by the dairy industry [54]. The main source of probiotics is known to be LAB from dairy products and of intestinal origin [69]. *Enterococcus faecium* is mainly used as an animal probiotic but also for human use in the genus *Enterococcus* , while *Enterococcus faecalis* is primarily used as a human probiotic [66]. *B. longum* and *B. animalis* are the most important species in the genus *Bifidobacterium* in terms of its use as a probiotic [66].

4.3. *Bacillus* spp. as probiotics

Spore-forming *Bacillus* spp. has been referred to for its beneficial qualities for human and animal health as probiotics [70]. *Bacillus* spp. essential characteristics include its ability to survive and germinate in the gut, to form biofilms and to secrete antimicrobials. [71]. Along with probiotic strains, the genus *Bacillus* contains pathogenic species, such as *B. Cereus* community, which raises

the issue of taxonomic bacterial identification [72]. In order to promote growth, feed use, and digestive health, a large number of *Bacillus*-based preparations have been found and subsequently recorded as probiotics for animal feed [73]. Three *Bacillus* spp., i.e. *B. subtilis, B. licheniformis* and *B. cereus*, are mainly based on commercial preparations, while the probiotic ability of other *Bacillus* spp. remains poorly investigated. [74].

4.4. Propionibacteria as a probiotic

Dairy *Propionibacterium* (PAB) has been successfully used as an animal growth promoter [75]. *Propionibacterium* strains originally classified as *Propionibacterium* and its 4 species originate from cheese or other dairy products and some have been isolated from soil, silage, olive fermentation and rat intestines. [76]. The less studied characteristic is the bacteriocin production of the species of the genus *Propionibacterium*, since only 3 bacteriocins have been identified from propionibacteria [77]. Probiotic food products primarily combine propionibacteria with lactic acid and/or bifidobacteria. [78]. A number of studies have clearly demonstrated the probiotic activity of propionibacteria and the effect is derived from the synthesis of propionic acid, along with some minor acids, bacteriocin, vitamin B12, as well as the availability of nutrients, increased feed exploitation and the ability to serve as growth stimulants for other beneficial intestinal bacteria[78].

4.5. *Escherichia* spp. as a probiotic

Escherichia coli species incorporates both non-pathogenic (commensal) and pathogenic strains. [79]. [80]. Possibly an ordinary example of a nonpathogenic, commensal E. coli isolate, E.coli strain Nissle 1917

(O6:K5:H1) forms the concept of the probiotic preparation Mutaflor, which is used to treat altered intestinal disorders and is considered to be a fruitful coloniser of the human gut. The lack of proven virulence factors (i.e., alpha-hemolysin, P-fimbrial adhesins, and hence the phenotype of semirough lipopolysaccharide) combined with the expression of fitness factors such as microcins, various iron absorption systems, adhesins, and proteases that can promote the survival and successful colonisation of the human gut contributes to the probiotic life of *E. coli* strain Nissle 1917[80].

5. Conclusions

Maintaining microbiota homeostasis in the intestine is highly vital for well-being. A few components can directly or indirectly affect the intestinal microbiota composition and the abundance of organisms. One such factor is the administration of antibiotics, which can have a major impact on the intestinal microbial population by reducing its diversity and number. In a few

cases, dysbiosis can lead to a significant increase in opportunistic pathogens. Subsequent advancements in science have found various mechanisms by which probiotics exert health- promoting effects on humans and numerous other species. In order to restore the safe structure and work of the intestinal microbiota, probiotics have been suggested as preventive and therapeutic step. By enhancing its intestinal microbial equilibrium, they ultimately control the host. Present types of probiotics or medicinal compounds derived from microbiomes may be used as possible methods to promote well-being, avoid diseases and treat various disorders.

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