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Review Article

**USE OF PROBIOTICS AND ITS EFFECTS ON OVERALL HEALTH; A
REVIEW OF RECENT LITERATURE****Mashaal Belal Alrubaian¹, Hana Khateam Alonazy², Sarah Nasser Alshehri², Aisha Hussain Hothan³, Ahmad Abdulla a Alnahwi⁴, Ahmed Hussain Alalawi⁵, Mohammad Saud S Aljohani⁶, Shahad Ahmed Albalawi⁷, Ali Hussain a Alabdullah⁸, Inad Mutlaq Alotaibi⁹, Abdulrahman Faleh Almutairi¹⁰**

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Abstract:

Introduction: Probiotics are living microorganisms that can be administrated in specific amounts to a certain host to achieve health benefits. There are several criteria that should be met by a substance to be considered as a probiotic. Several studies have been conducted lately regarding the use of probiotics and their effects on different body systems and in different health issues.

Aim of work: We aim to provide a review of recent evidence on the use of probiotics and their beneficial effects on health.

Methodology: We conducted a systematic comprehensive search in literature review using Medline, Pubmed, and Embase. We used the term 'probiotics, supplement, multivitamin, health benefits of probiotics' as search item.

Conclusions: Most proven applications of probiotics target the gastrointestinal tract, many probiotics have been successful in targeting health conditions in other organs including the mouth, the teeth, the skin, and the urinary tract. For probiotics to achieve these mentioned benefits, they need special delivery methods to make sure the strains survive their way to the target organ. Probiotics are also essential in treating disturbed balance of the microbes in a specific region, which is called dysbiosis. Some organisms and bacterial strains produce vitamins making them beneficial to the host by helping compensate for vitamins need. Vitamin K, pyridoxine, biotin, vitamin B12, nicotinic acid, folate, and thiamine can all be produced by organisms present in the bowels. Health issues of the gastrointestinal tract that can benefit from probiotics include acute diarrhea, traveler's diarrhea, constipation, H. pylori infection, along with other diseases.

Keywords: Probiotics, health supplements

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INTRODUCTION:

According to the World Health Organization and the joint Food and Agriculture Organization, the definition is probiotics is 'living microorganisms that can be administrated in specific amounts to a certain host to achieve health benefits' (1). Examples of these probiotics include the powder milk that has living lactic acid organisms. For a kind of food to be considered a probiotic, there are several criteria that must be met (1). These criteria include:

- Proper assessment of the genetic identity of strains and type of species.
- Performing in-vitro experiments to detect possible benefits and characteristics of this probiotic (resistance to bile acids or digestive enzymes, activity against pathogenic organisms...).
- Complete safety profile and sufficient assessment of this probiotic to establish it is safety.
- Performing in-vivo experiments to detect health outcomes of the probiotic on the body of the host.

More recently, and in their joint meeting, the European Food and Feed Cultures Association, and the International Life Science Institute (ILSI) have defined probiotics as 'living food ingredients that can be consumed in specific amounts to achieve proven health benefits in the host' (2). From these definitions, we can understand that the main use of probiotics is to get possible health-related benefits following ingestion. Studies on probiotics and their use to improve health are not old and have been increasing and improving lately. Probiotics are generally administrated as supplements, components of a medication, or simply present in food. Regardless of the way of administration, it must have the ability to survive the whole digestive tract (including gastric secretions and bile salts) and to proliferate in the bowels. This is because the benefits of probiotics occur mainly through proliferation and exerting activity in the body. Some recent data have proposed the application of local probiotics, making viability and persistent efficacy a main target for a probiotic to be successful. Moreover, it is essential to conduct trials not only isolated probiotics strains, but also on commercialized probiotics. However, this is not always applicable, as companies refuse to publicly declare information on strains present in their products (3).

Specific mechanisms in which probiotics improve health status are not clear in most cases. Recent studies have suggested that probiotics could possibly

have effects on the immune system. However, it is still not clear if, supposing this hypothesis is true, do probiotics need to be living in order to be able to stimulate the immune system? Whatever the answer of this question is, the current definitions of probiotics must be improved accordingly.

When regarding safety of probiotics, the European Food Safety Authorities still is still conservative regarding the use of probiotics, and they think that many of them have not yet been assessed sufficiently. According to the European Food Safety Authorities, in order for a probiotic to be used, several questions should be first addressed and answered (4). These include:

- Have the characteristics of this probiotics been sufficiently described?
- Have the potential benefits of this probiotics been sufficiently described and studies? And have its physiological benefits been studies?
- Have clinical trials been conducted on human subjects to provide solid evidence on these potential benefits?

Moreover, the World Health Organization and the joint Food and Agriculture Organization, in their guidelines regarding probiotics, they recommended that any commercial probiotic product should display all of the following information on its label (1):

- The strain, species, and genus of this probiotic, which should be clearly mentioned to avoid misleading.
- The minimum number of living strains within the probiotic when it reaches the end of its shelf-life.
- Suggested effective doses of the probiotic that will achieve health benefits.
- Potential health benefits.
- Proper conditions for storage of the probiotic.
- detailed contact information available for consumers.
- When available, mentioning specifically health benefits rather than using general and vague words. For example, it would be preferred to state on the label of the probiotic that it decreases the incidence of rotavirus infection in children, rather than stating just that it improves the digestive tract function.

METHODOLOGY:

We did a systematic search for blunt abdominal trauma and imaging using PubMed search engine

(<http://www.ncbi.nlm.nih.gov/>). EMBSE, and Google Scholar search engine (<https://scholar.google.com>) from January 1997 to March 2018. All relevant studies were retrieved and discussed. We only included full articles. The following search terms were used: probiotics, supplement, multivitamin, health benefits of probiotics

The study was approved by the ethical board of King Abdulaziz University.

Functional characterization of probiotics:

As we previously mentioned, the main goal of probiotics use is to enhance health condition in different body organs. Although, most proven applications of probiotics target the gastrointestinal tract, many probiotics have been successful in targeting health conditions in other organs including the mouth, the teeth, the skin, and the urinary tract (5). Applications of probiotics on the skin include the control of skin inflammation by orally consuming a specific type of probiotics that will affect this inflammation (6). Another use of probiotics has been their use to prevent the occurrence of infections in both the respiratory tract and the gastrointestinal using *Lactobacillus (L.) rhamnosus GG* probiotic (7). When it comes the applications in the gastrointestinal tract, there are a plethora of applications where different strains of probiotics are beneficial. These applications include the reduction of colonization of certain pathogens, decreasing bloating, improving immune response, enhancing synthesis of certain proteins, and improving transit of intestines.

For probiotics to achieve these mentioned benefits, they need special delivery methods to make sure the strains survive their way to the target organ. These delivery methods can be in the shape of matrix that will carry the probiotic. For example, a chocolate matrix has been recently produced and led to improved survival of the strain (8). Milk, yoghurt, kefir, cheese, cookies, cereals, sausages and other nutritional products have been used as matrices for the delivery of probiotics (9). Moreover, many probiotics have been used in infants' formulas to decrease the incidence and severity of diarrhea in infants (10).

Delivery of the probiotic does not necessarily have to always be through food. There has been some attempts to produce special ointments or sprays that will deliver probiotics to target organs (11).

The delivery of the probiotic to the target organ is not enough. In most cases, health effects of the probiotic

will only occur when the strain is delivered to the organ in an active state and in large numbers that are enough to establish effect. For example, when delivering a probiotic orally, the strain will have to be able to survive enzymes, and acidity throughout the gastrointestinal tract so it reaches the target while still viable. Previously mentioned food matrices have been found to significantly improve viability of probiotics strain throughout the gastrointestinal tract by altering PH and protecting these strains against enzymes. It is also possible to find another strain that has similar effects but higher resistance against these conditions (12).

After the probiotic strain has already been delivered and in sufficient concentrations and viable state, the next step is to establish its proliferation. It is clear that this strain will be considered foreign by other strains and organisms that are already there, making this step relatively hard. In order to achieve proper proliferation of the strain in the target organ, specific types of nutrients are supplied for the probiotic to help it survive and compete with other organisms. The probiotic then requires effectively adhering to the mucus surface of the target organ and surviving in it. This adhesion depends mainly on the properties of the probiotic cell wall (13).

Health benefits of probiotics:

The use of probiotics has been increasing for several health issues and possible benefits. Generally, a probiotic can be effective in an ill or health subject, and this effect could be curative or preventive. In general terms, we can assume that the target will be to fight the underlying etiology of the disease and to decrease signs and symptoms associated with it.

We can conclude that the use of probiotics in a healthy individual will mainly aim at preventing the disease and decreasing its incidence. However, this use should still be done with caution, and with strong emphasis that probiotics are still considered strains that are foreign from the body, making it necessary to accurately evaluate them and carefully administrate them for healthy individuals. This becomes of special importance when these individuals belong to certain sensitive subgroups, like infants, who require more care and attention before considering the use of probiotics. Most studies on different subgroups have concluded that probiotics have beneficial effects in all studies subgroups, including preterm infants and infants. For example, the use of milk that includes strains of *L. casei* has been proven to enhance the immune response of healthy infants and to decrease the rate of gastrointestinal infections (14).

Probiotics are also essential in treating disturbed balance of the microbes in a specific region, which is called dysbiosis. For example, dental caries is associated with the development of dysbiosis and a decrease in the concentrations of *L. rhamnosus*. On the other hand, administration of *L. rhamnosus* strains will lead to significant lowering of the incidence of dental caries in children (15). Studies have suggested that probiotics are also beneficial when performing orthodontic therapy (16). Bacterial vaginosis is another example of dysbiosis consequences that could be treated using probiotics. Drinking milk that contains *L. casei* strains has been proven to prevent and treat helicobacter colonization (17).

Nutritional functionality of probiotics:

Some organisms and bacterial strains are capable of producing vitamins making them beneficial to the host by helping compensate for vitamins need. Vitamin K, pyridoxine, biotin, vitamin B12, nicotinic acid, folate, and thiamine can all be produced by organisms present in the bowels (18). This production of vitamins is certainly beneficial for the body and could be considered as a probiotic activity. Another example of nutritional functions of probiotics are the use of lactase-positive probiotics strains that will treat symptoms of lactose intolerance and lactase deficiency (19).

Specific health benefits of probiotics:

Acute infectious diarrhea:

Several studies have been conducted to assess the effects of probiotics in the prevention and treatment of acute diarrhea. Some probiotics strains have been found (in large trials) to have statistically significant clinical benefits in the prevention of community-acquired acute diarrhea. These strains include *L. reuteri* and *L. rhamnosus* GG. However, despite being statistically significant, it is still debatable whether this effect is actually clinically significant or not (20).

On the other hand, *L. rhamnosus* GG strains have been tested for the prevention and treatment of diarrhea that is acquired in day-care centers. Trails on these strains have also found that the effects of probiotics in these cases are minimal and not always apparent, but they also find them to slightly decrease the occurrence of upper respiratory tract infections (21).

When studying hospitalized infants with diarrhea, the use of probiotics (that have actually been proven

efficient in outpatient treatment of diarrhea) have been found to have no significant effects on prevention and treatment of hospital-acquired diarrhea (22).

In general, evidence is currently present in the literature to support the use of the following bacterial strains for the management of acute gastroenteritis in children: *L. rhamnosus* GG, *S. boulardii*, for *L. reuteri* DSM 17938, and and heat-inactivated *L. acidophilus* LB (23). *Enterococcus faecium* SF6873 probiotics have also been studied and found to significantly decrease the incidence of diarrheal attacks that last for more than four days (23).

In conclusion, the use of probiotics in acute diarrheal attacks and gastroenteritis, especially in children, is still controversial and debatable. The studying of its cost effectiveness is essential before recommending their use, especially when taking into consideration that most attacks already resolve on their own (24).

Antibiotic-associated diarrhea (AAD):

A recent meta-analysis that included more than eleven thousand patients concluded that probiotic administration led to a significant reduction in the risk and severity of antibiotics-associated diarrhea (25). Probiotics that include *S. boulardii* strains were reported to be effective against diarrhea caused by *C. difficile* (26).

Traveler's diarrhea:

Traveler's diarrhea is a common disease that has significant social and economic burden. Several randomized trials have been conducted to assess the efficacy of probiotics in the prevention and treatment of traveler's diarrhea. Both *L. acidophilus* and *L. rhamnosus* GG strains have been found to cause no benefits in the prevention and treatment of travelers' diarrhea (27). On the other hand, probiotics containing *S. boulardii* strains were found to have small clinical effects in the prevention of traveler's diarrhea (28).

Due to the limited number of trails on the use of probiotics in traveler's diarrhea, and the opposing results in their efficacy, it is still not recommended to use routinely use probiotics neither for prevention nor for treatment of traveler's diarrhea.

Irritable Bowel Syndrome (IBS):

Several trials have assessed the use of probiotics for the treatment of irritable bowel syndrome in adults. However, no enough data is present on children. In 2009, a systematic review was published in Cochrane

and stated that most probiotics have had limited or no effects on reducing symptoms of irritable bowel syndrome (29).

Helicobacter pylori:

Many studies have assessed the use of probiotics for the treatment of patients who have *H. pylori* colonizations and/or gastritis. Strains that have been used against *H. pylori* include *Lactobacillus* and *Bifidobacterium* strains, and work by releasing bacteriocins that kill the *H. pylori* organisms. These mechanisms have been observed in several animal studies. Moreover, clinical trials have proven that probiotics are efficient in the reduction of *H. pylori* load and improving immunity against it (30). Despite their efficacy in decreasing colonization of *H. pylori* and improving immune response against it, probiotics have not been found effective in total eradication of the organism (31). It is thought to be beneficial to use probiotics as an adjuvant therapy during triple therapy against *H. pylori* (32).

Constipation:

It is frequent for children to suffer from constipation. In such cases, probiotics have been found to possibly have some benefits regarding stool frequency and consistency. However, these benefits have not been established due to the contradictory results by different trials. *B. breve* strains were found to improve constipation and increase frequency of stool in an open trial (33). *B. breve* strains were also found to improve consistency and decrease the severity abdominal pain (33). On the other hand, *B. lactis* strains have been found to be ineffective in the management of constipation in children and infants (34). In a Brazilian study, the administration of yogurt that included *B. longum* strains was found to cause improved stool frequency in cases of severe constipation (35).

Colic:

Almost all infants frequently suffer from colic making parents desperate and afraid of serious medical cases. Several studies have assessed the use of *L. reuteri* probiotics to decrease these colic attacks in breastfed infants (36). However, results are not consistent regarding the benefits for colic reduction. In fact, a study has concluded that probiotics administration led to longer crying spells in infants (37).

CONCLUSION:

Probiotics are defined as living organisms that are generally prescribed and ingested by a host to achieve certain health benefits. The use of probiotics

has been increasing recently due to their low costs and proven efficacy in improvement of several health problems. Most probiotics target the gastrointestinal tract. However, they can also have benefits in the mouth, teeth, urinary tract, skin, and other organs. For example, probiotics have been used to treat bacterial vaginosis and skin inflammations. To work efficiently, probiotics need to be well delivered to the target organ and reach it with sufficed counts and viable state. Then the probiotic will have to survive the environment and compete with other microorganisms in order to be able to proliferate and achieve its benefits. Benefits of probiotics can be preventive or curative. They can also be used to restore the balance of microorganisms in a specific organ after being disrupted. Probiotics can also have a significant nutritional role by synthesizing vitamins and other necessary nutrition. Acute diarrhea, traveler's diarrhea, constipation, *H. pylori*, and many other causes can be treated and/or prevented using probiotics.

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