THE IMMUNE POTENTIALS OF PROBIOTICS

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Abstract
Probiotics are vaccine allied biologics, vaccine adjuvants, oral vaccines, vaccine prim-boost and, vaccine delivery systems. They are formed from commensal bacteria and commensal yeasts. Such candidate preparation are developed and evaluated in a way similar to that of vaccine development and evaluations with less stringent control measures. They can be of therapeutic and preventive uses both for infectious and lympho-proliferative diseases.

Introduction
The concept of using bacteria for treatment and prevention as well as health insurance is not modern but it is rooted back to 1930s of the 20th century. However in the current days there is a renewal of the interest of probiotic use. Probiotic technology covers the theme of selection of strains, preparation of starters, studying the strain physiology and strain immune potentials as well as cell immobilization techniques. Probiotics displayed their preventive and/or therapeutic influences through their immunogenicity, immune-modulating as well as tumor reducing activities [1]. The objective of the present mini-review was to introduce probiotics as an immune-prophylactants and immunotherapeutics.

CONCEPT
Originally probiotics as a term is referred to a secretory product of a microbe that promotes the growth of the other microbe living within the same ecologic niche. Such term means in the straight English language“ For the life”[2]. Parker in 1975[3] have demonstrated that probiotics denoted to substances of microbe that posses positive role in restoration of the equilibrium of the intestinal microflora. Fuller in 1989[4], have been assured that probiotics means microbes which have certain biological and immunological determinants by which they can pass through mouth till intestines (ceccum).

FEATURES
The immune-biologic features of the probiotic microbes are being depicted in Table 1. They adhere to the intestinal and uro-genital cells and reduce pathogens through steri-hinderence, production of bio-surfactants, production of biocines and competition for nutrients. After instillation in the intestines and vagina they persist for three days in the intestines and seven weeks in the vagina. Some probiotic strains resist the micro-bicides and spermicide activities in intestines and vagina respectively. They formed coaggregates, biofilms and overgrow other pathogens, though they are nonpathogens. Probiotic bacteria are mainly from Lactobacilli and bifidobacter, while probiotic yeasts are from the genera Saccharomyces and Candida.[1,4].

MODE OF ACTION[5,6,7]
Probiotics performed their immune-biologic functions via several immune mechanisms like;

i-Adherence and colonization of mucosal surfaces.

ii-Competition for nutrients.

iii-Antagonism

iv-Production of Organic acids
v-Co-aggregation and overgrowth

vi-Immune mechanisms like antibody responses induction of cytokine network, immune-adjuvant action, tumor reducing ability.

TECHNOLOGY[8,9,10]

Cell immobilization techniques have pre-requests, such pre-requests are being stated in the following:

i-Candidate Probiotics: After the starter of the probiotic microbes are being propagated and thoroughly evaluated using a series of evaluation parameters then they are ready for loading to a specified carrier.

definition

ii-The chemical nature of the carrier materials are heterogeneous including, polysaccharides, starch, dextran and agarose derivatives. Alternatively, proteins can be of use as loading carriers such as gelatin, albumin and resins.

iii-Cell immobilization: Cell immobilization processes are, loading, linking, entrapping of microbial probiotic cells and encapsulation.

definition

iv-Entrapping: Probiotic cells are trapped inside synthetic tissues made from gel such as polyacrylamide, K-carrageenan and calcium alginate. Though, calcium alginate, carrageenan and starch are preferred.

Table 1: Characteristic features of the probiotics[1,4].

<table>
<thead>
<tr>
<th>Nature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiologic</td>
<td>- Acid tolerance</td>
</tr>
<tr>
<td></td>
<td>- Digestive juice tolerance</td>
</tr>
<tr>
<td></td>
<td>- Antibody tolerance</td>
</tr>
<tr>
<td></td>
<td>- Bile acid resistance</td>
</tr>
<tr>
<td></td>
<td>- Production of volatile acid to restore the equilibrium of microflora</td>
</tr>
<tr>
<td></td>
<td>- Resist killing by blood</td>
</tr>
<tr>
<td></td>
<td>- Compete for nutrients</td>
</tr>
<tr>
<td></td>
<td>- Host compatibility</td>
</tr>
<tr>
<td></td>
<td>- Persist and overgrow other microbes</td>
</tr>
<tr>
<td>Immunologic</td>
<td>- Adhere to mucous membrane</td>
</tr>
<tr>
<td></td>
<td>- Form biofilm</td>
</tr>
<tr>
<td></td>
<td>- Reduce pathogens</td>
</tr>
<tr>
<td></td>
<td>- Reduce cancer growth</td>
</tr>
<tr>
<td></td>
<td>- Induce immune response events</td>
</tr>
<tr>
<td></td>
<td>- Acts as an immune modulant</td>
</tr>
</tbody>
</table>

v-Encapsulation System: The use of starch as an encapsulation system for probiotics will be as in the following steps:

i-Large granules are treated with enzyme to obtain porous structure.

ii-If starch found as amylase it should be solubilized and cooled.

iii-The treated starch is of use as carrier in which probiotic suspension derived from broth culture media is precipitated on the surface of the starch granules to fill up the porous structures allowing chemical and physical bonding to starch surface.

iv-The final product is lyophilized to be obtained in dried form.

CAPSULE MIGRATION[8,9,10]

The capsule production in this way is known as simple precipitation and it is most sound in use and of high efficiency for production of coats for this stable and resistant capsules. The probiotic starch encapsulation is resistant to action of acids, juices and enzymes on passage through; mouth, esophagus, stomach and small intestines, when the capsule reach colon it hydrolyzed and probiotic materials are released after grow and increase in numbers due starch formation by the colonic bacteria and by the probiotic growing cells.
EVALUATION CRITERIA

Both of the small and large scale production of probiotics should fulfills several evaluation criteria[8,9,10] which includes the followings

i-Reliability, strain nature.

ii-Viability.

iii-Adhesion Ability.

iv-Antagonistic Activity.

v-Safety, proof to be non-toxic

vi-Stability, genetic back ground.

vii-Immunogenicity, antibody and cytokine response.

viii-Immuno-modulating activity.

ix-Immune Protectivity.

x-Tumor Regression Ability.

PROBIOTIC HOST IMMUNE RESPONSES[11,12]

When the probiotic cell clones reached, thereby in the colon they are taken up by M cells onto the surface lining of the Peyer's patches or across the normal epithelium overlying the lamina propria. In Peyer's patches the M cells transport the intact probiotic cells to the phagocytes to be phagocytized by the antigen presenting cells (APC) the macrophage and dendritic cells. The APC process and express the antigenic peptide along with MHCII molecules onto its surface. The peptide MHC combinations on the surface of APC, in turn presented to T cells through helper effect will activate B lymphocyte to grow, proliferate, expand and then differentiated to plasma cells. While if the probiotic antigen crosses the normal epithelium, it will has the potential to activate the lamina propria T cells and induce T cell immune responses.

When the mucosal immune responses are stimulated, primed T and B lymphocytes migrate through lymphatic vessels, then entered the peripheral blood circulation via the thoracic lymph duct. Extravasation do happened to the immune cells and then enrolled in traffic, migrate and homed into the common mucosal immune system compartments; lamina propria, respiratory tissue, uro-genital tissue, mammary and salivary glands. Such migration is referred to as an IgA cycle. Though on the contrary to the migration and homing stories. If the probiotic cells are bounded to epithelial cells, then they will have only local effects on the gut. They are unable to induce IgA cycle or to increase CD4+ T cells. Their effects only exerted through the induction of cytokine release by the stimulated cells without the need for antigen processing. Probiotics, during the passage through the gut, they will raise up S IgA, cytokine responses as well as they will induce their own specific mucosal antibody responses of the gut.

PROBIOTICS VERSUS VACCINE

Probiotics are vaccine and vaccine allied Biologics. There are some similarities and difference in between them[13].

<table>
<thead>
<tr>
<th>Features</th>
<th>Probiotics</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starter</td>
<td>Certain commensal bacteria</td>
<td>Pathogens or their subunits</td>
</tr>
<tr>
<td>Specificity</td>
<td>Nonspecific in most cases</td>
<td>Specific in most cases</td>
</tr>
<tr>
<td>Evaluation attitude</td>
<td>Less stringent for human favor</td>
<td>Stringent for human favor</td>
</tr>
<tr>
<td>Dispensing</td>
<td>Drug-like dispensing menu</td>
<td>Needs special dispensing menu</td>
</tr>
<tr>
<td>Specificity</td>
<td>Nonspecific, mostly</td>
<td>Specific mostly</td>
</tr>
<tr>
<td>Indication</td>
<td>Biotherapy of various immune defects in man and animals</td>
<td>Immunoprphylaction</td>
</tr>
<tr>
<td>Use</td>
<td>On individual basis more than massive</td>
<td>Massive use rather than individual cases</td>
</tr>
<tr>
<td>Disease nature</td>
<td>Infectious and non-infectious</td>
<td>Infectious, epidemic and pandemic threat or on travel to epidemic or endemic areas</td>
</tr>
<tr>
<td>Mode of action</td>
<td>Bacteriocin, immunomodulatory, antinecancerous</td>
<td>Based on affinity of B and T memory cells</td>
</tr>
<tr>
<td>Side Effect</td>
<td>No apparent side effect</td>
<td>Mild short duration like fever and ill</td>
</tr>
<tr>
<td>Failure</td>
<td>Due to probiotic or host born causes</td>
<td>Due to vaccine or host born causes</td>
</tr>
</tbody>
</table>

Table 2 gives rather logical comparison between probiotic and vaccines;
BIOTHERAPY[14,15,16,17,18,19]

Probiotics have been tempted in rather many therapeutic protocols of human and animal diseases to modulate immunity in autoimmune diseases like rheumatoid arthritis, inflammatory bowel disease and, allergic diseases like atopic dermatitis. They, also possess the potential of tumor growth reduction and prevention of diarrhea and urinary tract infection. Diarrhea occur in around 20% of patients whom received antibiotic treatment. Antibiotic associated diarrhea results from microbial imbalance that lead to decrease in the endogenous micro-flora that is usually responsible for colonization resistance and decrease in colonic capacity for fermentation. It has been found that probiotic treatment restore patient normal state in a range of 5 to 17%. Several controlled randomized trails have shown the beneficial effects of probiotics in therapeutic and preventive measures of gastroenteritis patients. In a group of 116 patients with IBD were given probiotic preparations. It was found that it is effective as that of Mesasalalin (R) in inducing remission and preventing relapse of IBD patients.

IMMUNE POTENTIALS[20,21,22]

Probiotics are responsible for about 70% of human immune responses and anti-cancerous ability[18]. They have anti-inflammatory influences[19]. Probiotics posses vaccine adjuvant effects and vaccine prime-boost potentials as well as vaccine and vaccine delivery system, Tables 3 and 4.

<table>
<thead>
<tr>
<th>Immune potentials</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal mucosal adjuvant,</td>
<td>22</td>
</tr>
<tr>
<td>Probiotic Lactobacillus adjuvant</td>
<td>23</td>
</tr>
<tr>
<td>T cell immunomodulatory</td>
<td>24</td>
</tr>
</tbody>
</table>

**Table 3:** Probiotic vaccine adjuvants.

<table>
<thead>
<tr>
<th>Immune Potentials</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probiotic oral vaccine</td>
<td>25</td>
</tr>
<tr>
<td>Probiotic oral live vaccine and vaccine delivery system</td>
<td>26</td>
</tr>
<tr>
<td>Probiotic based malaria vaccine</td>
<td>27</td>
</tr>
<tr>
<td>Drinkable HIV vaccine</td>
<td>28</td>
</tr>
<tr>
<td>Specific probiotic boost antibody response to oral and systemic vaccine</td>
<td>29</td>
</tr>
</tbody>
</table>

**Table 4:** Probiotic vaccine

CONCLUDING REMARKS

Finally to put-forward a concluding remarks to this mini-review one may state the basic immune features of probiotics as in the following:

i-Anti-inflammatory.

ii-Anti-autoimmune disease.

iii-Anti-cancerous.

iv-Immunonogen.

v-Immuono- adjuvant.

vi-Vaccine.

vii-The boost part of the prime boost protocol.

viii-Vaccine delivery System.

REFERENCES


16. Allen S, analysis of 63 studies show that probiotics are safe J Martinez EG, Gregio GV, Dems LF, 2010, A meta analysis of 63 studies show that probiotics are safe and have clear benefit in treatment of infectious diarrhea, when used with rehydration therapy, Cochrane Data Base System Rev, Epub No. 10.


