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HUMAN PROBIOTIC GLYCOCONJUGATES RECOGNIZING SYSTEMS AGAINST DISEASES OF MICROBIOCENOSES IN HUMAN ORGANISM

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ABSTRACT

The representations of diseases of biotope microbiocenoses are given and developed using the example of mucosal biotopes of open cavities of the human body. Various aspects including ways and factors influencing the prevention and treatment of such diseases are considered. Potential of influence of human probiotic glycoconjugates recognizing systems (HPGRS) with respect of infective process, prevention of diseases of human organism biotope microbiocenoses and reduction of their severity is systemized. HPGRS represent new class of natural bioeffectors functioning in biocontrol of biotope status. They counteract conditionally pathogenic microorganisms and acting pathogens at the level of niche organization of biotope microbiocenoses. They are characterized by (Genus, species or strain(s))-directed antimicrobial action. HPGRS, probiotic and leader microorganisms of protection significance decrease infective risk in biotope microbial societies. These indicated factors can increase final effectiveness of antiinfection preparations and procedures usually used in treatments. Combinative application of HPGRS and other important agents in organism biotopes is perspective for prophylaxis and therapy of microbiocenose of states before (Importance for early effective antimicrobial action), during (When direct and indirect possible therapeutic effects take place) and after (In prolongation of convalescence achieved) the human diseases. Among applications the combination of the synergy of HPGRS and antibiotics is look like as the most perspective in prophylaxis and therapy of the human biotope microbiocenosis diseases.

KEYWORDS: Probiotics; Lectins; Glycoconjugates; Microbiocenoses; Mucosal biotopes; diseases; Human.

ABBREVIATIONS

ac	acidic
al	alkaline
DHBM	diseases of human biotope microbiocenoses
GC	glycoconjugates
GRS	glycoconjugates recognizing systems
HPGRS	human probiotic glycoconjugates recognizing systems
LB	lectins of bifidobacteria
LL	lectins of lactobacilli
MCB	microbicenosis communicative bodies
QS	Quorum Sensing
YLF	yeast like fungi

1. INTRODUCTION

Glycoconjugates recognizing systems (GRS) refer to multifunctional (Carbohydrate and glycoconjugates [GC])-recognizing proteins and protein assembly complexes.[1-7] GRS of symbiotic microorganisms (Including probiotic ones) are an important communicative constituent of functioning microbiocenoses. Probiotic and symbiotic GRS reflect the properties of probiotics. GRS represent dynamic directional (With summary dynamic vector) systems, and belong to metabolombiotics - carriers of metabiotics; are (Bacteriocins and antibiotics)-similar metabolites of a new type (With new combinative mechanisms); mimic the action of probiotics, manifest themselves as functional organizers (Fixators, stabilizers, protectors of complexes, carriers, deliverers, assemblers of molecular and cellular ensembles, participants of labeling of complexes; controllers in *Quorum Sensing* [QS]), regulators and navigators of remote/ distant events (Including distributors of microbial pools in microbiocenoses, different biotopes and organs) with initiating response networks; GRS participate in the infrastructure organization, balancing and protection of biotopes and tracts of the human body; they co-function with other defense systems of human organism.[8-28] The action of probiotic GRS is aimed at preventing the initiation and development of an infectious process with established features of microbiocenoses.[29-44]

The concept of a healthy biotope of the human body presupposes the functioning of a normal (Healthy) biotope microbiocenosis. Violations within the framework of biotope microbiocenosis, including in the direction of biotope pathologies, should be considered as diseases of human biotope microbiocenoses (DHBM). At the same time, it is obvious that the influence of the symbiotic (Including probiotic) component of the biotope should and will influence the conditionally pathogenic component of the biotope microbiocenosis in the direction of restoring the normal initial balance of the patient's microorganisms. Thus, it is important to consider DHBMS in the aspects of their prevention and therapy, including those involving probiotic effectors. Among the probiotic effectors, glycoconjugates recognizing systems (HPGRS) remain poorly understood.

The aim of the work is to evaluate and summarize the ways and mechanisms of HPGRS influence on DHBM (HPGRS—DHBM as human organism interacting super-system).

2. RESULTS

2.1. Ways and mechanisms of HPGRS influence on the infectious process for prevention and therapy of DHBM.

2.1.1. HPGRS and *Quorum Sensing* (QS)

HPGRS together with probiotic bacteria affect the QS of microbiocenoses.[10,11]

2.1.2. HPGRS as growth inhibitors of opportunistic pathogens

- The growth of suspension and film massifs of *Candida* of group I representatives (*C. albicans* and *C. tropicalis*) is inhibited in the presence of free and sorbed HPGRS (acidic and alkaline lectins of lactobacilli and bifidobacteria: acLL, alLL, acLB, alLB), mainly as acLB > acLL, and in the case of group II (*C. krusei*) - as acLL > acLB.[18, 20, 29]
- HPGRS suppress the growth and biofilm formation of antimycotic-resistant YLFS.[18,38]

2.1.3. HPGRS as lysins

With prolonged exposure to HPGRS, YLF massifs undergo strain-dependent lysis.[18]

2.1.4. HPGRS – Broad-profile synergists in human organism (Classification of results)

- Diversity of representatives of HPGRS against DHBM:
- In molecular mass:
- Low molecular weight;
- High molecular weight (> 27 kD)

- Functional diversity:
- Against microfungi;
- Against *Gram* positive bacteria;
- Against fungi and bacteria;
- HPGRS – Synergists among themselves. For example, a multi-synergism of HPGRS combined action is implemented against the massifs of *C. albicans* and *C. tropicalis* of group I *Candida* (According to epidemiological significance): acLL and caLB, acLL and acLB.[21]
- HPGRS – Synergists with GRS of plants. For example, a multi-synergism of HPGRS combined action is implemented against the massifs of group I *Candida*: caLB and phytolectins.[21,31]
- HPGRS reveal potential of synergistic action against fungal and bacterial infections such as candidiasis-bacteriosis (against *C. albicans* [acLB > acLL] and against *S. aureus* [acLL > acLB]).[13,18,20]

2.1.5. The growth of suspension cultures of YLF (*Candida*) for 1-3 days in the presence of HPGRS is accompanied by biorhythmic fluctuations above and below control levels, which differ in *Candida* of group I (*C. tropicalis*) when compared with *Candida* of group II (*C. krusei*).[22] At the same time, LB exhibit modulating, unbalancing properties of the YLF culture that are superior to those of LL.

2.1.6. Mosaically localized HPGRS to varying degrees in time and space, and using various mechanisms (Due to specificity to glycopolymers; manifestation of early and late, synergistic, territorial action; within the subnishes of an initially unipolar conditionally pathogenic array) inhibit the growth and cause delayed lysis of antimycotic-resistant pathogens (On example of *C. albicans*) as a result of remote HPGRS synergism.[18,31]

2.1.7. HPGRS-sensitive YLF strains with leader properties in fungal pools and counteracting probiotic niches in microbiocenoses have been identified.[39,40] Thus, HPGRS (Bioeffector carriers) have the potential for direct (Coupled with subsequent initiation of bioeffector reactions) effects on fungal leader pathogens.

2.1.8. HPGRS can act as surface cell reagents of probiotic microorganisms. Thus, the species-dependent distribution of biofilm-forming *Candida* in microbiocenoses is disrupted in the presence of pools of probiotic-like lactobacilli with leader properties [37, 40], as a result of which the rupture of intercellular fungal communications leads to a weakening of pathogen protection and their greater availability to antimicrobial agents (for example, antibiotics such as Nystatin).[18,31]

2.1.9. The effectiveness of the HPGRS reactivity depends on the behavior of the cell pools (Consortia and Leaders) of the suspension-biofilm microbial conditionally pathogenic compartment of the biocenosis. Microbiosis “communicative bodies” (MCBs) reflect the patterns of functioning of ecological niches of biotope microorganisms.[31-35] Considering pathogen niches as landscape MCB with infrastructure that counteract the probiotic component (probiotic consortia, including enhanced sets of HPGRS delivered) of microbiocenosis, it allows predicting the suppression of the development of the infectious process in epithelial-mucosal tract biotopes by HPGRS.[31,34] It has been established that opportunistic pathogens (*Candida*) in protected "internal" survival-friendly areas of the MCB are subject to predominant attacks by "mucins"-recognizing HPGRS, and in borderline unprotected areas of the MCB with maximum stress - to predominant attacks by "mannans"-recognizing HPGRS.[18,31]

2.1.10. In response to the presence of HPGRS, YLF massifs (For example in case of some *C. albicans* strains with potentially increased pathogenicity) are forced to switch from aerobically dependent niches to anaerobic mycelium-like structures composed of hydrophilic porous polysaccharide-containing matrices that mimic polysaccharide-protected biofilms.[18] However, even under anaerobic conditions, HPGRS exhibit antimicrobial (antifungal) effects (no involvement of oxidoreductase systems is required).[29,30]

2.1.11. In the case of a mixed infection, the resistance of combined fungal niches (fungal super niche) to HPGRS may increase as a result of seasonal (in March) mycosymbiosis (for example, *Candida* with *Aspergillus*). Thus, in case of a mixed infection, germination of *A. niger* is initiated in the area of residual HPGRS-resistant *C. albicans* massifs. The complete lack of growth in the areas of *Candida* suppression by GPRS indicates the potential of using HPGRS (in special regimes) and anti-*C. albicans*-drugs against *A. niger* (interruption of mycosymbiotic biorhythmic chains of fungal activity).[19]

2.1.12. HPGRS have the potential to prevent the development of biotopes towards precancerous conditions by maintaining the normal functioning of mucosal organs.[14,15,17] At the same time, it is possible to support the probiotic microflora with prebiotics from complexes with HPGRS.[20]

2.1.13. HPGRS have the potential of action of carbohydrate metabolism enzymes.[45,46] including oxidoreductases (EC 1.11.-.-.) and glycosyl hydrolases (EC 3.2.1.-.).

2.1.14. The oxidoreductase antimicrobial potential of *Acylact*, including its ability to discolor pigments (Potential indicators of pre-disease as in case of the appearance of melanoma-like pre-oncological skin neoplasms), is realized with the participation of HPGRS with pI 5-6.[16] Such HPGRS are co-localized with oxidoreductase systems and have the potential to co–function with them under conditions of oxidative stress, while neutral and cationic HPGRS are associated with polysaccharides and other exopolymeric antioxidants, which can be used in the preparation of metabolic cell ointments, creams, and suppositories based on multipro/synbiotic ingredients.[20,28]

2.1.15. The maximal effectiveness of the HPGRS pathways on the infectious process in the biotope microbiocenosis can be achieved by coordinating the actions of HPGRS, protective microbes (Symbiotic, including probiotic) and antibiotics (developing personalized regimes).[20, 21, 37]

2.1.16. HPGRS systems implement an anti-infective effect in the body within the framework of existing macro-action axes through a communication network of epithelial-mucosal barriers.[41] The complexity of the pathways of the antipathogenic action of HPGRS increases when considering the combined coordinated *Cross-Talking* effect of all additional metabolic and cellular protectors of the body.[5, 6, 17]

2.1.17. Strategies for choosing probiotics (Commercial and as a result of the process of developing targeted probiotics) for regional prevention and personalized therapy are possible.[26]

2.1.18. HPGRS and Microbial niches

- HPGRS redistribute the niches of microorganisms (for example, YLF) through disruption of communication between yeast and mycelium-like forms); they serve as characteristic signs of the functional personalized and population cohesion of fungal niches in microbiocenoses.[27,28] At the same time, the independence and resistance of *Candida* species niches in urban populations are a consequence of increased resistance of opportunistic fungi and their communities (Including biofilm fungi and fungal-bacterial) to antimicrobial agents (Antibiotics, HPGRS, and others) and factors (Physical and physico-chemical).

- HPGRS prevent the expansion of the former and the formation of new fungal niches of pathogens (*C. albicans*).[18,38]

2.1.19. HPGRS and antibiotics

- HPGRS and antibiotics rebuild microbiocenoses towards a healthy status with the elimination of pathogens and pathogenic factors and the restoration of probiotic microflora. An increase in the occurrence of antimycotic-resistant YLF, which increase the risk of candidiasis, other fungal and fungal-bacterial infections in urban populations of individuals, is accompanied by a regular change in the ranking sequences of specific antibiotic sensitivity, the appearance of characteristic resistance blocks in the sequences, for example (Fluconazole, Ketoconazole).[42-44]
- HPGRS are synergists with antibiotics: alLL/alLB and Nystatin; acLB and Amphotericin, Itraconazole and/or Ketoconazole.[21]
- Under prolonged conditions of HPGRS contact with the YLF massif, the phenomenon of regeneration of the antimycotic's ability is observed (The space around the antimycotic is freed from the presence of the previous massif of the antimycotic-resistant variant of the fungus).[18]
- HPGRS themselves exhibit the properties of antibiotics.[47]

3. CONCLUSION

Concept of DHBM will help in simplification of development of the new effective combinative constructions for prophylaxis and therapy of himan diseases.

The biological activities of HPGRS, a new class of systemic effectors with a wide potential for positive effects on the infectious process, are characterized, investigated and systematized. HPGRS function as a biocontrol system for the infectious process. They are opposed to opportunistic microorganisms at the level of niche organization of biotope fungal, bacterial and fungal-bacterial microbiocenoses, characterized by genus/species/strain-directed antimicrobial action. The results suggest that HPGRS and protective sets of leader microorganisms (Symbiotic, probiotic-like, and probiotic), disrupting the initially balanced communication bodies of populations of potential pathogens (Which is important for therapeutic attacks on a destabilized opportunistic pathogenic massifs) in niches and subnishes. HPGRS purposefully and for a long time reduce the protection of microbial communities of infectious risk in biotopes and thus create comfortable conditions for increasing the effectiveness of antimicrobial drugs, factors and regimes of their use.

The combined use of HPGRS and antibiotics, along with the use of our proposed methodologies for studying suspension-biofilm prolonged (Delayed) states of biotope microbiocenoses and their effects, is promising for the development of optimized co-functioning (Synergistic) antimicrobial mixtures, procedures and regulations for the prevention of pre-diseases and the treatment of diseases of microbiocenoses, both within the population of individuals in the region and on a personalized the level. The patterns of HPGRS influence on the infectious process can be used as new factors and criteria for assessing the temporary status of dynamic biotope microbiocenosis niches and subnishes, identifying indicators (For status) of conditionally pathogenic pools and associates of microorganisms, and applying patterns in other diagnostic procedures of a broader profile.

Disclosure of conflict of interest

The authors declare no conflict of interest.

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