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Evaluation of sugar content in probiotics products prescribed for children - a review

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Abstract: The interest in nutritional supplement and functional food has risen significantly in recent years. Many of the products that are marketed to the consumers have the benefits of the probiotic for general good health and for a wide variety of conditions and situations. Although most of the products have been used safely for years, careful analysis and see scientific research should be conducted before routinely recommendation these products, especially for children.A basic understanding of intestinal flora, properties of probiotic and clinical research findings is necessary for clinicians to delineate probiotic agents in paediatric population. Therefore, the aim of this paper will be to summarize available evidence of probiotic use in well-defined clinical indications of importance for pediatricians. Sweetened oral medications are widely used for children to facilitate compliance. A variety of natural and artificial sweeteners are used in these drug formulations to augment the sweetness and thereby palatability of the product. There is growing concern among dentists about the increased consumption of sugars in these medications by children, especially those who are chronically ill as it may contribute to diabetes mellitus, dental erosion, and dental caries. This literature review provides information about the sweetener content and cariogenic potential of commonly prescribed pediatric oral medications that are used for managing acute and chronic conditions in children and measures for oral health prevention.

Keywords: Children; caries; dentistry; probiotics; sweetener.

INTRODUCTION

Most widely used definition of probiotics was given by the Food and Agriculture Organization of the United Nations and the World Health Organization in 2002[(Food and Agriculture Organization of the United Nations and World Health Organization, 2001*)]. That definition was accepted with minimal change by an expert panel (International Scientific Association for Probiotics and Prebiotics) in 2014 stating that probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host [(Hill *et al.*, 2014)]. The same document panel tried to emphasize the probiotic action, emphasizing that some of probiotics effects can be attributed only to specific probiotic strain, but some effects can be ascribed to probiotics in general or certain species of probiotics [(Hill *et al.*, 2014)]. Same recognition of clinical effectiveness was also approved and highlighted by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Working Group (ESPGHAN WG) on pre- and probiotics. Stating that recommendations for probiotic use should always be strain specific and aim is to recommend only the strains which have proven efficacy by well-designed randomized controlled trials (RCTs). There are many papers about probiotics produced on a daily basis which makes clinical up-date on their effectiveness extremely difficult. Therefore, the aim of this paper will be to summarize available evidence of probiotic use in well-defined clinical indication including the treatment of acute gastroenteritis, prevention of antibiotic associated diarrhea and prevention of infections in children.

Probiotics are defined as a living organism with potential health benefits for the host if consumed in an adequate amount[(Reid *et al.*, 2003)]. Probiotic benefits have been investigated for improving immune function lowering blood pressure[(Khalesi *et al.*, 2014)] and improving lipids(Guo *et al.*, 2011)]. Data from animal models suggest that probiotics can reduce blood glucose level and insulin resistance[(Tabuchi *et al.*, 2003)]. Interestingly, research shows that gut microbiota are involved in diabetes and metabolic disorders, revealing that diabetic children have altered gut microbiota compared to non-diabetic counterparts[(Cavalcanti *et al.*, 2012)]. Children or the future of our society and ensuring their good health is to the utmost importance. Mouth is a mirror of our

body, and oral health is essential for the growth of children, development and general health. A variety of probiotic agents have been studied as single agents or as combination therapies. Examples of such strains include lactobacilli, bifidobacteria, saccharomyces, Escherichia coli and streptococci. Considerable differences exist in the bioavailability, biological activities, doses and composition among probiotic preparations. Moreover, most studies have not been reproduced or confirmed. Further studies are necessary to increase understanding of how probiotic agents produce effects on the host as various strains of probiotic bacteria may work by distinct mechanisms. It is important to recognize that in vitro effects of a probiotic may display opposite behavior in vivo [(Nunn *et al.*, 2001)]. Therefore, although probiotics are promising agents to unravel the mystery of gut microbial interactions, our understanding of their use for children in the appropriate clinical circumstances is just beginning. Considerably more supporting evidence beyond what is currently provided in the literature is required as numerous fundamental questions remain unanswered.

Previously our team conducted numerous studies evaluating the properties in effect of various substances used regularly and clinical trials[(Jeevanandan, 2017)][(Somasundaram, 2015)][(Jeevanandan and Govindaraju, 2018)][(Govindaraju, Jeevanandan and E. Subramanian, 2017)][(Lakshmanan *et al.*, 2020)], as well as reviews[(Packiri, Gurunathan and Selvarasu, 2017)][('Fluoride, Fluoridated Toothpaste Efficacy And Its Safety In Children - Review', 2018)] and surveys[(Govindaraju, Jeevanandan and E. M. G. Subramanian, 2017b)] and in vitro studies[(Govindaraju, Jeevanandan and E. M. G. Subramanian, 2017a)][(Ravikumar, Jeevanandan and Subramanian, 2017)][(Veerale Panchal, Jeevanandan and Subramanian, 2019)][26][(Gurunathan and Shanmugaavel, 2016)][(Govindaraju and Gurunathan, 2017)][(Subramanyam *et al.*, 2018)]. As a step towards discovering new technologies as well as new innovation in existing literature, the aim of this review is to summarise the current understanding "Sugar content in probiotic products" which is an update in the currently in use and to present an overview of its merits, demerits, types and so on to get an understanding of its technique and properties and use in clinical dentistry.Our team has rich experience in research and we have collaborated with numerous authors over various topics in the past decade (Deogade, Gupta and Ariga, 2018; Ezhilarasan, 2018; Ezhilarasan, Sokal and Najimi, 2018; Jeevanandan and Govindaraju, 2018; J *et al.*, 2018; Menon *et al.*, 2018; Prabakar *et al.*, 2018; Rajeshkumar *et al.*, 2018, 2019; Vishnu Prasad *et al.*, 2018; Wahab *et al.*, 2018; Dua *et al.*, 2019; Duraisamy *et al.*, 2019; Ezhilarasan, Apoorva and Ashok Vardhan, 2019; Gheena and Ezhilarasan, 2019; Malli Sureshbabu *et al.*, 2019; Mehta *et al.*, 2019; Rajendran *et al.*, 2019; Ramakrishnan, Dhanalakshmi and Subramanian, 2019; Sharma *et al.*, 2019; Varghese, Ramesh and Veeraiyan, 2019; V. Panchal, Jeevanandan and Subramanian, 2019; Gomathi *et al.*, 2020; Samuel, Acharya and Rao, 2020)

Probiotic Properties:

In order for a potential probiotic strain to be able to exert its beneficial effects, it is expected to exhibit certain desirable properties. The ones currently determined by in vitro tests are

(i) acid and bile tolerance which seems to be crucial for oral administration,

(ii) adhesion to mucosal and epithelial surfaces, an important property for successful immune modulation, competitive exclusion of pathogens, as well as prevention of pathogen adhesion and colonisation,

(iii) antimicrobial activity against pathogenic bacteria,

(iv) bile salt hydrolase activity.

Nevertheless, the value of these parameters is still under debate as there are matters of relevance, in vivo and in vitro discrepancies, and lack of standardization of operating procedures to be considered. As there are no specific parameters essential to all probiotic applications, the best approach to establish a strain's properties is target population and target physiologic function specific[(Peres *et al.*, 2005)][(Edgar, 1998)].

Mechanisms of Probiotic Activity:

Probiotics have various mechanisms of action although the exact manner in which they exert their effects is still not fully elucidated. These range from bacteriocin and short chain fatty acid production, lowering of gut pH, and nutrient competition to stimulation of mucosal barrier function and immunomodulation. The latter in particular has been the subject of numerous studies and there is considerable evidence that probiotics influence several aspects of the acquired and innate immune response by inducing phagocytosis and IgA secretion, modifying T-cell responses, enhancing Th1 responses, and attenuating Th2 responses[(Strickley *et al.*, 2008)].

Dental caries is a common disease and the most prevalent infectious disease in the oral cavity. Among the theories that explain caries onset Universally accepted is the action of acid is produced by bacterial fermentation of carbohydrate from the diet. However, some diseases or medications may increase the risk or severity of caries, and dental erosion is one of them[(Cavalcanti *et al.*, 2012)]. Dental erosion is defined as the progressive loss of dental heart tissue by chemical dissolution without bacterial involvement[(Allen, 2008)]. Liquid oral medications are usually prescribed for children in order to avoid difficulty encountered in taking medicine in other forms [(Durward and Thou, 1997)]. Several liquid medications can be part of the daily routine of children with chronic disease[(Russell, 2009)]. Even antibiotics and cough syrup are the most common sugar containing medication regularly used for young children. Off late, where sugar substitutes have been introduced and are

widely used in food products to avoid tooth decay from sugar and other fermentable carbohydrates. Many studies have shown sugar substitutes to be non-cariogenic[(Saarela *et al.*, 2000)].
The use of sugar medicine by children from long period, specially those with chronic disease, thus the aim of the research study was to access in vitro, with stating that there are no effect of conventional and sugar free paediatric syrup or probiotics formulation on primary tooth enamel hardness.Solution or preparation in which the drug substance is completely dissolve predominantly in an aqueous wheel. Solution are of many types, simple formulations based on the constituent solvent and buffer, flavour or preservative and complex formulation comprises multiple solvents, solubilising excipients, buffers, sweeteners,Flavour, preservatives and dyes(Ibnou-Zekri *et al.*, 2003). Set up with some solution that uses sucrose solution as a vehicle, resulting in a viscous preparation. Most of the probiotic syrup contains 60 to 80% sucrose, and little or no alcohol. The role of sweetener in the paediatric probiotic medication is generally related to compliance[(Guarner and Malagelada, 2003)].

DISCUSSION

More than 70% of the most consumed liquid oral medicines by children in Tubarão presented sugar in their ingredients. The prevalence of pediatric medicines with sugar found in this study was similar to 2 those results from the international literature. Two out of the five studies that showed significant improvement in growth, noted that the children in the probiotic groups had growth curves that were significantly higher than or closer to the WHO reference value than the children in the control groups. Notwithstanding, it is important to emphasize that these studies were conducted in the 80's. The list of the UK National Pharmaceutical Asso- ciation (1984) shows that, for the available liquid oral medicines (prescribed and over-the-counter), 23% of a total of 210 were identified as sugar-free. By 1986, this proportion had risen to 35%. Therefore, another important point relates to the labeling of these drugs. In the current study 50% of all medicines ana- lyzed were labeled as containing sugar, while in New Zealand about one-third of sugar-free medicines were labeled as such and only one-quarter were confirmed to be sugar-free in the New Ethical Catalogue. It seems that there is a misconception among parents due to lack of information. Consequently, the pres- sure on drug companies makes it more difficult to remove sugar from liquid medicines or to use non- cariogenic substitutes. Reducing the cariogenic potential of children's medications should be of concern to all health pro- fessionals. From an individual point of view it would be possible through educating children and their parents regarding the need to brush the teeth after taking each dose, to take medicines at meal times rather than between meals, to avoid taking medi- cines before bed, and the need to fluoride applica- tions and regular preventive dental care. On the other hand, manufacturing children's medicines containing no fermentable carbohydrates with low prices should be the best public health policy. In addition, research should be developed in order to find acceptable levels of carbohydrates to help preserve medicines' palatability.Our institution is passionate about high quality evidence based research and has excelled in various fields ((Pc, Marimuthu and Devadoss, 2018; Ramesh *et al.*, 2018; Ezhilarasan, Apoorva and Ashok Vardhan, 2019; Ramadurai *et al.*, 2019; Sridharan *et al.*, 2019; Vijayashree Priyadharsini, 2019; Mathew *et al.*, 2020)

CONCLUSION

The advent of supernatural sugar and the advances in the understanding of neuro biological mechanisms for this test perception, improved drug palatability And paediatric closing, paediatric specialist and physicians should be able to provide medicine and probiotics for each child with least adverse affect in the near future.

AUTHORS CONTRIBUTION

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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