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Overview of Probiotics Available in Pharmacies in Turkey

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ABSTRACT

Objective: In this study, we aimed to provide a general assessment of the probiotic preparations actively sold in pharmacies in Turkey in December 2021 to health professionals and interested parties. **Materials and Methods:** We examined the probiotic preparations that were actively sold in pharmacies in Turkey in December 2021 by using the Rx Mediapharma® 2021 Interactive Drug Information Resource Program. **Results**: There were 249 preparations in the program. Most of them were capsules (n=103). 39% of preparations contained one type of microorganism (n:97) and the rest more than one type. Genres of Lactobacillus and Bifidobacterium are the main content (84%) in the probiotic preparations. 97% of preparations were approved as Food Supplements by the Ministry of Agriculture, and 99% of the probiotics are sold without a prescription. 59% of them were imported. **Conclusion:** Probiotics are evaluated into categories as food/supplement that can claim or not claim to be beneficial to health, and probiotic drugs. The probiotics we examined are evaluated under the title of 'Nutritional Products' and are not separated according to the grouping in the consensus. Investigation and inspection by the Ministry of Health will make the use of probiotics safer.

Keywords: Probiotics, Microbiota, Nutraceutical, Pharmacy.

Türkiye'deki Eczanelerde Bulunan Probiyotiklere Genel Bakış

ÖZ

Amaç: Bu çalışma, Türkiye'de eczanelerde aktif olarak satılan probiyotik preparatları hakkında sağlık profesyonellerine ve ilgililere genel bir değerlendirme sağlamak amacıyla yapıldı. **Gereç ve Yöntem:** Çalışmada Rx Mediapharma® 2021 İnteraktif İlaç Bilgi Kaynak Programını kullanılarak, Aralık 2021'de Türkiye'de eczanelerde aktif olarak satılan probiyotik preparatlar incelendi. **Bulgular:** Değerlendirmeye alınan 249 preparatın, çoğunun kapsül formunda olduğu tespit edildi (n:103). Preparatların %39'u tek tip mikroorganizma (n=97) içerirken geri kalanı birden fazla tip mikroorganizma içermekteydi. Probiyotik preparatların içeriğini başlıca Lactobacillus ve Bifidobacterium türlerinin (%84) oluşturduğu tespit edildi. Preparatların %97'si Tarım Bakanlığı tarafından Gıda Takviyesi olarak onaylanmış olduğu ve neredeyse tamamının (%99) reçetesiz satıldığı görüldü. Tüm preparatların %59'unu ithal ürünler oluşturmaktaydı. **Sonuç:** Probiyotikler sağlık otoritelerince; sağlığa yarar iddiası olan ve olmayan gıda/takviye maddeleri ile probiyotik droglar olarak sınıflandırılmaktadır. İncelediğimiz programda probiyotiklerin "Nutrisyonel Ürünler" başlığı altında listelenmekte olduğu herhangi sınıflandırma yapılmadığı görüldü. Sağlık Bakanlığı tarafından yapılacak değerlendirme ve denetlemeler probiyotik kullanımını daha güvenli hale getirecektir.

Anahtar Kelimeler: Probiyotikler, Mikrobiyota, Nutrasötik, Eczacılık.

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INTRODUCTION

Probiotics are live microorganisms that are beneficial to health; When it comes to probiotics, fermented products come to mind first. Findings on the use and benefit of fermented products date back to prehistoric times. In the excavations made in different continents of the world, it has been determined that the preparation and use of fermented foods are depicted in many figures, which are generally determined to belong to the neolithic age. The use of fermented foods obtained from milk dates back to 10000 BC and was first found to be used in the Middle East and Ancient Egypt (Gasbarrini et al., 2016). Yogurt, one of the most important fermented milk products, according to legends, was discovered by a Turkish shepherd who carried his milk in a goatskin pouch while traveling in the desert. In addition, the word yogurt is derived from the Turkish word "yoğuşmak", which means to solidify and condense (Ozen & Dinleyici, 2015). The findings belong to 7000-5000 BC show, that fermented beverages were made from rice in Asia and fruits, cereals, and honey in whereas Mesopotamia and Ancient Egypt (Gasbarrini et al., 2016). The production and use of fermented foods have continued until today; yogurt, kefir, pickles, cheese, wine and beer are among the most popular fermented foods (Bell et al., 2017).

It was discovered by the scientist Pasteur in 1864 that the fermentation of foods is carried out by microorganisms (Barnett, 2000). In 1905, Bulgarian Doctor Grigoroff found that the microorganism that enables the formation of yogurt by fermentation was a bacillus, and this microorganism was named *Lactobacillus bulgaricus* (Grigoroff, 1905). Nobel Prize-winning scientist Elie Metchnikoff described the hypothesis that the longevity of Bulgarians is due to Lactobacillus found in yogurt in his book ''The Prolongation of Life'' in 1907 (Metchnikoff, 1908). Then, many scientists began to be interested in this subject and search for beneficial microorganisms.

The definition of these beneficial bacteria as probiotics was first made by R. Fuller in 1989 and was used for animal feeds containing beneficial microorganisms (Fuller, 1989). The definition of probiotics was finalized by scientists working on behalf of the United Nations Food and Agriculture Organization (FAO) and the World Health Organization (WHO) as "live microorganisms that provide health aid to the host organism when taken in sufficient quantities", in 2001 (Cordoba, 2001). As of this date, almost more than 1000 studies have been published annually (McFarland, 2015). Thereby, the number of probiotic products on the market and the interest of society in these products have increased rapidly.

In this study, we aimed to provide a general assessment of the probiotic preparations actively sold in pharmacies in Turkey in December 2021 to health professionals and interested parties.

MATERIAL AND METHODS

The present study examined the probiotic preparations that were actively sold in pharmacies in Turkey in December 2021 by using the Rx Mediapharma® 2021 Interactive Drug Information Resource Program. By searching the data bank on "Pharmacological Group Structure"; "Probiotics" under the sub-title of "Vitamins, Minerals and Other Nutritional Products" were evaluated in the study. Preparations whose production or import was stopped were excluded from the study. In addition, only one of the preparations with the same drug names and pharmaceutical forms but with a different package amount was included in the evaluation. The numbers, pharmaceutical forms, contents (single/combined microorganism), microorganism types in its content, approval status by official institutions, sales (prescription/nonprescription), and production status (domestic/imported) of selected probiotic preparations were investigated in the present study.

Statistical analysis

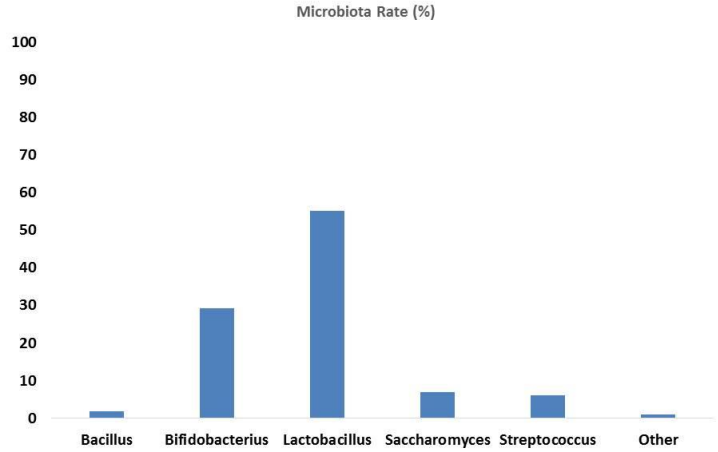
Statistical calculations were not used in our article.

Ethics committee approval

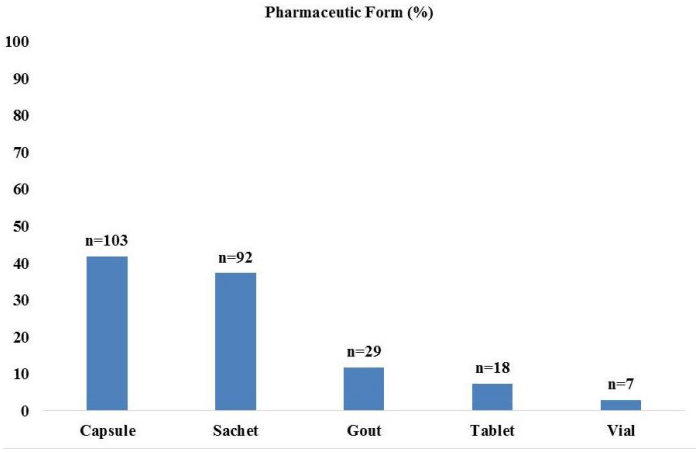
The author declares that this study does not include any experiments with human or animal subjects.

RESULTS

There were 323 probiotic preparations registered in the program. 35 of them have not been imported or produced, and one of them has been approved by the Ministry of Health but has not been put into use yet.



Graph 1. Microbiota type rate of probiotics (n=764).

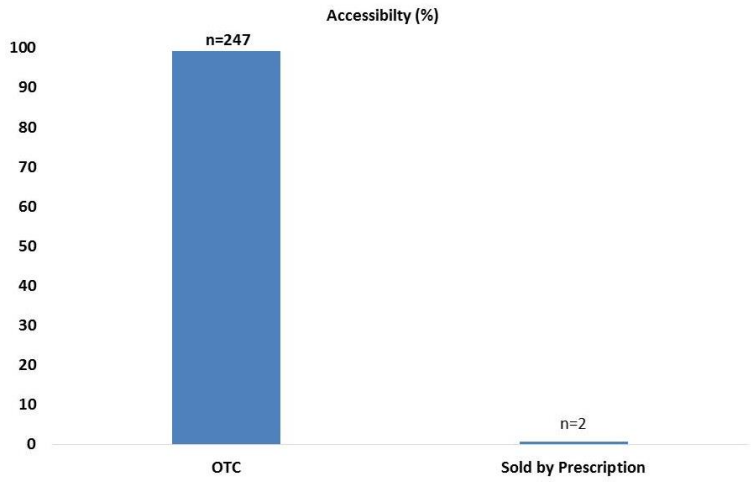


Graph 2. Pharmaceutical form of probiotics (n=249).

The remaining (n:287) preparations are actively sold in pharmacies. Only one of the same preparation and pharmaceutical forms with different package quantities were included in the study, it was determined that 249 preparations met our criteria. The most common bacteria of microorganisms in preparations used as probiotics are Lactobacillus and Bifidobacterium species, but there are other bacteria like some strains of Streptococcus and yeast such as *Saccharomyces boulardii* (Table 1, Graph 1).

Table 1. Type of microorganism of probiotics (n:764).

Type of microorganism	**n**
Lactobacillus	n:420
Lactobacillus rhamnosus	118
Lactobacillus acidophillus	117
Lactobacillus plantarum	34
Lactobacillus casei	29
Lactobacillus paracasei	28
Lactobacillus bulgaricus	24
Lactobacillus reuteri	24
Lactobacillus salivarius	10
Lactobacillus helveticus	7
Lactobacillus gasseri	6
Other	23
Bifidabacterium	n:223
Bifidabacterium lactis	61
Bifidabacterium longum	59
Bifidabacterium bifidum	48
Bifidabacterium infantis	26
Bifidabacterium breve	17
Other	12
Streptococcus	n:47
Streptococcus salivaricus	1
Streptococcus thermophilus	46
Saccharomyces	n:53
Saccharomyces cerevisia	1
Saccharomyces boulardii	52
Bacillus	n:13
Bacillus clausii	7
Bacillus coagulans	5
Bacillus subtilis	1
Other	n:8



Graph 3. Accessibility of probiotics (OTC; Over the Counter/ Sold by Prescriptions) (n=249).

Most of the 249 probiotic preparations were pharmaceutical in capsule form (n:103) and followed by sachet (n:92), drop forms (n: 29) (Graph 2). When evaluated in terms of content, it was seen that 39% contained only one type of microorganism (n:97), and 61% contained more than one type of microorganism (n:152). It was determined that almost all of the probiotics (97%) in the active sale were approved as Food Supplements by the Ministry of Agriculture, and the number of products approved by the Ministry of Health was just seven (3%). In addition, 99% of the probiotics were sold without a prescription (n:247), and only two of them were sold under prescription (Graph 3). We also established that 59% (n:146) of the 249 preparations sold actively were imported.

DISCUSSION

Demonstration of many benefits in the studies on probiotics, the interest of the society in fermented foods such as yogurt, kefir, boza, and pickles that can contain probiotics has increased (Bell et al., 2017). In order for the beneficial effects of probiotics to occur, they must contain a certain number of live microorganisms; The reasons such as the inability to determine the amount and type of microorganisms in fermented foods, the fact that they may contain toxins due to poor storage conditions or contamination, and that they may lose their nutritional value with pasteurization and heat treatments applied for food safety make the effectiveness of these foods controversial (Motarjemi, 2002). In order to rationalize the benefit to be obtained from probiotics, the basic features that these microorganisms must have are; a) reaching the target organ alive and in the desired amount; b) providing health benefits to its host; c) having an anti-pathogenic effect; d) be safety; e) can be produced and stored (McFarland, 2015). As a result, the fact that a product contains beneficial microorganisms does not mean that it will have a beneficial effect on health unless it has all the properties specified.

Lactobacillus and Bifidobacterium genuses are the microorganisms that meet these specifications and are most frequently used as probiotics. these microorganisms are also most frequently (84%) used in our country. However, only certain species and even certain strains of the Lactobacillus and Bifidobacterium genuses show probiotic properties. In the study of Domig et al. (Domig et al., 2014), just 3% of the lactobacilli obtained by vaginal isolation showed probiotic properties; Gu et al. (Gu et al., 2008) examined 567 lactobacilli in their study and found that only 36 of them could reach the intestine without being affected by stomach and bile acids. In order for the beneficial effects of probiotics can be occurred; scientific studies have shown that it should contain a minimum of 10^6-10^8 colony-forming units (CFU)/gram or 10^8-10^{10} CFU/day live microorganisms (may differ according to the type of and strain the microorganism it contains), at the time of consumption (Champagne et al., 2011). Probiotics have positive effects on many diseases such as inflammatory bowel diseases, ulcerative colitis, Crohn's disease, antibiotic-associated diarrhea, Clostridium difficile-associated diarrhea, infective diarrhea, constipation, obesity, hypercholesterolemia, allergy, eczema, atopic dermatitis, depression, sleep disorder and anxiety (Hill et al., 2014; Bermúdez-Humarán et al., 2019). However, probiotics' some theoretical and clinical adverse effects have been reported. Probiotics may theoretically cause autoimmune disease by excessive immunostimulation, pathogenicity and antibiotic resistance by gene transfer, colon cancer by toxin production however, no evidence of these effects was found in clinical studies (Snydman, 2008; Doron et al., 2015). The most common clinically reported adverse effects are; bacteremia, fungemia, endocarditis, and intestinal ischemia (Didari et al.,

2014). It has been emphasized that these effects are frequently observed in immunosuppressed individuals, premature infants, those with short bowel syndrome, elderly patients, and patients with heart valve disease or with central venous catheters, and therefore caution should be exercised when using probiotics in these individuals (Snydman, 2008).

Probiotics are evaluated into three basic categories as food or supplement that do not claim to be beneficial to health, food or supplement that claim to benefit health, and probiotic drugs in the Consensus Statement held in 2013 (Hill et al., 2014).

The probiotics we examined in our study are evaluated under the title of ''Vitamins, Minerals and Other Nutritional Products" and are not separated according to the grouping in the consensus. Of the 249 probiotic preparations we examined, 7 were approved by the Ministry of Health, and only 2 are sold by prescription. The remaining 242 preparations are subject to the approval of the Ministry of Agriculture.

According to the regulation numbered 26221 in the Turkish Food Codex (TGK) dated 07/07/2006, for a product to be probiotic, it must contain a sufficient number of live probiotics (at least $1.0x\ 10^6$ CFU/g) microorganisms until the end of its shelf life (Turkish Food Codex, 2006). The contents of only 99 of the 249 preparations in our study were specified CFU, and we observed that this information was not included in the prospectus of the remaining preparations.

In order to provide the desired benefit and minimize possible side effects, content determination and inspection by the Ministry of Health will make the use of probiotics safer. In addition, studies have shown that probiotics have the potential to change the bioavailability of drugs taken together (Koziolek et al., 2019). Therefore, some arrangements should be made in the sale and use of probiotics, and at least they should meet the quality, safety, and efficacy conditions sought in modern drugs.

The increasing interest in probiotics in recent years has also affected its place in the global market; The market volume, which was 49.4 million dollars in 2018, is expected to increase to 69.3 million dollars in 2023 (Trush et al., 2020). In our study, we found that 59% of the preparations we examined were imported. It is important for the economy of the country that this situation is evaluated by the relevant authorities and that domestic products play a competent role in the domestic market and even in the global market by making the necessary investments.

CONCLUSION

In this study, in which we examined probiotics that are actively sold in pharmacies in Turkey as of December 2021, we identified 249 different preparations meeting our criteria. This number may vary depending on the changes that may occur in the production, import, and license processes. The number of studies on the subject in our country is limited, and we expect our current study to provide a general assessment of the probiotics sold in pharmacies in Turkey to healthcare professionals and interested parties.

Conflict of Interests

The author declares that for this article they have no actual, potential, or perceived conflict of interests.

Author Contributions

Plan, design: OG, FS**; Material, methods and data collection:** FS; **Data analysis and comments:** OG; **Writing and corrections:** OG, FS.

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