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THE ROLE OF PROBIOTIC UPTAKE ON SOME BIOCHEMICAL PARAMETERS IN RATS INFECTED BY *E. COLI*

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THE ROLE OF PROBIOTIC UPTAKE ON SOME BIOCHEMICAL PARAMETERS IN RATS INFECTED BY *E. COLI*

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~~August~~ October 2022

We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science

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Sajir Abed Nuhair NUHAIR

ABSTRACT

THE ROLE OF PROBIOTIC UPTAKE ON SOME BIOCHEMICAL PARAMETERS IN RATS INFECTED BY *E. COLI*

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This research aims to identify the effect of the role of probiotic uptake on some biochemical variables in rats infected with *Escherichia coli*. Experimental design was performed on 6 groups of rats and the first control group was provided daily with food and drinking water only, The second group was given *Escherichia coli* orally (1x1010)/200 g/bw for 3 days. And the third group *Lacteol* Fort treated with *Lactobacillus* spp orally. (1x108)/200g/b.w to 11 days, Group IV: *Saccharomyces boulardii* treated orally for 11 days (1×106)/200 g/body weight for erythroid. And the fifth group *E.coli*+*Lacteol* Fort: This group was treated with *E.coli* (1x1010)/200 g/live weight after 3 days of oral treatment with *Lactobacillus* spp. (1x108) /200g/b.w to peroid 11 days, And the sixth group *E.coli*+*Saccharomyces boulardii*: This group is 3 days after oral treatment with *E.coli* (1×1010)/200g/bw with peroid, *Saccharomyces boulardii* (1×106)/200g/bw with peroid 11 days has been treated, At the end of the experiment, blood was collected from the jugular vein and from the blood site in the separator tubes without EDTA. Serum glucose, urea, creatinine, total protein, albumin, electrolytes, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) concentrations were determined using a clinical chemistry analyzer according to the manufacturer's recommended procedure

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Keywords: *E. coli*, Infection, Probiotic, Rat

ÖZET

E.COLİ İLE ENFEKTE SIÇANLARDA PROBİYOTİK ALIMININ BAZI BİYOKİMYASAL PARAMETRELER ÜZERİNDEKİ ROLÜ

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Bu araştırma, Escherichia coli ile enfekte sıçanlarda probiyotik alımının rolünün bazı biyokimyasal değişkenler üzerindeki etkisini belirlemeyi amaçlamaktadır. Deney tasarımı 6 grup sıçan üzerinde gerçekleştirilmiştir. Birinci kontrol grubuna günlük olarak sadece yiyecek ve içme suyu verilmiş, ikinci gruba, 3 gün süreyle *Escherichia coli* ağızdan (1x1010)/200 g/v.a verilmiş olup üçüncü grup 11 gün boyunca (1x108)/200g/v.a ağızdan *Lacteol* Fort ve *Lactobacillus* spp ile tedavi edilmiştir. Dördüncü grup, eritroid için 11 gün boyunca *Saccharomyces boulardii* ile (1×106)/200 g/v.a oral olarak tedavi edilmiştir. Beşinci grup ise *E. coli*+*Lacteol* Fort grubu olup, *Lactobacillus* spp ile 3 günlük oral tedaviden sonra *E. coli* (1x1010)/200 g/v.a. 11 gün boyunca (1x108) /200g/b.a) ile tedavi edilmiştir. Son olarak altıncı grup *E. coli* + *Saccharomyces boulardii* grubu olup, *E. coli* (1×1010)/200g/v.a. ile oral tedaviden 3 gün sonra, *Saccharomyces boulardii* (1×106)/200g/va ile 11 gün tedavi edilmiştir. Deneyin sonunda, juguler venden ve EDTA'sız ayırıcı tüplerdeki kan bölgesinden kan alınmıştır. Serum glukoz, üre, kreatinin, toplam protein, albümin, elektrolitler, alanin aminotransferaz (ALT), aspartat aminotransferaz (AST) ve alkalin fosfataz (ALP) konsantrasyonları, üreticinin tavsiye ettiği prosedüre (8,9,10) göre bir klinik kimya analizörü kullanılarak belirlenmiştir.

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Anahtar Kelimeler: *E. coli*, Enfeksiyon, Probiyotik, Sıçan

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Sajir Abed Nuhair NUHAIR
Çankırı-2022

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LIST OF SYMBOLS

%	Percentage
μL	Microliter
μm	Micrometer
mL	Milliliter
ºC	Degrees Celsius

LIST OF ABBREVIATIONS

AAD	Antibiotic-associated diarrhea
ALP	Ambulance loading post
ALT	Alanine transaminase
AST	Aspartate aminotransferase
EDTA	Ethylenediaminetetraacetic_acid
EMB	Education and manpower bureau
EMB	Eosin methylen-blue
GALT	Characterization of gut-associated lymphoid tissue
IBS	Irritable bowel syndrome
PCR	Polymerase chain reaction
TD	Toxoid

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1 INTRODUCTION

Probiotics are bacteria that are widely coexisted in humans and animals as normal flora, which is one of the biotherapeutic agents that have been used recently to improve animal and human health (Wynn 2009). Lactobacilli bacteria are considered one of the most important probiotic preparations, due to their characteristics and properties in showing their beneficial effects within the gastrointestinal tract against pathogenic bacteria, Its ability to adhere to the epithelial cells lining the gastrointestinal tract (Ouwehand *et al.* 2002) as well as its stimulation of the immune system by stimulating both humoral and cellular immunity (Casey *et al.* 2007, Meydani and Ha 2000) and an increase in the activity of enzymes responsible for nutrient absorption. and necessary minerals (Ibnou-Zekri *et al.* 2003). The species of Lactobacillus, Bifidobacterium are considered among the greatest important bio-enhancers because of their great beneficial effects on the health of the host as they are not pathogenic and do not produce toxins and with their high ability to survive inside the digestive canal and their high ability to withstand the manufacturing and storage conditions of fermented milk products and the possibility of isolation from the natural host (Borriello *et al.* 2003, Wynn 2009). Escherichia coli It was first described by Theodore Escherich in 1885 and it was 'initially considered harmless, non-injurious and present in the colon as a normal flora. Subsequently, it was found that it has a relationship with some clinical syndromes resulting from urinary tract infections (UTIs) to infections of the central nervous system and diarrheal diseases (Mahon *et al.* 2018). They are classified within the *Enterobacteriaceae* family and are characterized as bacilli with dimensions between (1.11.5.-×6.5) microns and they are Gram-negative Bacteria (G-Ve). Therefore, it was isolated from the colon in the intestine, as it is the first evidence of fecal contamination, in food and water, and it appears distinctly as smooth, convex pink colonies with clear ends. It is fermented with lactose, in contrast to the rest of the other intestinal types, and it is surrounded by a region of yellow salts precipitated in the McConkey agar, so it appears on the middle Eosine Methylene Blue(EMB), it has a green metallic luster. Most strains of *Escherichia coli* are motile, non-spore forming, and generally have Fimbriae for adhesion, Sex Pili and (K,O,H) antigens, as both *Escherichia coli* and *Shigella sonne* i possess the autoantigen Somatic antigen (Clermont *et al.* 2000).

It is also positive for the catalase test and negative for the oxidase test. It is also facultative anaerobic and produces lactase enzyme and has the ability to ferment different sugars coupled with gas production, which is one of the main characteristics of this type (Jawetz *et al.* 2004). It is also positive for Indole and Methyl Red, but negative for Voges Proskaur and Citrat Utilization. (Holt *et al.* 1994)

The aims of the study includes the following:

- Probiotics as a live microbial food that benefits human or animal health and Lactic acid bacteria, which ferment when ingested, are believed to positively affect the bacteria in the colon and reduce toxic microbial activities.
- Identification of food additives that can improve the utilization of important types of sugars and types of lactic acid bacteria containing 45-60% rich in crude protein, multiple enzymes, high biological value, vitamin B complex, biotin and niacin. And pantothenic acid, thiamine, the most important minerals and foods with functional ingredients.
- Stimulating the immunity of the intestinal mucosa.
- Increased protection against toxins caused by pathogenic Escherichia coli, as well as the effects of functional food components that reduce malnutrition and the negative effects of stress with unknown pathways functions.

2 LITERATURE REVIEW

The history of probiotics began with human records through the consumption of the famous fermente meals regularly ate up with the aid of the Greeks and Romans (Gismondo *et al.* 1999, Guarner *et al.* 2005). In 1908, the Russian researcher Ili Mitchnikov, a Nobel Prize winner, advised the beneficial effects of probiotic microorganisms on human health. It become postulated that Bulgarians have been healthy and lengthy-lived humans due to the consumption of fermented dairy merchandise such as rod-fashioned micro organism (*Lactobacillus* spp.). These bacteria have a tremendous effect on the intestinal microflora and reduce the toxic interest of microbes (Gismondo *et al.* 1999, Duru *et al.* 2003, Chuayana *et al.* 2003).

According to him, harmful bacteria are the purpose of many diseases and useful bacteria, specially the ones lively in fermented milk, can suppress diseases as a result of disease-inflicting bacteria and as a consequence extend everyday lifestyles (Soccol *et al.* 2010, Lourens-Hattingh and Viljoen 2001).

2.1 Definition of Probiotics

The phrase "probiotic" come from the Greek "pro bios" which means "for existence" in preference to "antibiotic" which means "towards life". The time period "probiotic" become first utilized in 1965 via (Lilly and Stillwell 1965) to explain substances that stimulate the development of other microorganisms. After this year, the word "probiotic" was usage in a special feel, relying on its mechanism and consequences on human health. The which means changed into subtle to the closest we usage today by way of Parker in 1974. Parker described 'microorganisms' as 'substances and organisms that make contributions to the intestinal microbial stability'. In 1989, the usage of the meaning these days turned into improved upon by Fuller. Thus, probiotics are a stay microbial supplement that positively impacts the health of the host by using enhancing the intestine microbiome balance. This definition become then prolonged via (Havenaar and Huis In’t Veld 1992) to include monoculture or mixed tradition of microorganisms relevant to animal and human (Duru *et al.* 2003, Guarner *et al.* 2005, Sanders 2003). In the following years, many researchers studied probiotics and provided many definitions. They are listed underneath.

- “Living microorganisms, which, when ingested in sure numbers, achieve fitness advantages beyond their inherent simple vitamins”.
- “A microbial food complement beneficially affecting host body structure with the aid of modulating mucosal and systemic immunity, in addition to improving dietary and microbial stability within the intestine” with the aid of (Naidu *et al.* 1999).
- “A live microbial food ingredient beneficial to health” by means of (Salminen *et al.* 1999).
- ‘‘A guidance or product containing feasible microorganisms diagnosed in sufficient numbers, which alters the microflora (with the aid of implantation or colonization) in a compartment of the host and thereby exerts beneficial health results in that host’ with the aid of (Schrezenmeir and De Vrese 2001).
- “Living microorganisms which when administere in enough portions confer a health benefit to the host” (Table 2.1), common by using FAO/WHO (Klaenhammer 2000, Sanders 2003, Guarner *et al.* 2005) .

To exercise any probiotic impact, the microorganism should meet strict standards (Heller 2010) as follows:

- It must be obviously immune to stomach acid (eg belly acid and bile acid pH variety from 1 to 4).
- They ought to continue to exist the impact of bile salts and digestive enzymes (eg lysozymes) present inside the gut.
- It have to be completely secure for the host and give useful consequences on human health.
- They must attain the gut in sufficient portions and be able to adhere to the intestinal wall so that it will have an impact.

Table 2.1 The microorganisms showing used aprobiotics. (Prado *et al.* 2008, Leroy *et al.* 2008)

Genus	Species	Genus	Species
Cryptococcus	*Mujuensis*	*Lactobacillus*	*Brevis*
Cryptococcus	*Curvatus*	*Lactobacillus*	*Bulgaricus*
Cryptococcus	*Cuniculi*	*Lactobacillus*	*Cellobioses*
Yarrowia	*Lipolytica*	*Lactobacillus*	*Curvatus*
Metschnikowia	*Lochheadii*	*Lactobacillus*	*Delbruekii*
Candida	*Humilis*	*Lactobacillus*	*Fermentum*
Candida	*Pintolepsii*	*Lactobacillus*	*Lactis*
Candida	*Saitoana*	*Lactobacillus*	*Plantarum*
Candida	*Utilis*	*Lactobacillus*	*Casei*
Candida	*Pararugosa*	*Leuconostoc*	*Mesenteroides*
Debaryomyces	*Hansenii*	*Ediococcas*	*Acidilacticicii*
Debaryomyces	*Cereviae*	*Ediococcas*	*Cervisiae*
Kluyveromyces	*Marxianus*	*Ediococcas*	*Damnosus*
Kluyveromyces	*Lodderae*	*Propionibacterium*	*Freudnreichii*
Kluyveromyces	*Lactis*	*Bacillus*	*Lentus*
Pichia	*Anomala*	*Bacillus*	*Lincheniformis*
Saccharomyces	*Cerevisiae*	*Bacillus*	*Pumilus*
Isaatchenkia	*Orientalis*	*Bacillus*	*Subtilis*
Aspergillus	*Oryza*	*Bacteroides*	*Amylophilus*
Aspergillus	*Niger*	*Bacteroides*	*Capillosus*
Bacteroides	*Ruminocola*	*Bacillus*	*Coagulans*
Bifidobacterium	*Suis*	*Propionibacterium*	*Sheranii*
Bifidobacterium	*Odolesntis*	*Streptococcus*	*Diacetylactis*
Bifidobacterium	*Animalis*	*Streptococcus*	*Faecium*
Bifidobacterium	*Bifidum*	*Streptococcus*	*Intermedius*
Bifidobacterium	*Infantis*	*Streptococcus*	*Lactis*
Bifidobacterium	*Longum*	*Streptococcus*	*Thermophilus*
Lactobacillus	*Thermophiles*		
Lactobacillus	*Acidophilus*		

2.1.1 Yeast probiotic

Probiotics are live microbial food dietary additions that beneficially have an result on the host animal by way of refining the intestinal microbial balance, or by using a broader meaning, probiotic are arrangements of microbial cells or additives of microbial cells which have a useful result on human health and properly-being. Host (Salminen *et al.* 1999). The probiotic houses of yeasts, along with S. Cerevisiae, have been said to be the aptitude to survive via the gastrointestinal (GI) tract and to engage reversibly with gastrointestinal pathogen together with *Esherichia coli*, *Shigella* and *Salmonella.*

Specifically, *S. boulardii*, a refractory, non-pathogenic yeast, has been usage for over 50 years as a probiotic addition to live animal feed in addition to as a healing agent to deal with a selection of intestinal disorders along with diarrhea. This yeast is safe, proof against antibiotics, achieves excessive cell counts within the gut in a brief time, does now not completely colonize the gut, and is quickly cleared after you prevent taking it. The effects of probiotics are also stronger by their capability to produce polyamines, compounds that strongly have an effect on cellular growth and differentiation (Lourens-Hattingh and Viljoen 2001, Costalos *et al.* 2003, Golubev 2006). Several yeast species were determined, consisting of D. Hansenii and Torulaspora delbrueckii (Psani and Kotzekidou 2006), Kluyveromyces lactis, Yarrowia lipolytica (Chen *et al.* 2010), K. Marxianus, K. Sporting the passage thru the gastrointestinal tract. A rare in vitro examine, (Etienne-Mesmin *et al.* 2011) investigate the impact of the probiotic S. Cerevisiae CNCM I- 3856 against Escherichia coli O157:H7. The effects confirmed that yeast probiotics have opposite consequences within the distal a share of the small intestine and this could be owing to ethanol manufacture. But, handiest S. Boulardii is considered a probiotic (Czerucka *et al.* 2007). S. Boulardii is broadly usage and is to be had in various profitable formulations. Other yeasts accepted and usually utilized in animal feeds as probiotic components are Candida pentolopisi, C. Saitoana, and S. Cerevisiae (Bovill *et al.* 2001, Leuschner *et al.* 2004).

2.1.1.1 ***Saccharomyces boulardii***

Non-pathogenic yeast S. has been remoted and defined for the reason that mid-twentieth century, presenting empirical proof for its effectiveness as an adjunct in the remedy of diarrhea and the deterrence of AAD. Beginning inside the Nineteen Eighties, research become lead to assess the welfares of *S. boulardii* for the host organism and to control its mechanism of action. In unique, research have investigate the impact of this yeast on bacterial infections, its effect on the mucous membrane, and greater these days on its immune properties. Yeast *boulardii* is the best yeast whose result has been assessed in double-blind clinical research. *Saccharomyces boulardii* changed into to begin with diagnosed as a separate class of the genus *Saccharomyces hemiascomycete* (Farland 1996). In 1994, Cardinali and Martini (1994) categorised S. Yet, the speedy growth of molecular genetics in latest years has caused adjustments inside the category of many yeast species (Vaughan-Martini 2003). Polymorphic DNA taxonomy-polymerase chain response, polymorphic evaluation of restrict fragment period of the rDNA spacer place and PFGE] *S. boulardii* within the class S. Cerevisiae (Mitterdorfer *et al.* 2002). Usage relative genomic hybridization for entire-genome evaluation, it turned into also decided that S. Cerevisiae and S. Boulardii belong to the similar species. However, *S. boulardii* is genetically distinctive from the *S. boulardii* genome. S.). The authors advocate that overexpression of a gene connected to protein mixture and strain replies ought to make a contribution to the elevated growth fee and advanced existence of *S. boulardii* at acidic pH. Indeed, from the metabolic and physiological point of view, *S. boulardii* may be very extraordinary from S. Metabolism takes place at a temperature of 30°C, *S. boulardii* is a warmness-resistant yeast that produces optimally at 37°C, that is, the physiological temperature of the host. New research have proven that *S. boulardii* seems to be additional resistant than the S. Pressure. Augmented devotion to epithelial cells or transit via the intestine of mice (Edwards-Ingram *et al.* 2007). Pharmacokinetic studies in human beings and rats confirmed that once repeated management, it become achieved that S. Boulardii has strong concentrations inside the colon within three days and is excreted in the feces 2-five days after discontinuation. (Blehaut *et al.* 1989, Elmer *et al.* 1999)

2.1.1.2 Resistance to antibiotics

Since *S. boulardii* is naturally resistant to antibiotics, it could be set to patient getting antibiotic (Bergogne-Berezin *et al.* 1995). Investigation on the administration of *S. boulardii* to patient with recurrent C. Difficile infection has proven that the variety of fecal yeast is drastically better in patient who do now not relapse as likened to sufferers who do now not relapse (Elmer *et al.* 1999). Thus, *boulardii*'s treatment appears to be related to the concentration of fecal yeast.

2.1.1.3 Taxonomy

Probiotics might be either bacterial microbes or yeast. Yeast probiotic, together with S. Boulardii, differ from bacterial probiotic (extraordinary physiological structures, massive in size, do no longer accumulate antibiotic resistance genes and are not tormented by antibiotic) (Czerucka *et al.* 2007). Not lone is there a complicated collection of probiotic crops on the world marketplace, the taxonomy of *Saccharomyces* traces has been mentioned (Sankoff 2009, Farland *et al.* 1996). Nomenclature (Farland 1996, McCullough *et al.* 1998). It changed into initially called *S. boulardii* in the Fifties. Loans in printing strategies have unlocked a discussion as to whether or not this pressure must be reclassified as a subspecies of S. Cerevisiae or stay a separate class. Initial work the usage of PCR electrophoresis or rRNA sequencing techniques stated that *S. boulardii* changed into indistinguishable from different strains of *S. cerevisiae* (McCullough *et al.* 1998, Mitterdorfer *et al.* 2002) that show more recent metabolic tools (polymorphism evaluation). Micro-satellite and lower back-hybrid analyzes display that *S. boulardii* has a unique population that differs from different traces of *S. boulardii* from different traces from S. 2007). Boulardi perseveres lengthier in southern rat models (10 d) than fast removal of other strains of *S. cerevisiae* (<1 d) (Pecquet *et al.* 1991). *boulardii* is likewise physiologically and metabolically specific, its most advantageous growth temperature is 37°C, it is proof against low pH and tolerates bile acids. While other traces of *S. cerevisiae* select cooler temperatures (30–33°C) and do now not live on nicely in acidic pH tiers (Fietto *et al.* 2004, Graff *et al.* 2008). *S. boulardii* can be illustrious from the lines of S (As mentioned inside the Work Mechanisms segment).

2.1.2 The effects of probiotics on health

There are a whole lot of studie looking on the fitness advantages of fermented meals and probiotic. Though, in greatest of those studie, investigators did no longer usage sufficient test subject or they usage microorganisms which have no longer been conclusively diagnosed (Duru *et al.* 2003). Therefore, even as some of the said outcomes have simplest been partly confirmed, a few can be taken into consideration as well-hooked up and clinically properly-documente for positive traces. These health-associated results can be careful as defined under (Duru *et al.* 2003, Schrezenmeir and De Vrese 2001, Dunne *et al.* 2001, Dugas *et al.* 1999).

2.1.2.1 Prevention of diarrhea

Bacterial probiotics inhibit pathogens through opposition for vitamins and adhesion websites and/or by generating diverse antimicrobial compounds/metabolites. However, the scenario can also vary slightly among kinds of probiotics. Several traces of probiotics, particularly *Lactobacillus rhamnosus*, have been exposed to save you or relieve diarrhea in youngsters, which is in particular due to rotavirus. It is likewise recognized that some strains of probiotics can save you and shorten antibiotic-related disorders. (Fuller *et al.* 2008).

There is a overall agreement that yeast probiotics absence the capability to provide some antimicrobial metabolite and/or inhibit pathogen (Martins *et al.* 2005, Kourelis *et al.* 2010). But numerous intelligences designate the fruitful inhibition of several pathogen consisting of *Clostridium albicans*, *Escherichia coli*, *Salmonella typhi*, *Shigella dysentery*, *Vibrio cholerae*, *Salmonella enterica* and *Clostridium difficile* by using probiotic yeast (FilhoLima *et al.* 2000, Czerucka and Rampal 2002). Pathogens commonly attach to the epithelium to shape a deadly infection. But yeast probiotic can save you pathogens from binding to intestinal cells through direct hostile impact and/or secretion of diverse metabolites/enzymes. Furthermore, *S. cerevisiae* var *boulardii* lines can contest with pathogenic microorganism for meals and mucosal receptor in the gut, for that reason preventing pathogens from colonizing within the host gut (FilhoLima *et al.* 2000). Likewise, some pathogens together with Escherichia coli or Salmonella possessing such kind I mannose traumatic inflammation bind to mannose remains on epithelial cellular membranes (Ofek and Beachey 1978). Yeasts which include *S. cerevisiae* cover mannan in the outer layer in their cellular wall and hence can exert a shielding impact in opposition to pathogens. These pathogens quite simply bind to the mannan at the yeast floor instead of adhere to intestinal epithelial cells (Gedek 1999; Spring *et al.* 2000) and are then removed from the host's peptic tract afterward agglutination through yeast.

One kind of diarrhea is visitor's diarrhea (TD) that touches healthy vacationers not handiest in growing republics but additionally in Europe. Probiotics have helpful results in stopping some types of TD. Oksanen *et al.* (1990) assessed the effectiveness of *Lactobacillus* species in stopping diarrhea in 820 people journeying from Finland to Turkey. In a double-blind study by means of Black *et al.* (1989), A freeze-dried bacteria (*Lb. acidophilus*, *Bifi. bifidum*, *Lb. bulgaricus*, *Str. thermophilus*) assumed to fifty six Danish travelers on a-week trip to Egypt. The prevalence of diarrhea in the institution getting lactic acid bacteria became forty three% even as it became seventy one% within the placebo group (Gismondo *et al.* 1999).

2.1.2.2 Stimulation of the immune system

Probiotics have additionally been exposed to stimulate each innate and adaptive immunity which in turn might also make contributions to the best health and disease resistance of the host. Yeasts are a wealthy supply of many bioactive substances which can cause the functioning of various organic systems together with the host's immune device (Buts *et al.* 1990, Rodrigues and Pais 2000, Martins *et al.* 2005). Yeast mobile wall components consist predominantly of complex polymers of b-glucans, a-mannans, mannoproteins and the amino thing of chitin (Smits *et al.* 1999). These massive molecules can in the long run stimulate the host's immune system, specially the provocative reply, and the reticuloendothelial system. Lately, Pothoulakis (2009) mentioned at duration the anti-inflammatory device of *S. cereviceae* var *boulardii*. *S. cereviceae* traces have been located to be a higher stimulator of the immune device. In a relative observe, Martins *et al.* (2005) stated higher immunostimulating hobby (in phrases of sIg A and IL10 manufacturing) of *S. cereviceae* var *boulardii* in comparison to bacterial probiotic which include *Bifidobacterium* animals, *E. coli* and *Lactobacillus casei*. Probiotic traces of *S. cereviceae* var *boulardii* had been exposed to improve phagocytic interest in addition to production of numerous cytokines (Rodrigues and Pais 2000, Czerucka *et al.* 2007). Kourelis *et al.* (2010) located the aptitude of hypothetical probiotic yeast strains fitting to *S. cerevisiae* and K. Lactis to growth pleomorphic mobile inflow, phagocytic activity, and several cytokines in the air pouch model. Yet, extended immune responses are often associated with strain. Recently, a few research has reported good sized variability within the capacity of different probiotic strains to induce increased manufacturing of TNF-a, IFN-g and IL-10. But, strains together with K. Latis and K.

Saccharomyces species were discovered to stimulate the level of SIgA in extraordinary animal fashions. In gnotobiotic mice, this grew to become at the phagocytic gadget in conjunction with improved sIg A (Rodrigues and Pais 2000) whilst Buts *et al.* (1990) observed a vast increase in sIgA and the secretory issue of immunoglobulins in mice by using ingestion of *S. immunity* by using cumulative herbal killer cell pastime and phagocytosis, altering cytokine outlines, and cumulative immunoglobulin ranges. Two probiotic strains were evolved with specific emphasis on their ornamental results on immune replies: *Bifidobacterium lactis* and *Lactobacillus rhamnosus*. Both traces have been established in numerous research to beautify everyday immune feature in healthful topics (Fuller *et al.* 2008).

(Perdigón *et al.* 2001) Feeding mice by *lactobacilli* or milk and activated macrophages extended secreted IgA attentions (Scheinbach 1998). Too in a human trial by Fooks *et al.* (1999) feeding 450 grams of yoghurt daily for 4 months, eventually a vast boom within the production of beta-interferon was located.

2.1.2.3 Lactose intolerance

Most non-Caucasians normally broaden lactose intolerance after weaning. Those individuals who are lactose illiberal can't metabolize lactose due to a lack of the number one enzyme β-galactosidase (Ouwehand *et al.* 1999). When they eat milk or merchandise covering lactose, symptoms which includes abdominal ache, bloating, flatulence, cramping and diarrhea. If the lactose permits from the small gut, it is rehabilitated into gasoline and acid inside the huge gut through colon micro organism. The presence of hydrogen in the breath is likewise an indicator of lactose malabsorption (Lin *et al.* 1993). Studies show that including 5 precise starter farms to dairy merchandise, allows humans with lactose intolerance to devour those products with out the usual elevation of breath hydrogen or accompanying signs (Scheinbach 1998, Fooks *et al.* 1999).

The useful consequences of probiotics on lactose bigotry are clarified in two ways. One of them is the lower awareness of lactose in agitated meals owing to the higher lactase pastime of the bacterial arrangements usage inside the production. The different is lactase interest increases whilst the lactase enzyme arrives the small intestine with the agitated creation or with possible probiotic micro organism (Salminen *et al.* 2004).

In yogurt, lactose is transformed to lactic acid and is shaped via bacteria able to generating the enzyme beta-galactosidase; It is a useful stop and appropriate for intake by means of people who are lactose illiberal. Moreover, LAB used in the production of yogurt, *Lactobacillus bulgaricus* and *Streptococcus thermophilus*, is not immune to stomach acidity. Thus, merchandise containing probiotic micro organism are greater effective for people with lactose intolerance. It is believed that the primary element that improves digestibility by way of hydrolysis of lactose is the bacterial enzyme β-galactosidase. Extra component is the slow draining of the belly from semi-solid dairy crops including yogurt. So the β-galactosidase hobby of other probiotic traces and lactic acid micro organism utilized in dairy merchandise is virtually significant. The activity of β-galactosidase within probiotics varies in a wide variety. Both the enzyme interest of the probiotic pressure and the residual pastime inside the very last creation need to be considered to be used in lactose bigoted topics (Salminen *et al.* 2004, Li *et al.* 2012).

2.1.2.4 Toxin neutralization activity

The lethal pollution produced with the aid of pathogens bind to unique receptors in intestinal epithelial cells and as a consequence motive mucosal injury and inflammation. Yeast probiotics often wreck bacterial pollution and factors in their receptors through freeing various enzymes together with protease (Castagliuolo *et al.* 1999). In vitro research advise that proteases present in both whole yeast and the cell wall portion *of S. cerevisia*e var *boulardii* may be worried in inhibiting the adhesion of *Clostridium difficile* to Vero cells regardless of their incapability to adhere to micro organism or Vero cells (Tasteyre *et al.* 2002)

Yeasts can't most effective inhibit the manufacturing of pollutants for plenty pathogens such as *Clostridium difficile*, *Vibrio cholerae* and *Escherichia coli* however also inhibit their harmful outcomes (Vidon *et al.* 1986, Corthier 1997,). The serine protease of *S. cerevisiae* actively degrades pollutants A, one of the two energetic pollutants (A and B) shaped by means of *C. difficile* (Pothoulakis 2009). Likewise, *S. cerevisiae*/*S. cerevisiae* var *boulardii* to decrease fluid secretion and mannitol penetrability brought on by way of *Clostridium difficile* toxin A in the rat ileum (Pothoulakis *et al.* 1993). The fifty four kDa serine protease of *S. cerevisiae* can decrease murine toxin A-precipitated beam secretion and stop toxin A-triggered infection and villous injury by inhibiting the binding of toxin A to the glycoprotein receptor at the brush border (Pothoulakis *et al.* 1993, Castagliuolo *et al.* 1996). However, some other one hundred twenty kDa protein from *S. cerevisiae* var *boulardii* is chargeable for blocking the movement of cholera toxin and turned into observed to lessen cholera toxin-mediated stimulation of cyclic adenosine monophosphate within the intestinal loops of mice (Brandao *et al.* 1998, Czerucka and Rampal 2002, Neves *et al.* 2002, Czerucka *et al.* 2007).

2.1.2.5 Cancer reduction

Epidemiological studies recommend that in case you devour a number of saturated fats for your weight loss plan, this ends in an multiplied prevalence of colon cancer. Recent information support the potential of β-glucans in yeast to gain immune characteristic while ate up and the frame's labors to defend himself from ailment. Preclinical trials have exposed that an industrial yeast-soluble beta-glucan creation, resulting from the cellular partitions of *Saccharomyces cerevisiae*, in aggregate with sure monoclonal antibodies or most cancers vaccines, recovers long-time period survival higher than monoclonal antibodies alone (Vetvicka *et al.* 1996, Ross *et al.* 1999). β-(1 → 6) and β- (1 → three)-glucan branching had been cleansed from the mobile partitions of *Saccharomyces cerevisiae* (Hong *et al.* 2003). The antitumor pastime is triggered by way of a murder mechanism concerning neutrophils organized with a beta-glucan training that is not normally worried in antitumor hobby. When neutrophils bind to cancer cells, the practise of β-glucan permits them to understand cancer, as it become a fungal pathogen and this system presents the kill. Indeed, beta-glucan uses neutrophils to fight most cancers cells, synergistically enhancing the efficacy of monoclonal antibodies and vaccines thru a distinctive killing mechanism.

β-glucan enhances the effect of all activated monoclonal antibodies of the examined supplements, counting breast, liver and lung cancers. Complementary antibody complexes kill most cancers cells. Bacterial enzymes including β-glucornidase, nitroreductase and azoreductase change cancer agents into energetic cancer agents inside the colon. It is believed that probiotics can lessen the threat of cancer by using reducing the pastime of bacterial enzymes, and other guidelines were made through McIntosh as shadows (Scheinbach 1998, Fooks *et al.* 1999).

- Carcinogens/cancer agents are suppressed by way of binding, blocking off or elimination.
- Suppression of bacterial boom by means of enzymatic activities which could convert carcinogens into carcinogens.
- Altering the intestinal pH and therefore changing the interest of bacteria and the solubility of bile.
- Change the colon transit time to remove mutated stool extra correctly.
- Stimulating the immune device.

There are in vitro and in vivo research in people and laboratory animals which have evidence that probiotics have useful results in suppressing most cancers. Oral management of lactic acid micro organism has been exposed to lessen DNA injury because of carcinogenic chemical substances inside the gastric and colonic mucosa of mice. It has been shown that intake of lactobacilli by healthy volunteers reduces the genetic mutations in urine and excretion related to ingestion of cancer causing agents in cooked essence. When it involves epidemiological studies, they demonstration an connotation between agitated dairy crops and colorectal most cancers, and it seems that consuming a big amount of dairy products particularly fermented foods which includes yogurt products containing Lactobacillus or Bifidobacterium caused a decrease incidence of colon cancer (Hirayama and Rafter 2000). A quantity of research have proven that carcinogenic chemical compounds from unique resources within the colon are undoubtedly altered through the intake of positive probiotics (Brady *et al.* 2000). The boom of tumor cells in mice changed into avoided orally through management of insoluble yeast beta-glucan at a awareness of 28.4 mg/kg for 21 consecutive days (Vetvicka *et al.* 1996).

2.1.2.6 Respiratory tract infections

The respiration belongings of probiotics in animal models protected attenuation of allergic airline replies and protection towards respiratory pathogens. Dendritic cells look like principal to guiding the helpful immune response to probiotic bacteria and in interpreting microbial indicators from the innate immune machine to the adaptive immune device, at the same time as regulatory T cells grow to be capability key influences of probiotic-mediated responses, particularly in desensitizing flare-ups. Despite advances in primary research, scientific trials of probiotics in allergic reaction/allergies and respiration infections have been incredibly variable at first-rate, undermining self belief on this ability remedy approach (Forsythe 2011).

2.1.2.7 Constipation

Studies of the impact of lactic acid micro organism on constipation and bowel movement have proven reduced constipation severity and stepped forward bowel motion incidence and stool constancy in constipated however otherwise wholesome topics after consuming agitated dairy products covering *Lactobacillus casei* pressure Shirota. Administration of *Bifidobacterium longum* BB536 to constipate women meaningfully lengthy the frequency of defecation and softer stools. A nice impact of *Bifidobacterium longum* BB536 on 'regularity' within the elderly has too been suggested (Ouwehand *et al.* 2002).

2.1.2.8 Diabetes and hypertension

Diabetes and hypertension are comorbidities that regularly occur collectively in the identical sufferers. Induction of insulin resistance frequently leads to diabetic dyslipidemia, and this is greatly extended with the aid of accelerated stages of plasma entire cholesterol, low-density lipoprotein ldl cholesterol, very -low-density lipoprotein ldl cholesterol and ldl cholesterol (Yadav *et al.* 2006). The effectiveness of probiotics in lowering serum cholesterol levels as proven in exceptional in vivo models can recover insulin resistance. It has been advised that intake of probiotics can lessen the onset of insulin resistance and as a consequence lessen the incidence of excessive blood strain intently related to diabetes.

Previous research additionally hypothesized that the start of diabetes is related with poor provocative fame in people who consumed high-fat diets for extended intervals (Cani *et al.* 2007) assessed the results of a excessive-fats weight loss plan on lipopolysaccharides the use of mice. As a version. The authors showed that the arrangement of the ordinary intestinal microflora frequently determines the grade of irritation that contributes to the start of diabetes and weight problems. The attentiveness of lipopolysaccharides in plasma, that's the stimulating thing for inflammation, is contrariwise associated with the organization *Bifidobacterium* spp. The concentration of *Bifidobacterium* spp has too been pronounced in high-fats diet-brought about diabetes. In the intestine favorably with better glucose tolerance and glucose-prompted insulin secretion in addition to reduced inflammatory cytokines for glucose, plasma, and adipose tissue (Cani *et al.* 2007), numerous research have additionally proven that Bifidobacteria can decrease tiers of intestinal endotoxins and enhance the mucosal barrier and hence lessen Systemic inflammation and thus abridged occurrence of diabetes (Cani *et al.* 2007).

In a randomized, double-blind, placebo-managed human take a look at of 25 healthful aged volunteers (imply age 69 years; range 60 ± 83 years), low-fat milk covering 1.Five x 1011 CFU of Lactobacillus lactis two times daily to find a six week period To decorate the immune reaction of the elderly, without liberating inflammatory cytokines, thereby lowering the onset of inflammatory-caused diabetes (Arunachalam *et al.* 2000). Another observe through (Matsuzaki *et al.* 1997) showed a massive lower in plasma glucose in four-week-vintage non-insulin-based male rats that have been fed 2 mg of lyophilize *Lactobacillus casei* 5 instances in keeping with week for a 16-week trial period.

The authors decided that intake of probiotics suppresses the manufacturing of pro-inflammatory cytokines that could principal to diabetes, and in the end prevent the onset of diabetes-related high blood pressure.

The prevalence of diabetes mellitus due to systemic inflammation has been found with a low ratio of Gram-high-quality: Gram-negative intestinal micro organism. This decrease ratio inclines to boom the obtainability of proinflammatory molecules and lipopolysaccharides in the frame which might be chargeable for systemic infection, leading to diabetes.

These consequences suggest the useful outcomes of probiotics inside the treatment of diabetes in synergy with different diabetes medicines and as a result reduce the occurrence of diabetes-related high blood pressure.

The authors additionally found that plasma total cholesterol, low-density lipoprotein ldl cholesterol and low-density lipoprotein levels of cholesterol have been reduced, resulting in decreased insulin resistance. The proposed devices are inhibition of insulin reduction, protection of diabetic dyslipidemia and inhibition of lipid peroxidation and nitrite formation in mice. This result designated that ingesting of probiotic merchandise decreased the risk of diabetes and associated problems in people with fructose- persuaded insulin resistance (Al-Salami *et al.* 2008).

A range of probiotic straining have also been discovered useful in lowering the onset of insulin confrontation and diabetes in animals. The parts of probiotics in lowering the onset of insulin resistance, hyperglycemia, and dyslipidemia have led to fine consequences. It is thought that probiotics may be usage as an other preventative measure and remedy for diabetes and for this reason lessen the risk of excessive blood strain associated with diabetes (Tabuchi *et al.* 2003)

2.1.2.9 Cholesterol reduction

Several researchers have advised that probiotics have cholesterol-reducing results. Though, the device of this impact can't be conclusively explained. There are two hypotheses that try to clarify the device. One is that the micro organism might also bind or include ldl cholesterol immediately into the cell membrane. The different approach is bile salt hydrolysis enzymes damage down the conjugate of bile salts that is possibly to lead to extra cholesterol used inside the synthesis of bile salts (Duru *et al.* 2003, Prakash and Jones 2005).

Yeast β-glucan is normally known as a safe product (GRAS), which can be used as a meals preservative. In addition, β-glucans from various bases have efficacy in reducing cholesterol and lipids (Mason 2002). Human research round the arena have proven beta-glucan to be a safe, powerful, and cheaper way to decrease ldl cholesterol and multiplied lipids (Bell *et al.* 2001, Keogh *et al.* 2003, Ronald Steriti 2007). Reducing blood lipids, total ldl cholesterol and LDL cholesterol is the fine manner to save you high blood stress and atherosclerosis. Natural β-glucans arrangements consisting of oat or barley milk or yeast-glucans additional to juice liquids can be utilized in location of costly medicines with extreme aspect effects (Naumann *et al.* 2006).

Several human research have evaluated the consequences of dairy products containing cultured or probiotic bacteria on cholesterol levels, with vague effects. Agitated milk covering *Enterococcus faecium* and *Streptococcus thermophilus* has been suggested to supply a small but considerable reduction in general cholesterol and LDL ldl cholesterol in sufferers with number one hypercholesterolemia (Pereira *et al.* 2002)

2.1.3 Mechanism of probiotics actions

Microorganisms are careful probiotics to guide host health. Though, support devices have not been elucidated (Holzapfel *et al.* 1998). There are studies on how probiotics paintings. Therefore, numerous devices from those studies try to provide an explanation for how probiotics can also defend the host from intestinal complaints. These mechanisms are in short noted underneath (Castagliuolo *et al.* 1999, Salminen *et al.* 1999,Duru *et al.* 2003).

- Production of inhibitory materials: production of a few natural acids, hydrogen peroxide and bacteriocins that inhibit Gram-fantastic and Gram-negative bacteria.
- Blocking sites of adhesion: probiotics and pathogenic micro organism in opposition. Probiotics inhibit pathogens with the aid of attaching to intestinal epithelial surfaces by way of bridging the adhesion websites.
- Competition for Nutrients: Although there aren't any in vivo research, probiotics inhibit pathogens by ingesting vitamins wanted with the aid of pathogens.
- Immunity stimulation: Stimulation of specific and non-particular immunity can be one of the feasible mechanisms for probiotics to shield the host from intestinal illnesses. This device isn't properly recognized, however it's miles supposed that additives of the cell wall or certain cell layers might act as adjuvants and increase the humoral immune reply.
- Toxin receptor degradation: Due to the deterioration of toxin receptors in the intestinal mucosa, *S. boulardii* has been shown to defend the host from *Clostridium difficile*. Some of the other mechanisms on display are conquest of toxin manufacture, reducing gut pH, and mitigating virulence (Fooks *et al.* 1999).

2.2 *E. Coli*

(Holt *et al.* 1994) indicates that the colon bacteria are gram negative bacilli, whose length ranges between (6-2) µm and width (1-0.6) µm. (Quinn *et al.* 1994) indicated that these bacteria do not form non- spores. spore forming, and they are motile by peritrichous flagellae, and there are non-motile strains of them as well. And (Holt *et al.* 1994) showed that coliform bacteria grow at a temperature of 37°C ideally and can also grow within a temperature range between 20-45°C, and on most normal culture media, whether these media are liquid or solid. It was also shown (Jawetz *et al.* 2004) that *E.coli* bacteria are characterized by the ability to produce indole, ferment mannitol and produce gas from glucose. All *Escherichia* strains are positive for Methyl Red test and give negative reactions to Vogas-proskaur and Phenylalanin diaminase, and they are generally urease negative and do not produce hydrogen sulfide H_2S in Triple agar iron medium. Count (c) The type *E.coli* is commonly isolated from feces. As for the agronomic properties, *E.coli* bacteria can grow on simple laboratory media containing glucose as a major carbon source, the optimum temperature for growth (37-36). Holt *et al.* (1994) confirmed that most strains isolated in medical laboratories ferment the sugar lactose and therefore grow as soft, radiant pink colonies on the medium of Maconkey agar, and that (80%) of the strains are motile and others are immobile when Primary isolation, most strains give a metallic green color when grown on Eosin Methylene Blue (EMB) medium. According to what was indicated by Curran and Murray (1999) *E. coli* is part of the normal flora in the intestines of healthy individuals, but there are strains that can cause diseases in the digestive system as well as infections of the urinary system. The researchers noted

to its role in causing *Peritonitis*, *Septicem*ia, *Meningitis*, *Cholecystitis*, *Pneumonia*, Wound Infections, and and intestines in infants (Feder *et al.* 1986). *E.coli* bacteria are one of the most important types of the intestinal family, due to their natural presence in different areas of the body, and this makes them able to infect the body opportunistically whenever the opportunity arises, and they are abundant in ulcers as they are facultative anaerobic and may lead to Peritonitis and cholecystitis
Cholecystitis and Bacteraemia. It also affects the lower parts of the respiratory system, especially in surgical operations. It was mentioned Ewbank and Creighton (1993) that coliform bacteria may lead to infection in the lower parts of the urinary system and bladder, and colon bacteria have many virulence factors that help them to cause diseases. Among these factors, according to Shapiro and Senior (1999), the ability of bacteria to invade, and this is mediated by one of the surface antigenic structures represented by the somatic antigen.

O antigen somatic antigen

Flagellar antigen called H antigen (Brooks *et al.* 1998) and colonization factor (Brito Neves *et al.* 1999) and the interaction between cell receptors in the body. Colonization factors antigen CFA of all kinds help in this process, in addition to the role of velvet hairs (Lee and Schneewind 2001) and capsular antigen (K-antigen) are important for bacterial attachment to host cells (Bounous *et al.* 1994). As for hemolycin, as indicated by many investigators (Waalwijk *et al.* 1983, Opal *et al.* 1990, Oswald *et al.* 1993), it is of great importance in increasing the virulence of colon bacteria, and thus this is reproduced in the augmented pathological effects of this bacteria. It works on being on the surface of the red blood cell and forming holes in it, causing the hemoglobin to come out and thus iron loss. And because they are talented to grow in anaerobic circumstances, indicated that they are characterized by wide and varied capabilities to highlight their different functional activities, and they usually use them to adapt to external conditions, especially when they exist in environments outside their characteristic habitats, and to indicate these capabilities The simplicity of its growth requirements mentioned (Prescott *et al.* 2015) that, for example, it can grow in a medium consisting of a very simple solution that does not contain any food ingredients except glucose sugar as a single organic compound in it, and Dozois *et al.* (1997) showed that the wild type The wild-type of these bacteria does not need any specific growth factors in order to assign its various metabolic activities when it is present in different other conditions, as its bacilli, without any growth aid factors, can employ glucose molecules alone to form macromolecules that block them The needs of its cellular structure, whether when oxygen is available in aerobic conditions or when it is not available in anaerobic conditions, through fermentation of this sugar and generating products Composed of a different mixture of acids and gases (Prigent *et al.* 2001). In addition, it is also able to grow using the anaerobic respiration process by consuming nitrates NO_3, nitrite NO_2, and fumarates by using these compounds as final electron acceptors to conduct the electron exchange process required for this type of respiration (Roos *et al.* 2006).

2.2.1 Pathogenicity

Krieg and Melton (1984) indicated that although *Escherichia coli* is one of the bacterial species that naturally coexist in the intestine microflora for humans and other vertebrates, but it is considered an opportunistic bacteria because it causes a wide range of different pathological infections, whether in humans or in animals. As Simpson and Smith (1992) showed that the mechanism through which infection with strains of this bacteria occurs is a complex mechanism, and the available information about it is still incomplete. Certain adhesion, viability in various body fluids in the presence of low iron concentration. pointed

Falk *et al.* (1990) indicates its ability to escape from phagocytosis and to resist intracellular killing when ingested by phagocytes. Also Tesh, (1998) indicated that strains of *Escherichia coli* use virulence factors directly or indirectly through their products, or both in directing the immune response in their favour.

The following is a brief presentation of the most important diseases caused by these bacteria in humans

2.2.1.1 Urinary tract infections (UTI)

The two researchers Joklik *et al.* (1950) and, Brooks and Endler (2001) stated that the infections caused by this bacteria in the urinary tract and resulting from its pathogenic strains of this system uropathogenic E. coli are among the most important infections caused outside the intestines of extraintestinal human infections, as they constitute about about 80-90% of the total infections caused by other bacterial species. Some reports issued in this field also indicate, as indicated by him

Dillman *et al.* (1998) indicated that the total number of people infected with UTI diseases only as a result of hospitalization with Nosocomial infection is 900.000 cases annually in the United States of America alone, and more than half of them are due to *Escherichia coli*. Watanabe *et al.* (2009) also indicated that most urinary tract infections caused by these bacteria, including cystitis, occur due to contamination of fecal origin in the lower parts of the urinary tract from the contents of the intestine contaminated to the area surrounding the opening of the urethra.

Urethral orifice, i.e. an ascending infection with strains of this bacteria, as this infection is transmitted towards the upper parts of this device, and infection may occur in these parts of this device with this bacteria also through the transmission of this infection from the bloodstream after a case of bacteremia. According to Conley *et al.* (2004), colonization of the tissues lining the bladder *by Escherichia coli* occurs through certain types of adhesions, represented by a special type called cilia or fimbria known as P-fimbria. Its presence when it was discovered in cases of pyelonephritis associated pili, called PAP for short, and it is unique of the greatest significant factors of adhesion to strains of Escherichia that infect the urinary tract, as it was found that it can attach to special receptors for it present on the epithelial cells lining the bladder. 99% of the strains that cause repetitive injuries are this type of injury.

2.2.1.2 Enteric infections

Brooks and Endler (2001) indicated that although colon bacteria in normal conditions, especially those that inhabit the intestines, are harmless to them, some of their strains are enterovirulant in various circumstances, because they possess special virulence factors that can These strains can be divided into several groups depending on their pathogenicity and virulence factors, as follows:

1. **Enterohemorrhagic E.coli EHEC**

It was mentioned Brooks and Endler (2001) that it includes strains of *Escherichia coli* that cause hemorrhagic injuries in the intestine, the most important of which are Hemorrhagic Colitis HC, and Hemolytic Uremic Syndrome HUS. The virulent strain symbolized by the O157:H7 antigen, as mentioned Palermo *et al.* (2009), is the prototype for this group, and one of its important characteristics is its production of the highly effective Virotoxin, which is similar in many properties to the toxin similar to Shiga-shiga. like toxin, which is secreted by some species of *Shigella bacteria*.

2. **Enteroinvasive E.coli EIEC**

The strains that cause acute diarrhea include dysentery caused by *Shigella bacteria*, and these infections usually occur as a result of the bacteria invading the mucous layer lining the colon (Brooks and Endler 2001).

3. **Enterotoxigenic E.coli ETEC**

The strains of this group are among the main causes of traveler's diarrhea Travellar`s diarrhea in adults, cases of diarrhea in infants. Infantile diarrhea. The strains of this group produce two types of intestinal toxins: heat stable toxins (ST) and thermally variable toxins (heat labile toxins (LT), both of which have a special effect on the intestines that lead to a state of disturbance in its functions, including its excretory system, which leads to cases of diarrhea (Brooks and Endler 2001).

4. **Enteropathogenic E.coli**

EPEC The strains of this group are one of the main reasons of diarrhea in infants, especially in poor regions of the world, and its members are characterized by a great ability to adhere to the epithelial layer of the layer of cells lining the intestine, causing important changes. In their cytoskeletal structures 2001, cytoskeletal changes (Brooks and Endler 2001).

5. **Enteroadhesive E.coli**

EAEC, which is the latest group that entered this classification for virulent strains of *E. coli*, and it was found that it causes about 30% of cases of traveler’s diarrhea in American citizens who enter the neighboring country of Mexico, according to what is mentioned (Dillman *et al.* 1998) in his research.

2.2.1.3 Meningitis *E. coli*

is one of the main causes of meningitis cases in neonates neonates, that is, children less than 28 days old, where the total meningitis infections caused by these bacteria in addition to similar infections caused by *Streptococcus* group BB. Most infections with this disease are in this age group of children, and it is responsible for about 8% of deaths in them (Brigotti *et al.* 2008). The researchers found, through one study in this field, that about 75% of the strains of *Escherichia coli* that cause this type of infection carry the 1-K antigen, and there is also evidence (Brooks *et al.* 2007, Chase-Topping *et al.* 2007). On the existence of a cross reaction between this antigen belonging to this bacterium with the polysaccharide antigens of the type *B. bacterium N. memingitidis*. It is mentioned Brooks and Endler (2001) that the real mechanism by which the 1-K antigen appears is still virulent in this type of infection. It is vague and subject to continuous studies in this field.

2.2.1.4 Other miscellaneous infections

Brooks and Endler (2001) also mentioned that there is another group of different diseases resulting from infection with this bacteria, the most important of which are: pneumonia, septic arthritic inflammation, conjnetivitis, suppurative thyroiditis, sinusitis, oesteomylitis, endocarditis, skin and soft tissue infections, among others.

2.3 Relationship of Probiotics and Bacteria Pathogen

Probiotics in the deterrence and treatment of diarrhea The usage of probiotic microorganisms for the deterrence or remedy of gastrointestinal problems is an clear measure and maybe the maximum not unusual software of probiotics since greatest

The health consequences credited to them are without delay or in a roundabout way (i.E. Mediated by using the immune system) associated with the digestive device. The devices and efficacy of the impact of probiotics frequently be contingent on connections with host-specific bacteria or immune-equipped cells inside the intestinal mucosa. The gut (or related lymphatic device, GALT) 5 is the largest immune-equipped organ inside the frame, and the most beneficial maturation and growth of the immune system after delivery relies upon on the growth and arrangement of the original micro organism and vice versa. Several strains of probiotic microorganisms had been exposed to inhibit boom and metabolic action as well as bond to intestinal cells of enteric pathogenic micro organism (*Salmonella*, *Shigella*, *Escherichia coli*, or *Vibrio cholerae*) (1-3) to (quickly) alter the intestinal microflora and feature immunological or controlling residences. The proposed devices of effects at the intestinal microflora are dropping the intestinal pH, manufacture of bactericidal materials e.g. organic acids (lactic, vinegar and acid) (Keersmaecker *et al.* 2006), H_2O_2 and bacteriocins, agglutination of pathogenic microorganisms, adhesion to the cellular floor of the mucous membrane, opposition for fermentable substrates or receptors, enhancement of the intestinal mucosal barrier impact (Eizaguirre *et al.* 2002, Mangell *et al.* 2002), release of intestine-protecting metabolites (arginine, brief-chain fatty acids, glutamine, conjugate linoleic acids), binding and metabolism of poisonous metabolites (Bingmark 1996, Oatley *et al.* 2000), immune mechanisms (Gill *et al.* 2001) or law of gut motility (Marteau *et al.* 2002) and mucus manufacturing (Mattar *et al.* 2002). In human and animal trials, bacterial totals in stool examples and in examples from the small gut occupied from circle of relatives patients have been changed by using probiotics. Though, a majority of these strategies have drawbacks and handiest not directly reflect the real scenario in the digestive device and its microflora. The connections among probiotic microorganisms and GALT or associated mucosal receptors, gesturing trails pathways, immune modulation mechanisms, and anti inflammatory results of probiotics aren't yet absolutely unspoken, but the usage of modern-day technology consisting of molecular biology is leading to rapid increase in information of the relationships amongst probiotics, the immune device and health. Protective or therapeutic consequences of probiotic microorganisms with indication of belongings at the intestinal microflora and antibacterial, immunomodulatory and anti-inflammatory properties examined in diarrhea as a result of (number one) lactose bigotry; acute diarrhea due to viral and/or bacterial infections, which includes rotavirus contamination in kids, gastrointestinal infections in kids in day care facilities, visitor's diarrhea; antibiotic-related diarrhea (AAD); *Clostridium difficile* gastroenteritis. Diarrhea in tube patient. Diarrhea resulting from chemotherapy or radiation. Inflammatory bowel illnesses (Crohn's ailment, ulcerative colitis, sinusitis); Overgrowth of micro organism within the small intestine. Irritable bowel syndrome with diarrhea.

2.4 Treatment of Infectious Diarrhea Using Probiotics

The majority of a hit probiotic treatments for communicable diarrhea (or probiotics, additionally known as clinically used probiotics) were achieved on younger kids (Elmer *et al.* 1996). Many of them suffered from rotavirus contamination in hospitals, or were diagnosed with viral and bacterial contagions within the studied institution. Analysis of nine or 18, correspondingly, randomize and blinded eligible topics for acute diarrhea in healthy babies confirmed a mean discount in length of episodes of 0.7 or 1 day (Huang *et al.* 2002, Niel *et al.* 2002) and a discount in stool incidence of 1.6 stools on the second day of remedy (Niel *et al.* 2002). In businesses getting probiotics (specially *lactobacilli*). Yet, it has been posted that *L. rhamnosus* strains have been only effective in treating diarrhea due to rotavirus in children but no longer in treating diarrhea of different etiologies (Szymanski *et al.* 2002). In other toddler scientific trials, LGG, one of the maximum a success probiotics ever, turned into ineffective in benign rotavirus contamination (Mastretta *et al.* 2002) and in severely dehydrating diarrhea (Costa-Ribeiro *et al.* 2003). The healing effectiveness of probiotic microorganisms is not enough in instances of acute communicable diarrhea, or probiotics manifest their healing result too gradually. This is constant with a current evaluate Szajewska *et al.* (2005) that the therapeutic results of probiotics in kids with acute diarrhea look like 1) moderate, 2) pressure- (LGG, L. Reuteri, B. Lactis Bb12) and three) dose-dependent, four) more pronounced while probiotics are used early within the bout, and five) simplest considerable in watery diarrhea and viral gastroenteritis but now not in invasive bacterial diarrhoea. A smaller range of randomized managed trials of every composition have been carried out on wholesome adults. A meta-analysis of 23 randomize skillful studies in adults and children with a complete of one,917 human beings concluded that probiotics decrease the common length of diarrheal incidents by 30.Five hours and seem to help deal with acute dehydration. Severe diarrhea (Allen *et al.* 2014). In end, the protective and healing outcomes of some dietary probiotics, especially LGG, against rotavirus (nosocomial) infection in kids are fantastically properly supported. The use of food or medicinal probiotics in opposition to different pathogens, in adults and children in 0.33 world countries, and for intense diarrhea (dehydration) has been much less a success. Therefore, at gift, the outcomes of randomized managed clinical studies are too contradictory to give particular tips for the scientific usage of probiotics. Too, in regards to the prevention of tourist's diarrhea, not one of the examined probiotics may be advocated with out booking, mainly since of inconsistent observe outcomes concerning the variety of tour approaches and placement-precise pathogens.

3 MATERIALS AND METHODS

3.1 Materials

3.1.1 Apparatus and instruments

The equipment's and apparatu, which usage in this study, are exposed in Table 3.1.

Table 3.1 Equipments and apparatus

No.	Apparatus	Company and Origin
1	Milko-Scan System	Lactostar, Germany
2	Microscope	Olympus, Japan
3	Water bath	Kottermann, Germany
4	Shaker incubator	Labtech/Korea
5	Incubator	Memmert, Germany
6	Centrifuge	Hettich, Germany
7	Shaker	Reichart, Germany
8	Electric Balance	Sartorius, Germany
9	Air Oven	Gallenkamr, England
10	Distillator	GFL, Germany
11	UV-Visible Spectrophotometer	Shimadzu, Japan
12	pH Meter	PHM, England
13	Plastic petri Dish	Syria
14	Flasks	Germany
15	Burette	Germany
16	Autoclave	Germany
17	Refrigerator	Concord
18	Micropipette	Dragon/China
19	Slides	Germany
20	Hood	Marubeni
21	Anerobic jar	Rod well, Germany
22	Thermometer	Savety
23	Haemocytometer chamber	Marienfeld
24	Vitek2 System	Germany
25	Auto-Hematology analyzer	Human, Germany
26	Reflotron	Roche, Germany

3.1.2 Biological and chemical materials

The following Biological and chemical materials usage in present study as follow in the Table 3.2

Table 3.2 Biological and chemical materials

No.	Material Names	Company and Origin
1	Ethanol, Chloroform.	BDH (England)
2	McFarland	Germany
3	Glucose kit	Giesse (Italia)
4	Urea kit	
5	Creatinin kit	
6	Sodium kit	
7	Potassium kit	
8	Calcium kit	
9	AST kit	
10	ALT kit	
11	ALP kit	

3.1.3 Dyes, reagents, solutions and buffers

The following Dyes, reagents, solution and buffer usage in present study (Table 3.3)

Table 3.3 Dyes, reagents, solution and buffer usage

No.	Reagents and solutions	Company and Origin
1	Gram Stain	BDH, England
2	Methyl Red	BDH, England
3	Methyl Blue	
4	Indicator Phenolphthalein (1%)	
5	Cyclohexamide Solution	
6	Phosphate buffer solution (PBS)	
7	NaOH 0.1N	
8	Hydrogen peroxide	

3.1.4 Cultural media

The cultural media used in present study is shown in Table 3.4

Table 3.4 Cultural Media

No.	Media	Company and Origin
1	Nutrient Agar (NA)	HIMEDIA, INDIA.
2	Sabouraud Dextrose Agar (SDA)	
3	Corn Meal Agar(CMA)	
4	Malt Extract Agar(MEA)	
5	Rose Bengal Agar (RBA)	
6	Yeast Extract Powder (YEP)	SIGMA, USA.
7	Carbohydrate Fermentation Medium	
8	Yeast extract peptone Dextrose Broth Medium (YPDB)	
9	DeMan Regosa Sharpe (MRS)	MERCK, GERMANY.
10	Potato Dextrose Agar (PDA)	
11	MacConkey Agar	
12	Skim milk	ALSAFI, SAUDI

3.1.4.1 Preparation of culture media

All Cultural Media were prepared (exception of synthetic Medium) according to the manufacturer's instructions label.

3.1.4.2 Synthetic culture media

Carbohydrate Fermentation Medium

This medium was prepared according to (MacFaddin 2000) as follow:

Basal medium: This media were prepared by dissolving 10g of peptone, 5g of NaCl, 50mL of phenol red reagent which prepared in one liter of distilled water, then the pH was adjusted to 7. And each 100 mL of medium dispensed into one flask and sterilized by autoclaving. The media cooled to 45-50°C.

Sugar solution: Prepared the solutions of sugars, sucrose, Mannose, Lactose, Galactose, D-glucose, Ribose, Sorbitol, Mannitol, Xylose, Maltose and Rafinose, by dissolving 1 g of each sugars in 100 mL of sterile distilled water, then sterilized solutions mediated by filter paper with diameters of 0.22µm.

The 10 mL of sugar solution (10%) which was prepared in (B) was added to give a concentration (1%) of each sugar in medium. Finally, the medium dispensed into test tubes (5 mL for each tube) then stored at 40° C until use. It was used to appearance the ability of yeasts and bacteria in ferment sugars and gas production. (Harrigan and MacCance 1976).

Yeast extract peptone Dextrose Broth Medium (YPDB): The preparation of this medium was done by dissolving the following components (g/L): Yeast extract powder 10g, Peptone 20g, Dextrose 20g. In 1000 mL of distilled water, pH adjustment at (7), and autoclaving at 121ºC, for 15 minutes.

Starch Agar Medium: This medium was prepared by dissolving (23) g Nutrient agar in (500) mL of distilled water and (10) g of starch in the (250) mL of distilled water, then mixed the ingredients, sterile using autoclave, and poured in sterile Petri dishes. This medium was used to test the ability of isolates in degradable starch. The appearance clear zones around colonies was indicated for the positive result, while the blue areas was indicated to negative result.

Skim milk broth: Skim milk supplemented with 5% (w/v) sucrose was boiled to 90°C, then autoclaved and placed in water bath at 35°C for until used.

3.1.4.3 Reagents and indicators preparations

They were prepared according to (MacFaddin 2000, Prescott *et al.* 2015) as follows:

Oxidase Test Reagent: Mix 1.0g of dimethyl-phenylenediamine hydrochloride in 100 mL of distilled water. Preferably, the reagent should be made up fresh, daily. It should not be stored longer than one week in the refrigerator. Tetramethyl-phenylenediamine dihydrochloride (1%) is even more sensitive, it was used for detecting the production of oxidase enzyme.

Catalase reagent: It was prepared in concentration (3%) H_2O_2. It was used for detecting the production of catalase enzyme.

Iodine, 5% Aqueous Solution: Dissolve 4 gm. of potassium iodide in 300 mL of distilled water and then add 2.0 gm. iodine crystals.

MacFarland standard solution: This solution was prepared by mixing 0.05 mL of aqueous solution of barium chloride concentration (1.175%) to (9.95 mL) solution of sulfuric acid concentration (1%) for a turbidity equal to the concentration of microorganisms amount at (1.5 × 108) cells / mL, then keeping this standard in clean and dry test tube and cover its exactly strong for preventing solution evaporation then keeping in dark until using

Phenol red reagent: It was prepared by adding 1g of phenol red to 10 mL NaOH (0.1M) and 20 mL distilled water then dissolved by gentle heating.Later10 mL HCl (0.1M) was added then the volume completed to 500 mL by distilled water. The final concentration of solution was (0.2%).

Methylene blue solution: It was used for the preparation of methylene blue milk broth medium. This solution was prepared by dissolving 1gm methylene blue in 10 mL distilled water then filtrated by Millipore filters (0.22μm).

Phosphate Buffer Solution (PBS): This solution was prepared by dissolving of 1.21 g of K_2HPO4 and 0.34 g of KH_2PO_4 and 8 g of $NaCl_2$ in 1000 mL of distilled water, and the pH was adjust to 7.2.

Acid dichromate solution: Prepared by adding 70 mL of concentrated sulfuric acid to 125 mL of D.W. in a 500 mL conical flask, add (carefully and with constant swirling). Cool under the tap then adding 0.75 g of potassium dichromate and diluted to 250 mL with distilled water.

Sodium thiosulfate solution: Prepared by dissolve 7.44 g of $Na_2S_2O_3.5H_2O$ in one liter of distilled water.

Starch solution: This solution was prepared at 1% by dissolve of 10g of starch in one liter of distilled water. Phenolphthalein Indicator 1%:

3.2 Methods

3.2.1 Microbial isolation

3.2.1.1 Yeast isolations

For isolation the Saccharomyces cerevisiae and Cryptococcus curvatus yeasts we collecting the sweets samples from different sources as, (Nestle Bluffer, Nestle cocoa, pretzels and nuts), sausages (Iyad Emirates origin, type Kescan Ihsanoglu, a Turkish origin), and a drug Antox. The samples were keeping in Polyethylene sterile containers. The necessary information were recorded and transferred to the laboratory immediately (Korn-Wendisch and Kutzner 1992).

After collection the sweets samples types mentioned above. each samples were leaves for five days as exposed to the normal laboratory environmental with humidity at 60% by adding distilled water, then incubation at 30ºC for 48 hours. After these process weight

25 grams of each sample and added to 225 mL of physiological saline solution, then mixed with a 15 mints with magnetic stirrer then take 1mL of diluted solution and streaking on Potato Dextrose Agar (PDA) and incubation at 30ºC for 48 hours.

Isolated the yeast *Saccharomyces cerevisiae* from drug Antox, Antox antioxidant tablets Produced By Arab Company for Pharm and Medicinal Plants Mepaco-Egypt, dissolving 1 tablet in the 10 mL of distilled water and taking 1mL and inoculating the petri dishes of NA and SDA her incubation a temperature 37ºC for 48 hours.

After the peroid of the incubation selected colonies questionable, and Subculture on petri dishes from the Medium of (NA) and the Medium (SDA) and the NA slants, and incubated conditions ideal temperature of 37ºC for 48 hours, and kept isolates pure at the Media of the (MEA) and (RBA) at a temperature of 4ºC, thru the period of diagnosis and work, making Subculture every 20 days, then make the tests were morphological, Physiological characteristics and biochemical study for the diagnosis of yeasts.

3.2.1.2 Lactic acid bacteria isolation

Bifidobacterium bifidum and *Lactobacillus casei* were obtained from the Food Science Department in College of Agriculture, Tikrit University were verified by conducting several tests. Subculturing each isolates on plates contains MRS medium by streaking method and cultivation anaerobically at 37ºC for 48 h on MRS-CaCO3 agar in anaerobic jar according to (Atlas 1995). Isolates on MRS or MRS-CaCO3 agar were selected and subculturing on the same medium.

3.2.1.3 Kefir grains

This was brought from HiMedia company, India and were prepared according to company manufactured illustrated

3.2.2 Microbial identification

3.2.2.1 Yeast identifications

Morphological and Microscopic Characterization: Isolated colony were tested for important phenotypic characterizes, color and types of ground and aerial mycelium and pigments produced after cultivated on Sabouraud Dextrose Agar (SDA), Malt Extract Agar (MEA), Corn Meal Agar (CMA) and Rose Bengal Agar (RBA) media

The suspected colonies were stained using gram stain and methylene blue, methods and their shapes, colors, and arrangements were observed under light microscope.

Biochemical characteristics: Biochemical tests were acquired according to (Van der Walt and Yarrow (1984) which included:

- **Catalase test:**

Catalase production was detected by adding the 3% H_2O_2 to an appropriately yeast culture incubated on PDA medium at 18 to 24 hours. Bubbles of O_2 represent a positive catalase test; the absence of bubble formation is a negative catalase test (Atlas 1995).

- **Oxidase test:**

The capability of yeast to produce cytochrome oxidase may be decided through adding the oxidase check reagent to the cultured colonies on a plate medium or the use of a timber stick, and the yeast sample may be rubbed on the dry slide oxidase reaction area, on clear out paper moistened with oxidase reagent. The light purple oxidase test reagent acts as a artificial substrate, giving electrons to cytochrome oxidase and within the system it's miles oxidized to a crimson after which darkish red compound within the attendance of O_2 and oxidase. The attendance of this dark red colour represents a tremendous take a look at. The absence of an alternate in shade or a mild crimson coloration on the colonies designates the nonappearance of oxidase and is a negative check (Prescott *et al*. 2015)

- **Sugar fermentation broth media**

These media were used to differentiate the species of yeast. The positive results were indicated by changed the broth medium to the yellow color.

- **Pseudo or true mycelium formation on CMA and NA**

This test was executing by prepared of CMA and NA by transfer of two colony to plates and pour of the medium individually then cultural of agar medium to note pseudo or true mycelium formation.

- **Germ tube formation**

This test was carried out by mixing small part of the yeasts colony with 0.5 mL of human serum in a sterile tube then incubate the mixture for 3 hours at 37ºC. After these take a drop from mixture on a glass slide and, examined under a microscope to observe the formation of germ tube that appears in a long stretch from the surface of yeast cells. (Atlas 1995).

- **Yeast resistant's to 0.1 and 0.01% of cycloheximide solution in NA.**

One mL of cycloheximide at 0.1 and 0.01% concentration were transferred to petri dish then the Sabouraud Dextrose Agar, was poured. The agar plates were inoculated with the yeast and incubated at 37º C for 24 hours. Then observed the growth of yeast.

- **Growth at different temperatures:**

This test was carried out according of (Buck and Gilliland 1994), by inoculated of YPDB Medium tube with 0.1 mL of activated yeasts broth and incubated with different temperatures 15, 25, 30, 37 and 45°C for 3-5 days. Then assay of yeast growth levels was obtained by measure the medium turbidity with the MacFarland solution (Holt *et al.* 1994)

3.2.3 Tests of yeast and LAB as probiotics

3.2.3.1 Ability to growth at different pH levels

The YPDB medium (yeast) and MRS medium (LAB) to was distributed to 5 mL in test tubes after moderate for serious pH from 2 to 9 through adding 0.1 N HCl or 0.1 N NaOH, each tubes then inoculated with 0.1% from each yeast and LAB isolates, and incubated at 35°C for 24 hours. Turbidity when occurred was indicated to positive result (Holt *et al.* 1994).

3.2.3.2 Ability to growth in different bile salts concentrations

This test was prepared by inoculates the 5 mL of YPDB medium (yeast) and MRS-Bile salt medium (LAB) at 0.05, 0.1, 0.2, 0.3, 0.4, and 0.5% in test tubes with 0.1% from yeast and LAB isolates suspensions, and incubated at 35°C for 24 hours. Turbidity when occurred was indicated to positive result

3.2.3.3 Ability of yeast and LAB cells to adhesion with epithelia's cells

In our study we used the Adhesion Index (AI) which define the ability of adhesion yeast and bacterial cells counts with epithelial cells counts dividable to epithelial cells counts. This tests was completed according to (Lee *et al.* 2021). As follow:

- **Epithelial cells suspensions prepared:** this suspension was perfect by securing some pieces of rats intestine under sterile conditions and washed with phosphate buffers at pH 7.2. Then scraping the intestine underlay with sterile glass slide and suspended with 10 mL of phosphate buffers.
- **Yeast and LAB Isolates suspension prepared:** Yeast and LAB suspensions have been prepared via taking 10 mL of remoted suspensions and spore medium at 2500 rpm for 10 min. The cell sediments had been amassed and the phosphate solutions had been gradually introduced with shaking, till a turbidity same to the 0.5 McFarland answer changed into received.
- **Promotions:** Depositing 1mL from epithelial cells suspensions in sterile test tube and adding to its 0.5 mL from each yeast and LAB isolates suspensions, then incubation in shaking water bath at 35°C for 30 mints at 20 rpm/mint.
- **Tested:** after incubation periods, three drops from suspensions were diffusing on glass slide and stained with gram stain, then tested under microscope to detect the adhesions ability. Yeast and LAB was stained with blue color, while the epithelial cells with orange color.

3.2.4 Pathogenic microorganisms tested

3.2.4.1 Diagnosis of bacteria

Pathogenic isolates from *E. coli* were obtained from the microbial laboratory in college of science, Tikrit University. The assurance identified was obtained by using the optimal parameter testes according to (Greenwood *et al.* 1998).

3.2.5 Bacterial and yeast isolates storage

Isolated from LAB was storage for daily working culture by cultivation in MRS broth and incubating aerobically at 30°C for 24 hrs. and anaerobically at 37°C for 48 hrs. then storage in refrigerator at 4°C. While the other bacteria was cultivation on Nutrient agar at 37°C for 48 hrs. Isolated from yeast was storage for daily working culture by cultivation in PDA broth and incubating aerobically at 30°C for 48 hrs. Then storage in refrigerator at 4°C. For long time storage the media broth from each above was used to cultivation then added to its with 20% glycerol and inoculated by bacterial or yeast species then incubated for optimal temperatures and periods, then keeping isolates in freezing at (-20°C)

3.2.6 Agar well diffusion method

The susceptibility test was done for two isolates of yeast and *Lb. casei* and *B. bifidum* isolates using the well diffusion method, which was described by (Vignolo *et al.* 2000). Its included the prepare of activated suspension from each tow isolates from yeast and LAB suspension by picked up from colony cultured and inoculated into sterile YPDB broth tubes and MRS broth for 24 hours, then centerfugated at 3000 rpm/ min for 5 minutes were separated supernatant from the precipitate and keeping in test tubes. Then 100 μL of *E. coli* was poured onto Mueller-Hinton agar plates and spread onto all the surface of the plate. The plates were left 10-15min until the surface of agar has dried. After this the each tow yeast isolates and LAB suspension were injected into the wells (prepared in the plate by using sterile crock borer at 4 mm in diameter), using sterile syringe with the distance between well and another more than 22mm. Plates were incubated at 35°C for 48 hrs. then diameters of inhibition zones were recorded in millimeter using metric ruler (Bauer *et al.* 2001, Pandey *et al.* 2004).

3.2.7 Fermented products preparation

3.2.7.1 Microbial activation

Activation of microbial were done by inoculation of Bifidobacterium bifidum and Lactobacillus casei in MRS broth and the S. cerevisiae and C. curvatus in PDA broth and incubation for 48 hrs. stored at 4°C as daily working culture. The kefir grains was stored with skim milk broth at 4°C.

3.2.7.2 Preparation of inoculum

Lactic acid bacteria and yeast inoculum was prepared by transferred of each two isolates of LAB broth and twoisolates of yeast broth at 10% (1.5×10 10 cells/mL) of pasteurized milk and incubated at 37°C for 17-19 hrs.

While kefir grains was activated by adding 30 g of kefir grains to one liter of pasteurized milk and incubation at 25°C for 21 hrs. (Yaman *et al.* 2010).

3.2.8 Fermented skim milk groups

- Group 1: 5% of S.cerevisiae inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and incubation at 30°C for 30 hrs.
- Group 2: 5% of *C.curvatus* inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and incubation at 30°C for 30 hrs.
- Group 3: 5% of *S.cerevisiae* inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and Incubation at 30°C for 15 hrs. completed with 1:1% of *B. bifidum* and *Lb. casei* at 35 °C for 15 hrs.
- Group 4: 5% of *S.cerevisiae* inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and incubation at 30 °C for 15 hrs. completed with 2:2% of *B. bifidum* and *Lb. casei* at 35 °C for 15 hrs.
- Group 5: 5% of *C.curvatus* inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and incubation at 30 °C for 15 hrs. completed with 1:1% of *B. bifidum* and *Lb. casei* at 35 °C for 15 hrs.
- Group 6: 5% of *C.curvatus* inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and incubation at 30 °C for 15 hrs. completed with 2:2% of B. bifidum and *Lb. casei* at 35°C for 15 hrs.
- Group 7: 1% of *B. bifidum* inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and incubation at 35°C for 30 hrs.
- Group 8: 2% of *B. bifidum* inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and incubation at 35°C for 30 hrs.

- Group 9: 1% of *Lb. casei* inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and Incubation at 35°C for 30 hrs.
- Group 10: 2% of *Lb. casei* inoculated into one liter of skim milk supplemented with 5% (w/v) sucrose, and incubation at 35°C for 30 hrs.
- Group (11): (Kefir Preparation) 3 g of kefir grains, inoculated in 100 mL reconstituted milk. and incubation at 25°C for 21 h, the grains were separated from the fermented milk by filtration through the cloth and store at 4°C. (Marshall and Cole 1985, Yaman *et al.* 2010).

3.2.9 Biochemical analysis for milk fermentation

pH determination: The pH of the sample was determined by using pH meter.

Acidity determination: With pipette were take 10 mL of the sample, 3 drops of phenolphthalein were mixed by shacked. The sample was measured with titration with 0.1N NaOH until appearance of slight pink color in one mint.

Lactose sugar, Protein, Total solid, and Fat%: were determined by Milko Scanner system.

Alcohol (%): determined by potassium dichromate method according to (Caputi *et al.* 1968).

3.2.10 Microbiological analysis

3.2.10.1 Enumeration of bifidobacterium bifidum and lactobacillus casei.

Fermented milk samples were diluted using 10-fold dilution with sterile saline with 0.85% NaCl. DeMan Rogosa Sharpe (MRS) agar used for enumeration of *Bifidobacterium bifidum* and *Lactobacillus casei*. After the agar solidified, the

Bifidobacterium bifidum and *Lactobacillus casei* plates were incubated anaerobically at 37°C for 48 hrs.

3.2.10.2 Enumeration of *S.cerevisiae* and *C.curvatus*

Fermented milk samples were diluted using 10-fold dilution with sterile saline with 0.85% NaCl. Potato Dextrose agar (PDA) was used for enumeration of *S.cerevisiae* and *C.curvatus*. After the agar solidified, the *S.cerevisiae* and *C.curvatus* plates were incubated at 37°C for 48 hrs.

Biçimlendirdi: Yazı tipi: İtalik

3.2.11 Antimicrobial activity of fermented milk samples

This tests was conducted at a same procedure in "Agar Well Diffusion Method" exception to replace the LAB and yeast with the fermentation products.

3.2.12 Initialization of laboratory animals

Sixty five of male Albino-Sprague Dawley Rats, were individually weighed, between 90-95 g, have been obtained from the house live stock in the Faculty of Veterinary Medicine, University of Mosel. Wing banded and housed in heated battery brooders under 12 hours fluorescent lighting daily with feed and water provided ad libitum. Rats were fed the optimal formula according to (Urdaneta *et al.* 2009). The experimental design consisted of thirteen dietary treatments. The Rats animals group that are orally dosage from Dairy fermented products at 3.6 mL/200 g bw/day (Judiono *et al.* 2014)

The Rats were randomly assigned to the following treatment groups;

- Milk fermented by (*S.cerevisiae* 5%)
- Milk fermented by (*C.curvatus* 5%)
- Milk fermented by (*S.cerevisiae* 5%) + (1:1% of *Bifidobacterium bifidum and Lactobacillus casei*)

- Milk fermented by (*S.cerevisiae* 5%) + (2:2% of *Bifidobacterium bifidum and Lactobacillus casei*)
- Milk fermented by (*C.curvatus* 5%) + (1:1% of *Bifidobacterium bifidum and Lactobacillus casei*)
- Milk fermented by (*C.curvatus* 5%) + (2:2% of *Bifidobacterium bifidum and Lactobacillus casei*)
- Milk fermented by (1% *Bifidobacterium bifidum)*
- Milk fermented by (2% *Bifidobacterium bifidum*)
- Milk fermented by (1% *Lactobacillus casei*)
- Milk fermented by (2% *Lactobacillus casei*)
- Milk fermented by (3% kefir w/v)
- Sterilized skim milk 5% sucrose.
- Water only.

These were replicates of five rats per dietary treatment and the rats were maintained on these treatments to 28 days period.

3.2.13 Studied characteristics

Blood characteristics: At the end of the experiment, we randomly selected from each treatment (4 rats of each iteration); five milliliters of blood were calm from Jugular Vein with EDTA for hematological limits willpower. The slow of trial as follows which working according to (Theml *et al.* 2004) and used Auto-hematology analyzer (Human Germany).

Hemoglobin concentration: For measuring hemoglobin concentration the manual cyanmethmeoglobin method has been used which is in brief mixing (20) microliter of the blood with (5) mL of Drabkin's solution was centrifuged for 15 minute to separate the free red cell nuclei after the red cell lysis, then the samples were measured by using spectrophotometer on the wave length of. For obtaining accurate results the same samples of blood were measured by using hemoglobin meter to compare the results.

Total Erythrocytes count. (RBCs): RBCs has been measured by standard manual technique using Natt and Herrick's solution (Theml *et al*. 2004), which requires using erythrocyte-diluting pipette and hemocytometer with improved Neubauer ruler. The blood was absorbed to the 0.5 sign, and the diluted solution was absorbed to the (101) sing, for diluting the blood. This makes the blood diluted 200 times. After mixing the blood with the dilution solution. the diluted blood was poured on the hemocytometer counting chamber and left for few minutes to stabilize before counting under the objective lens (40 X), the total count of the cells have been estimated by counting the four corner squares and the central square in the counting chamber, and the result was multiplied by (10000) to get RBC for each microliter of blood.

Total leukocyte count. (TLC): For measuring (TLC) the direct method has been used which, in brief, is using the same charged hemocytometer that used for (TLC) counting and using the same dilution ratio (200 times), the TWBC has been measured by counting all (TLC) in 9 big squares in the ruled area of the counting chamber in the hemacytometer.

Differential counts of White Blood Cells: After collecting blood samples, small drop of blood has been dropped immediately onto a clean slide to make a smear and the rest of the collected blood was poured into a special tube that contains (EDTA). Standard two-slide wedge technique has been used for preparing blood film; the blood was carefully spread on the surface of slide by the edge of the spreader slide to make a monolayer blood film. Then the smear was left to dry, after that the smears were immersed in absolute methanol for 7 minutes, then the smears were stained by Giemza stain by immersing the slides into the stain and leaving it for almost 40 minutes then the slides were rinsed by tap water and were kept to the time that they were examined under microscope by the immersion-oil objective lens (100 X).The differential count of WBC has been done according to the description of normal leukocytes in avian peripheral blood. It's worth mentioning that the smears were used to estimate differential count of WBC.

Biochemical blood characteristics: At the end of the experiment , we randomly selected from all treatment (4 rats of each iteration) were bled by Jugular Vein to collect about 5 mL from each animals, the blood was transferred to tubes that not contain EDTA. After that blood samples were centrifuged for 15 minutes and the supernatant liquid which signify blood plasma was collected by using micropipette and transferred to eppendorf tube and then kept in a freezer at -20°C until measurement biochemical traits included in this study.(Kaynakça)

For the serum collected using serum separator tubes. Serum concentration of glucose, cholesterol, triglycerides, HDL-C, LDL-C, VLDL-C, urea, uric acid, total protein, albumin, globulin, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and Alkaline phosphatase (ALP) were determine using a clinical chemistry analyzer according to the manufacturer's recommended procedure from Biolabo, Rondex Laboratories Ltd.

3.2.14 Total counts of intestine normal flora

Rats were then slaughter and small intestine were collecte and control the intestine microbial equilibrium after making the thoughtful thinning and incubation to appear the microbial species. One gram of intestine was collected from the small intestine. Homogenize with 5 mL of sterile PBS then serially weak and 100 μL of each dilution was plated into MacConkey agar, MRS plates, N.A agar and PDA. Plates were then incubated of the MacConkey agar, N.A agar and PDA at 37 ˚c for 24 hrs. and the MRS plates were incubated anaerobically at 37 ˚C for 48 hrs. and the number of colonies on the plates were determine and spoken as Enterobacteriaceae colony forming units on MacConkey agar and the LAB on MRS agar and the Aerobic Bacteria and yeast on N.A agar and PDA. All example run in duplicate plates. The final bacterial and yeast attentions were intended as the number of colonies per milliliters of harvested tissue. (Boke *et al.* 2010).

Determination of pH rats feces: Feces samples in intestine were diluted in distilled water (1:4, w/v) and homogenized with pipette tips. pH was determined using pH meter.

3.2.15 Statistical analysis

Data have been analyzed by means of ANOVA, the use of the General Linear Model of the Statistical Analysis System. Significant variations in remedy were assessed the usage of Duncan's more than one variety take a look at Duncan (1955). All importance statements are based on a 0.05 stage of probability.

4 RESULTS AND DISCUSSION

Data of current study revealed highest mean levels of urea at groups *E. coli* (64.60± 0.87), creatinine at *E.coli* plus Lacteol forte (2.53±1.23), while the least mean levels of urea and creatinine was at Lacteol forte (36.80±1.02 and 0.35±0.02) respectively compared to controls with significant different (LSD for urea =6.54 and creatinen = 0.96). In contrast, our study showed decrease levels of glucose at groups *E. coli* (82.80± 1.24), and the increased levels at group Lacteol forte (130.00±1.14) compared to controls with significant different (LSD =14.88) (Table 4.1).

Table 4.1 Comparative mean levels of glucose, urea, creatinene among study groups

N= 5 frequent for each group	Glucose		Urea		Creatinene	
	Mean	SEM	Mean	SEM	Mean	SEM
Controls	130.00	2.72	50.00	2.02	0.45	0.02
E. coli	82.80	1.24	64.60	0.87	0.78	0.04
Lacteol forte	130.00	1.14	36.80	1.02	0.35	0.02
Saccharomyces boulardii	127.60	1.17	44.20	0.73	0.44	0.02
E.coli+Lacteol forte	94.00	1.38	46.20	1.16	2.53	1.23
E.coli+*Saccharomyces boulardii*	95.40	1.75	50.20	1.07	0.54	0.01
LSD	14.88*		6.54		0.96	

SEM : Açılımı nedir? LSD değerlerinde olasılık oranlarının değeri yıldız indisi ile belirtilmelidir. p<0.05, Tüm tablolarda bu durum dikkate alınmalıdır.

We noticed the Lacteol forte and saccharomyces boulardii probiotics leaded to preserve on glucoses, urea, and creatinene with normal range. Moreover, these probiotics leads to regulate (increase or decrease) glucoses, urea, and creatinene in patients with gastroenteritis.

Probiotics are microorganisms which have beneficial outcomes once consumed. While probiotics in overweight human beings seem favorable for weight reduction, their use has been controversially mentioned to deal with diverse diseases, which include inflammatory bowel disease, *Clostridium difficile* contagions, and allergic diseases (John *et al.* 2018). Aside from mediating useful effects, probiotics ought to now not reason negative consequences, in particular infections. Several microorganisms have been usage, amongst them lactobacilli, *Streptococcus bifidobacteria*, (ie Streptococcus thermophiles*)*, *Escherichia coli* Nissle, and *Saccharomyces boulardii* (Sivananthan and Petersen 2018). Probiotics offer many health advantages such as improving intestine fitness, enhancing immune response, reducing cholesterol degree and blood stress through a variety of mechanisms and as a consequence improving the overall fitness of consumers. Competing for pathogen-binding websites for epithelial cells of the gastrointestinal tract consequently preventing contamination, generating unique metabolites inclusive of micro organism that lessen the boom of pathogenic micro organism, strengthen the epithelial barrier, and improve adhesion to the intestinal mucosa, leading to inhibition of pathogen longer adhesion and modulation of the immune machine Some of the main mechanisms of motion of probiotics.

The properly-studied probiotic yeast *S. boulardii* performs an crucial function in keeping and/or restoring intestinal barrier feature in a couple of disorders. This can be of awesome importance in diseases characterised through changes in intestinal barrier characteristic (Terciolo *et al.* 2019). *S. boulardii* shows anti inflammatory abilties and stops the attachment of pathogenic micro organism to the epithelium (Stier and Bischoff 2016). In medical settings, *S. boulardii* abridged the improvement of antibiotic-related diarrhea which includes diarrhea because of *Clostridium difficile* (Borgmann *et al*. 2019). The outcomes of the facts confirmed that patients who conventional probiotics had a notably decrease incidence of related gastrointestinal signs, a greater range of identical bacterial diversity, a better abundance of intestinal bacteria, and a decrease profusion of Bacteroides and Clostridia at treatment conclusion. The adding of *S. boulardii* CNCM I-745 led to a inferior incidence of GI symptoms that could be associated with vicissitudes in the intestine microbiota (Cifuentes *et al.* 2022). A current look at showed that the adding of *S. boulardii* CNCM-I 745 to traditional antibiotic eradication treatment for *H. pylori* abridged the profusion of antimicrobial resistance genes (ARGs), specially the ones genes conferring resistance to lincosamides, tetracyclines, MLS-B, and a few Genes are inside the beta-lactam magnificence (Cifuentes *et al.* 2022).

Among the pathogenic *Escherichia coli*, enteric *Escherichia coli* (EPEC) reasons infectious diarrhea in developing international locations, even as enterohemorrhagic coli

(EHEC), which produces a Shiga-like toxin, is complicated in foodborne infections in industrialize international locations. The attachment of those micro organism to the intestinal mucosa is a critical step in their capability to motive disease. After interaction with the mucosa, those micro organism vaccinate effector proteins into the host finished the kind III secretion machine. These effector protein set off vicissitudes inside the tight junction shape, stimulating the start of MAP and NF-κB kinases, and as a result activation of IL-eight synthesis. Studies of polarized human epithelial cellular monolayers showed that incubation with S. In addition, the tight junction structure is preserved in these ill cells after publicity to yeast. In cells inflamed with EHEC, S. *boulardii* CNCM I-745 inhibits phosphorylation of the myosin mild chain this is right concerned in keeping the integrity of tight junctions. *boulardii* CNCM I-745 also has an anti inflammatory impact that inhibits the activation of mitogen-activated protein kinases, NF-κB nuclear translocation, and therefore IL-8 synthesis (Wu *et al.* 2008). In a mouse model inflamed with *Citrobacter rodentium* (equal to EPEC in rodents) S. Boulardii CNCM I-745 reduces mannitol efflux and improves histological grade of infected animals. Another observe showed that S. (Buts *et al.* 2006) mentioned that the complex phosphatase in *S.injected* LPS mice exposed to phosphatase purified from S.

The latest observe indicates a few interesting consequences concerning the efficacy of mixes shaped by *S. cerevisiae* S3 on toxin gene languages in each enterohaemorrhagic and enterotoxin *Escherichia coli* (EHEC) (Koupaei *et al.* 2022).

The results of the study tested the capacity new therapeutic position of S. The outcomes of the statistics display, for the first time, that the management of S.

(Kvit *et al.* 2021) tested that the probiotic S. Most articles covered the high-quality effects pronounced for S.

Lacteol uniqueness probiotic includes *Lactobacillus acidophilus* LB 10 stress, that is a probiotic strain that propagates proper bacteria inside the stomach and treats digestive problems together with indigestion, diarrhea and irritable bowel syndrome (IBS). A current examine showed that management of *Lactobacillus acidophilus* LB

(*Lactobacillus boucardii*) is real and secure as an adjunct in the remedy of acute diarrhea, persistent diarrhea and antibiotic-associated diarrhea, even within the attendance of immunosuppression (María Remes-Troche *et al.* 2020). Study results indicate that *Lactobacillus acidophilus* remedy of pediatric acute gastroenteritis is real when administered at a every day dose of ≥109 CFU/day. The probiotic traces *Lactobacillus acidophilus* and *Lactobacillus rhamnosus* are endorsed for youngsters with acute gastroenteritis, whether or not the probiotic traces are usage collectively or alone (Cheng *et al*. 2022). *L. acidophilus* supplementation decreased mortality from *Escherichia coli* project, reduced serum C-reactive protein ranges, and LPS ranges at 14 and 21 days d; It upregulate the mRNA expression of claudin and ZO-1 inside the jejunum and ileum, and downregulated the mRNA look of iNOS, IL-8, and IL-1β in the jejunum of *E. Coli* animals at 21 days. Dietary supplementation containing L. Acidophilus can recover increase overall presentation, gut fitness, and existence of broilers with *Escherichia coli* (Wu *et al*. 2021).

Study results show that glycemic manage is better done by way of eating probiotic yogurt covering *L. acidophilus* and *B. lactis* in patients with complications of diabetes at some stage in pregnancy as compared to placebo. The fine outcomes of probiotics on glycemic manage can be translated into a tremendous result on lessening the occurrence of gigantism (Sahhaf Ebrahimi *et al*. 2019). Particularly, *L. acidophilus* KLDS1.0901 remedy reinstated the gut microbiota structure just like that of the manage group. The observe effects indicated that *L. acidophilus* KLDS1.0901 might be usage as a brand new kind of antidiabetic drug applicant (Yan *et al*. 2019). Study outcomes display that there may be a ten% decrease in blood urea concentration with *L. acidophilus* in patients with stage 3 and four CRF (Alatriste *et al.* 2014). The authors decided that the mixture of heat-killing probiotics and wheat bran reduces the attendance and harshness of gastrointestinal (GIS) symptoms in kids undergoing dialysis (decrese stages of creatinine and urea) (Youssef *et al.* 2019). *L. acidophilus* supplementation attenuates systemic irritation and proteinuria related to renal failure, suggesting that lactate in the intestine microbiota plays a defensive function against the development of persistent kidney ailment (Yoshifuji *et al*. 2016).

Data of current study revealed highest mean levels of GOT, GPT, and ALP at groups E. coli (192.80± 2.06, 59.40±1.36, and 828.00±23.30) respectively, while the least mean levelsof all were at Lacteol forte group (141.00± 1.38, 40.00±1.14, and 521.20±6.70) respectively, compared to controls with significant different (LSD GOT= 13.51, GPT=5.78, ALP=82.19) (Table 4.2)

Table 4.2 Comparative mean levels of GOT, GPT, ALP among study groups

N= 5 frequent for each group	GOT		GPT		ALP	
	Mean	SEM	Mean	SEM	Mean	SEM
Controls	145.00	1.34	40.00	1.14	525.20	1.85
E. coli	192.80	2.06	59.40	1.36	828.00	23.30
Lacteol forte	141.00	1.38	40.00	1.14	521.20	6.70
saccharomyces boulardii	145.20	1.32	40.00	1.14	539.20	2.48
E.coli+Lacteol forte	155.20	1.56	47.80	1.93	611.00	3.56
E.coli+saccharomyces boulardii	151.40	2.16	52.20	0.86	574.80	9.39
	13.51		5.78		82.19	

We noticed the Lacteol forte and saccharomyces boulardii probiotics leaded to preserve on GOT, GPT, and ALP with normal range. Moreover, these probiotics leads to regulate GOT, GPT, and ALP in patients with *E. coli* infection, where these investigations show importance Lacteol forte and *Saccharomyces boulardii* probiotics in regulation liver diseases that related gastroenteritis.

A latest examine proven the healing capability of S.. Study consequences show that management of *S. boulardii* to streptozotocin-triggered (STZ) diabetic mice reduces oxidative strain and restores the attention of renin-angiotensin machine (RAS) peptides, helping the speculation that this yeast can also have a role as a ability adjuvant therapy. To mitigate. Liver harm as a result of diabetes (Barssotti *et al.* 2021).

(Zoheir and Amara 2012) exhibit the importance of using yeasts as a probiotic in protecting towards liver damage. Study outcomes indicated that oral administration of *S. boulardii* should decorate liver function of carbon tetrachloride (CCl4)-dealt with animals, and probiotic yeast probiotic therapy would possibly gradual the development of cirrhosis. In addition, dietary management of the probiotic pressure (*Bacillus subtilis*, *Bacillus licheniformis*, and *Bacillus cereus*) extensively decreased the stages of serum ammonia, uric acid, general cholesterol, triglycerides GOT, GPT, and ALP in patients with inflammation (Gong *et al.* 2018). S. Boulardii CNCM I-745 has been found to secrete a number of one-of-a-kind digestive enzymes. Although those enzyme sports are definitely a strategy for yeast to metabolize proteins and peptides for his or her own functions, those sports may be considered beneficial inside the human gut—especially beneath situations which include intestinal contamination and/or infection, for those who lack a few enzyme pastime, or inside the intestine. The immature (Moré and Vandenplas 2018).

Bacteria belonging to the genus are located inside the oral cavity, intestines and vagina. *Lactobacillus* spp. It can enhance conditions which includes gastrointestinal disease, allergies, and liver sickness thru various mechanisms, consisting of the manufacturing of metabolites that could at once inhibit pathogens, show off immunological results, and modify the intestinal vegetation. It is likewise acknowledged that gut microorganisms have an effect on liver disease (Jeong *et al.* 2022). This is due to the fact the venous system of the portal move determines the axis of the intestine and the liver, and there is a close anatomical and useful interaction between the digestive machine and the liver (O'Hara *et al.* 2017). The consequences of diverse probiotics on disease development were showed in non-alcoholic and alcoholic liver disease.

Ingestion of *Lactobacillus*, together with *L. acidophilus*, *L. fermentum*, and *L. plantarum* facilitates the development of non-alcoholic steatosis with the aid of decreasing ldl cholesterol. The use of *Lactobacillus* may be considered a beneficial approach for the treatment of nonalcoholic fatty liver ailment (NAFLD) (Lee *et al.* 2021). In addition, using *L. acidophilus* in overweight sufferers with nonalcoholic fatty liver ailment (NAFLD) resulted in lower serum triglyceride tiers (Ahn *et al.* 2019).

The study consequences confirmed that oral management of *L. acidophilus* progressed ethephon-triggered liver and colon fibrosis as indicated through the downregulation of

TGF-β1 and α-SMA expression and collagen expression thru NF-kB inhibition. Thus, *L. acidophilus* can be used as a promising candidate against fibrosis (Bahr *et al.* 2019). Hepatic lipid metabolism additionally seems to be prompted by the presence of commensal bacteria, and probably probiotics. Although, the mechanisms via which probiotics may also act on the liver stay unclear. However, this could be of brilliant significance in the destiny because low-grade contamination, hepatic fat infiltration, and hepatitis may also turn out to be extra normal due to high fat intake and the increased occurrence of obesity (Gratz *et al.* 2010).

Data of current study revealed least mean levels of K and Ca at groups *E. coli* (3.97± 0.08 and 7.86±0.14), while the highest mean levels of K and Ca were at saccharomyces boulardii group (5.72±0.10, and 9.50±0.17) respectively, compared to controls with significant different (LSD K= 0.48, Ca=0.12). In contrast, our study showed increased levels of Na at groups *E. coli* (134.20± 1.24), and the decreased levels at group Lacteol forte (109.60±3.23) compared to controls with significant different (LSD =6.71) (Table 4.3).

Table 4.3 Comparative mean levels of Na, K, Ca among study groups

N= 5 frequent for each group	NA		K		Ca	
	Mean	SEM	Mean	SEM	Mean	SEM
Controls	119.80	1.71	5.46	0.11	9.04	0.15
E. coli	134.20	1.24	3.97	0.08	7.86	0.14
Lacteol forte	109.60	3.23	5.66	0.09	9.32	0.14
saccharomyces boulardii	119.20	1.39	5.72	0.10	9.50	0.17
E.coli+Lacteol forte	126.40	1.17	5.14	0.14	8.72	0.12
E.coli+saccharomyces boulardii	119.80	3.40	5.44	0.17	8.72	0.14
LSD	6.71		0.48		0.12	

We noticed the Lacteol forte and *Saccharomyces boulardii* probiotics leaded to preserve on Na, K, and Ca with normal range. Moreover, these probiotics leads to regulate a, K, and Ca in patients with *E. coli* infection, where these investigations show importance

Lacteol forte and *Saccharomyces boulardii* probiotics in regulation electrolytes that related gastroenteritis.

Hossain *et al.* (2020) results showed that *Saccharomyces boulardii* probiotics may exert beneficial effects in decrease sodium levels the gastrointestinal tract infection compared to controls, and these results matched with our results. Oral administration of *S. boulardii* reduced dextran sulfate sodium DSS-induced weight loss, ameliorated the histological damage and protected the colon barrier in mice with DSS-induced colitis (Zhou *et al.* 2018). Girard *et al.* (2005) show the *Saccharomyces boulardii* probiotics lead to decrease levels of electrolytes (eg., K) in patients with colitis, and these results not matched with our study that showed the *Saccharomyces boulardii* probiotics increase level of K in patients with gastrointestinal tract infection. The oral administration of *Saccharomyces boulardii* probiotics increased potassium and sodium while decrease chloride level in serum of patients with gastrointestinal tract infection (Mohamed and Ajah, 2020). Calcium is the most important nutrient, with about 99% of the calcium discovered inside the teeth and bones of the frame and handiest 1% in the blood serum. Several research have indicated that probiotics have an crucial role in enhancing the absorption and absorption of calcium (Dubey and Patel 2018).

The effects of the examine showed that *L. acidophilus*, *L. casei*, *L. rhamnosus*, *L. bulgaricus*, *B. breve*, *B. longum*, and *Streptococcus thermophilus* caused multiplied serum calcium concentrations and decreased degrees of alanine aminotransferase (ALT) in sufferers of the sort. 2 diabetes. (Asemi *et al.* 2015). A recent examine found out that a couple of species of the probiotic *Lactobacillus* spp. Altered hair calcium attention and femur magnesium stage, as well as the molar ratio of those elements in testes of healthful male rats (Suliburska *et al.* 2021).

Several researches have genuinely indicated the involvement of probiotics in human health via acting via a exceptional mechanism. Studies additionally reveal the position of probiotics in calcium bioavailability (Dubey and Patel 2018). Study results show the *L. acidophilus* probiotic lead to increase levels of calcium in geriatrics individuals (Gohel *et al.* 2016).

5 CONCLUSIONS AND RECOMMENDATION

They are classified within the *Enterobacteriaceae* family and are characterized as bacilli and they are Gram-negative Bacteria (G-Ve) Therefore, it was isolated from the colon in the intestine, as it is the first evidence of fecal contamination, in food and water, and it appears distinctly as smooth, convex pink colonies with clear ends It is fermented with lactose, in contrast to the rest of the other intestinal types, and it is surrounded by a region of yellow salts precipitated in the McConkey agar, so it appears on the middle (EMB) Eosine Methylene Blue It has a green metallic luster.

Increased protection against toxins caused by pathogenic Escherichia coli, as well as the effects of functional food components that reduce malnutrition and the negative effects of stress with unknown pathways function.

The mechanisms via which probiotics may also act on the liver stay unclear. However, this could be of brilliant significance in the destiny because low-grade contamination, hepatic fat infiltration, and hepatitis may also turn out to be extra normal due to high fat intake and the increased occurrence of obesity.

Despite advances in primary research, scientific trials of probiotics in allergic reaction/allergies and respiration infections have been incredibly variable at first-rate, undermining self belief on this ability remedy approach.

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