



## Probiotics for the prevention of human diseases

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### Abstract

While the human gastrointestinal microflora is getting a lot of attention these days due to alteration causing dysbiosis, the probiotics have been reported to heal this altered microbiota without any harm. These probiotics are live bacteria or yeasts found in fermented foods that when consumed in adequate amounts take residence in the human gut and improves our overall health. Therefore, they are often called as good bacteria because they help to keep our gut healthy. The present paper discusses the various ailments and diseases which are being cured with the use of probiotics in the light of recent researches done so far.

**Keywords:** probiotics, gastrointestinal microflora, prevention of human diseases

### 1. Introduction

Probiotics are the live microorganisms normally inhabiting in the human intestine naturally secrete antibiotic like substances having antagonistic potential providing immunomodulatory impact which stimulate the normal microbiocenosis. They are also being treated as the correctors of normal intestinal microflora acting as an important role in human ecology (Murat *et al.* 2016) [62]. The present paper is second in series of probiotic researches as the first paper describing probiotic good foods with microflora they contain has already been published (Masroor *et al.* 2018) [55].

Eli Metchnikoff in 1907, while working at Pasteur Institute in Paris suggested about the colonization of beneficial gut bacteria in human. He opined that some proteolytic bacteria such as *clostridia* which are normally inhabited in human intestines circumstantially produce some toxic substances causing auto-intoxication and aging in animals. He also felt that those people who were routinely consuming fermented milks with their diet have been away from gastric troubles and long lived. Lateron, He himself tried the same and got benefitted. Naturally, it was all due to the Lactic Acid Bacteria (LAB) present in the fermented milks inhibiting the growth of proteolytic bacteria because of the low pH produced by the fermentation of lactose (Metchnikoff 1907) [58].

Another scientist, Henry Tissier working in the same institute simultaneously isolated another bacterium from the gut flora of bottle fed infants. Though, after sometime recognizing as probiotic and finally named as *Bifidobacteria* were also found to be involved in replacing proteolytic bacteria (Tissier 1900) [86]. Further, Cheplin and Rettger in 1920 observed the desired effect with *Lactobacillus acidophilus*, when implanted in human's intestine especially in the relief of chronic constipation (Cheplin and Rettger 1920 and Rettger *et al.* 1935) [14, 69]. And, in the following decades several intestinal probiotics with alleged health beneficial properties like LAB species, *Bifidobacteria*, *Bacillus coagulans*, *Bacillus subtilis*, *Saccharomyces boulardii*, *Enterococcus faecium* and *Streptococcus thermophilus* have been introduced (Kim *et al.* 1994 & 2010, Agerholm *et al.* 2000,

Niedzielin *et al.* 2001, Sagioro *et al.* 2005, Leonetti *et al.* 2006, Yang *et al.* 2008, Hun 2009 and Wang *et al.* 2012) [1, 37, 46, 47, 49, 64, 72, 91, 94].

More than 100 trillion microorganisms weighing about a kilogram we harbour in our intestine to maintain good health and well being. While most of these microorganisms are beneficial some of them are harmful or sometimes they have been transformed to be harmful and an appropriate balance must be maintained in serving as a key line of defense against invading pathogens, aiding digestion enabling proper absorption of nutrients and producing vitamins (Jeavons 2003 and Johnston *et al.* 2012) [40, 42]. With 70 % of immune cells residing in our gut, they play an important role in boosting our immune system (Pascal *et al.* 2011) [65]. This critical and delicate balance is, however, often disturbed by stress, infections, indiscriminate use of antibiotics, inadequate sleep and aging (Fuller 1992) [23].

Basically, these probiotics containing good bacterial cultures have been used up for centuries. Currently, the benefits of some of the already improved diseases and ailments are improved digestion (Tabbers *et al.* 2011) [82], immune function (Pascal *et al.* 2011 and Masroor *et al.* 2015 & 2018) [54, 55, 65], vitamin synthesis (Strozzi and Mogna 2008 and Molina *et al.* 2009) [60, 79], lowering of cholesterol level (Agerholm *et al.* 2000, Kiebling *et al.* 2002 and Kumar *et al.* 2012) [1, 45, 48], blood pressure (Jauhiainen *et al.* 2005) [39], Crohn's disease (Guslandi *et al.* 2000 and Borruel *et al.* 2002) [5, 28], irritable bowel syndrome (Moayyedi *et al.* 2010 and Gugliemetti *et al.* 2011) [27, 59], inflammatory bowel diseases (Hedin *et al.* 2007) [32], diarrhoea (Cimperman *et al.* 2011) [16], ulcerative colitis (Naidoo *et al.* 2011) [63], colorectal cancer (Geier *et al.* 2006) [25], urinary tract infections (Barrons and Tassone 2008 and Reid 2008) [5, 68], vaginosis (Branco *et al.* 2010) [10], lactose intolerance (Salzman *et al.* 1999) [73], eczema (Kim *et al.* 2010 and Han *et al.* 2012) [29, 47] and allergy (Pascal *et al.* 2011) [65].

As probiotics are now scientifically proved to improve the overall health, the present paper deals with the study of prophylaxis, biotherapeutics and the treatment with the help of these probiotics of several ailments, disorders and diseases

abnormally developed in human.

## 2. Material and Methods

The present paper is prepared on the basis of researches done

so far in the field of probiotic therapies. Several research papers were consulted in order to explore the various human diseases cured by these probiotics in the light of recent researches.

**Table 1:** A list of some stomach and digestive disorders being treated with probiotics

S. No.	Name of disease	Probiotics involved	Source
1.	Loss of appetite and indigestion	<i>Lactobacilli</i>	Rial 2000 <sup>[70]</sup> , Vemuri <i>et al.</i> 2010 <sup>[89]</sup> , Kumar <i>et al.</i> 2012 <sup>[48]</sup>
2.	Acute diarrhoea	<i>Lactobacilli</i>	Francavilla <i>et al.</i> 2012 <sup>[22]</sup>
3.	Travellers diarrhoea	<i>Lactobacillus GG</i>	Hilton <i>et al.</i> 1997 <sup>[34]</sup>
4.	Antibiotics associated diarrhoea	<i>Lactobacillus reuteri</i> , <i>L. acidophilus</i> , <i>L. casei</i>	Gao <i>et al.</i> 2010 <sup>[24]</sup> , Cimperman <i>et al.</i> 2011 <sup>[16]</sup> , Johnson 2011 <sup>[41]</sup>
5.	<i>Clostridium difficile</i> associated diarrhoea	<i>Lactobacillus rhamnosus</i> , <i>Saccharomyces boulardii</i>	Johnston <i>et al.</i> 2012 <sup>[42]</sup>
6.	Gastroenteritis	<i>Lactobacillus reuteri</i> <i>Bifidobacteria breve</i>	Tojo <i>et al.</i> 1987 <sup>[87]</sup> , Teitelbaum and Walker 2002 <sup>[84]</sup>
7.	Chronic liver diseases and pancreatitis	<i>Lactobacilli</i> <i>L. acidophilus</i> , <i>Bifidobacteria</i> , <i>B. longum</i> , <i>Enterococcus faecium</i>	Read <i>et al.</i> 1966 <sup>[67]</sup> , Besselink <i>et al.</i> 2008 <sup>[7]</sup> , Sun <i>et al.</i> 2009 <sup>[80]</sup> , Liu <i>et al.</i> 2010 <sup>[50]</sup> , McGee <i>et al.</i> 2011 <sup>[56]</sup> , Wang <i>et al.</i> 2012 <sup>[91]</sup>
8.	<i>Campylobacter</i> enteritis	<i>Bifidobacteria breve</i>	Tojo <i>et al.</i> 1987 <sup>[87]</sup>

**Table 2:** A list of some intestinal colorectal and urinogenital disorders being treated with probiotics

S. No.	Name of disease	Probiotics involved	Source
1.	Inflammatory bowel disease (IBD)	<i>Lactobacilli</i> <i>Bifidobacteria</i>	Mach 2006 <sup>[52]</sup> , Hedin <i>et al.</i> 2007 <sup>[32]</sup> , Lorea <i>et al.</i> 2007 <sup>[51]</sup>
2.	Irritable bowel syndrome (IBS)	<i>Lactobacilli</i> , <i>L. plantarum</i> , <i>Bifidobacterium bifidum</i> , <i>Bacillus coagulans</i> , <i>saccharomyces boulardii</i>	Niedzielin <i>et al.</i> 2001 <sup>[64]</sup> , Brenner <i>et al.</i> 2009 <sup>[11]</sup> , Hun 2009 <sup>[37]</sup> , Moayyedi <i>et al.</i> 2010 <sup>[59]</sup> , Choi <i>et al.</i> 2011 <sup>[15]</sup> , Guglielmetti <i>et al.</i> 2011 <sup>[27]</sup>
3.	Abdominal pain	<i>Lactobacilli</i> <i>L. reuteri</i> ATCC, <i>L. reuteri</i> DSM 17938, <i>L. rhamnosus</i> GG, <i>Bacillus coagulans</i>	Hun 2009 <sup>[37]</sup> , Horvath <i>et al.</i> 2011 <sup>[36]</sup> , Szajewska <i>et al.</i> 2013 <sup>[81]</sup>
4.	Crohn's disease	<i>Saccharomyces boulardii</i>	Guslandi <i>et al.</i> 2000 <sup>[28]</sup> , Borruel <i>et al.</i> 2002 <sup>[9]</sup>
5.	Enterocolitis, Ulcerative colitis	<i>Lactobacilli</i>	Do <i>et al.</i> 2010 <sup>[19]</sup> , Alfaleh <i>et al.</i> 2011 <sup>[3]</sup> , Naidoo <i>et al.</i> 2011 <sup>[63]</sup>
6.	<i>Helicobacter pylori</i> infection	<i>Lactobacilli</i> , <i>L. reuteri</i> , <i>L. gasseri</i> , <i>L. johnsonii</i>	Sagioro <i>et al.</i> 2005 <sup>[72]</sup> , Sgouras <i>et al.</i> 2005 <sup>[75]</sup> , Leonetti <i>et al.</i> 2006 <sup>[49]</sup> , Imase <i>et al.</i> 2007 <sup>[38]</sup> , Shigeru 2012 <sup>[76]</sup>
7.	Chronic constipation, Evacuation disorder, Fecal microbes disruption, Small intestine bacterial overgrowth (SIBO)	<i>Lactobacilli</i> , <i>L. fermentum</i> , <i>L. casei</i> , <i>L. reuteri</i> , <i>L. rhamnosus</i> , <i>Bifidobacteria</i>	Stotzer <i>et al.</i> 1996 <sup>[78]</sup> , Bu <i>et al.</i> 2007 <sup>[12]</sup> , Chatoor and Emmnauel 2009 <sup>[13]</sup> , Coccorullo <i>et al.</i> 2010 <sup>[17]</sup> , Arif and Joshi 2012 <sup>[4]</sup> , Masroor <i>et al.</i> 2015 <sup>[54]</sup> , Masroor <i>et al.</i> 2018 <sup>[55]</sup>
8.	Urinary tract infections (UTI), Vaginosis, Vaginal thrush, Vaginal candidiasis	<i>Lactobacilli</i> , <i>L. casei</i> , <i>L. rhamnosus</i> , <i>L. reuteri</i>	Jeavons 2003 <sup>[40]</sup> , Barrons and Tassone 2008 <sup>[5]</sup> , Reid 2008 <sup>[68]</sup> , Branco <i>et al.</i> 2010 <sup>[10]</sup> , Romeo <i>et al.</i> 2011 <sup>[71]</sup> , Petrova <i>et al.</i> 2015 <sup>[66]</sup>
9.	Colorectal cancer	<i>Lactobacilli</i> <i>Bifidobacteria</i>	McIntosh 1996 <sup>[57]</sup> , Geier <i>et al.</i> 2006 <sup>[25]</sup> , Do <i>et al.</i> 2008 <sup>[18]</sup>
10.	Cervical cancer	<i>Lactobacilli</i> ,	Verhoeven <i>et al.</i> 2013 <sup>[90]</sup>

**Table 3:** A list of some other diseases being treated with probiotics

Sr. No.	Name of disease	Probiotics involved	Source
1.	Respiratory tract infections, Common cold, Sinusitis	<i>Lactobacillus gasseri</i> , <i>L. fermentum</i> , <i>Bifidobacterium longum</i> , <i>B. bifidum</i>	Winkler <i>et al.</i> 2005 <sup>[92]</sup> , Mukerji <i>et al.</i> 2009 <sup>[61]</sup> , Maldonado <i>et al.</i> 2012 <sup>[53]</sup>
2.	Leukemia	<i>Lactobacillus bulgaricus</i>	Esser <i>et al.</i> 1983 <sup>[21]</sup>
3.	Obesity	<i>Lactobacilli</i> , <i>Bifidobacteria</i>	Ehrlich 2009 <sup>[20]</sup> , Sandra <i>et al.</i> 2013 <sup>[74]</sup>
4.	Atopic diseases, Dermatitis, Eczema	<i>Lactobacillus sakei</i> , <i>L. plantarum</i>	Woo <i>et al.</i> 2010 <sup>[93]</sup> , Kim <i>et al.</i> 2010 <sup>[47]</sup> , Han <i>et al.</i> 2012 <sup>[29]</sup>
5.	Allergy	<i>Lactobacilli</i>	Vanderhoof 2008 <sup>[88]</sup> , Pascal <i>et al.</i> 2011 <sup>[65]</sup>
6.	Immune disorders, Gluten intolerance, Celiac disease, Lactose intolerance, Arthritis	<i>Lactobacillus acidophilus</i> , <i>Bifidobacterium infantis</i>	Salzman <i>et al.</i> 1999 <sup>[73]</sup> , Hatakka <i>et al.</i> 2003 <sup>[30]</sup> , Helmhorst <i>et al.</i> 2010 <sup>[33]</sup> , Pascal <i>et al.</i> 2011 <sup>[65]</sup> , Smecuol <i>et al.</i> 2013 <sup>[77]</sup>
7.	Neurological disorders	<i>Lactobacilli</i>	Romeo <i>et al.</i> 2011 <sup>[71]</sup> , Ahmad <i>et al.</i> 2014 <sup>[2]</sup>
8.	Oral health with dental manifestations	<i>Lactobacillus reuteri</i> , <i>L. rhamnosus</i>	Tasli <i>et al.</i> 2006 <sup>[83]</sup> , Hatakka <i>et al.</i> 2007 <sup>[31]</sup> , Keller <i>et al.</i> 2012 <sup>[43]</sup>

**Table 4:** A list of some probiotic biotherapeutics

S. No.	Name of biotherapeutics	Probiotics involved	Source
1.	Lowering of cholesterol	<i>Lactobacilli</i> , <i>Bifidobacteria</i> , Yeast	Agerholm <i>et al.</i> 2000 <sup>[1]</sup> , Kiebling <i>et al.</i> 2002 <sup>[45]</sup> , Kumar <i>et al.</i> 2012 <sup>[48]</sup>
2.	Lowering of blood pressure	Fermented milk with <i>Lactobacillus helveticus</i>	Jauhainen <i>et al.</i> 2005 <sup>[39]</sup> , Hiromitsu 2013 <sup>[35]</sup>
3.	Lowering the effects of Vit. B <sub>12</sub> deficiency	<i>Lactobacillus reuteri</i> CRL 1098	Molina 2009 <sup>[60]</sup>
4.	Quantification of folic acid in human faeces	<i>Bifidobacteria</i>	Strozzi and Mogna 2008 <sup>[79]</sup>
5.	Antagonistic biotherapeutics	<i>Lactobacilli</i> , <i>Bifidobacteria</i>	Beata <i>et al.</i> 2012 <sup>[6]</sup>
6.	Fecal matter transplantation (FMT)	Probiotic good bacteria	Masroor <i>et al.</i> 2015 <sup>[54]</sup> Masroor <i>et al.</i> 2018 <sup>[55]</sup>

### 3. Results and Discussion

Several human diseases being treated with probiotics have been tabulated in Table 1 to 3 with a list of some probiotic biotherapeutics in Table 4. These probiotics have now been proved experimentally to cure several human ailments and diseases like loss of appetite (Vemuri *et al.* 2010) <sup>[89]</sup>, indigestion (Rial 2000) <sup>[70]</sup>, constipation (Bu *et al.* 2007, Chatoor and Emmanuel 2009, Coccorulo *et al.* 2010 and Arif and Joshi 2012) <sup>[4, 12, 13, 17]</sup>, diarrhoea (Gao *et al.* 2010, Cimperman *et al.* 2011 and Johnston *et al.* 2012) <sup>[16, 24, 42]</sup>, gastroenteritis (Teitelbaum and Walker 2002) <sup>[84]</sup>, liver diseases (Liu *et al.* 2010, Mc Gee *et al.* 2011 and Wang *et al.* 2012) <sup>[50, 56, 91]</sup>, pancreatitis (Sun *et al.* 2009) <sup>[80]</sup>, inflammatory bowel disease (Hedin *et al.* 2007 and Lorea *et al.* 2007) <sup>[32,51]</sup> irritable bowel syndrome (Hun 2009, Moayyedi *et al.* 2010, Choi *et al.* 2011 and Gugliematti *et al.* 2011) <sup>[15, 27, 37, 59]</sup>, Crohn's disease (Guslandi *et al.* 2000 and Borruel *et al.* 2002) <sup>[9, 28]</sup>, enterocolitis (Alfaleh *et al.* 2011) <sup>[3]</sup>, ulcerative colitis (Do *et al.* 2010 and Naidoo *et al.* 2011) <sup>[19, 63]</sup>, colorectal cancer (Do *et al.* 2008) <sup>[18]</sup>, cervical cancer (Verhoeven *et al.* 2013) <sup>[90]</sup>, SIBO (Stotzer *et al.* 1996) <sup>[78]</sup>, UTI (Barrons and Tassone 2008 and Reid 2008) <sup>[5, 68]</sup>, vaginosis (Branco *et al.* 2010 and Petrova *et al.* 2015) <sup>[10, 66]</sup>, vaginal thrush and candidiasis (Jeavons 2003, Romeo *et al.* 2011) <sup>[40, 71]</sup>, obesity (Ehrlich 2009 and Sandra *et al.* 2013) <sup>[20, 74]</sup>, allergy (Vanderhoof 2008 and Pascal *et al.* 2011) <sup>[65, 88]</sup>,

dermatitis (Han *et al.* 2012) <sup>[29]</sup>, eczema (Kim *et al.* 2010, Woo *et al.* 2010 and Han *et al.* 2012) <sup>[29, 47, 93]</sup> and immunocompromised neurological and psychological disorders (Romeo *et al.* 2011 and Ahmad *et al.* 2014) <sup>[2, 71]</sup> (Tables 1, 2 & 3).

Further, studies have shown that pre-term babies do not develop good bacteria till about three weeks after birth and if they are administered with probiotics have improved their survival rate (Boehm *et al.* 2002) <sup>[8]</sup>. Similarly, probiotics reduce the risk of antibiotics associated diarrhoea and probiotics should commonly be given during antibiotic therapy to maintain the internal balance (Gao *et al.* 2010, Cimperman *et al.* 2011 and Johnson 2011) <sup>[16, 24, 41]</sup>. Studies also show that there are significant benefits outside the gastrointestinal tract too, such as improved immunity and possible cancer prevention. *Lactobacillus* bacteria have been found to restore the activity of Natural Killer (NK) cells in our bodies. Natural Killer cells protect us from viruses, bacteria and other diseases causing organisms and are the mainstay of our immune system. Natural Killer cells diminished due to smoking, lack of Physical activity and inadequate sleep (Gopalkrishnan and Clinthorne 2012). Prevention of cancer and its recurrence is closely related to the immune system, thus probiotics have a role in cancer prevention too (Kim *et al.* 1994, McIntosh 1996, Geier *et al.* 2006 and Hiromitsu 2013) <sup>[25, 35, 46, 57]</sup>.

In some cases, probiotics have proven to be a more effective form of treatment than even prescription medicine. Probiotic strains like *Lactobacilli* and *Saccharomyces* have incredible success rate in fighting inflammatory bowel disease (Mach 2006, Hedin *et al.* 2007, and Lorea *et al.* 2007) [32, 51, 52] and irritable bowel syndrome (Niedzielin *et al.* 2001, Hun 2009, Moayyedi *et al.* 2010, Choi *et al.* 2011 and Gugliemetti, *et al.* 2011) [15, 27, 37, 59, 64]. Similarly, the gastric ulcers caused by *Helicobacter pylori* may be more effectively treated with probiotics rather than conventional antibiotics (Sagioro *et al.* 2005, Sgouras *et al.* 2005, Lionetti *et al.* 2006, Imase *et al.* 2007 and Shigeru 2012) [38, 49, 72, 75, 76]. Supplementation with probiotics to boost the body's overall population of *Lactobacilli* may help restore the balance of microflora in the vagina and thus help prevent common female problems such as bacterial vaginosis, yeast infection and urinary tract infections (Jeavons 2003, Reid 2008, Branco *et al.* 2010, Romeo *et al.* 2011 and Petrova *et al.* 2015) [10, 40, 66, 68, 71]. Similarly, in cases where disbiosis has been reported to be as one of the causes of a disease, the probiotic therapy must be adapted. For example, in cases where *Clostridium difficile* recurrent infections occurred in the human gut, fecal microbiota transplantations (FMT) should be recommended (Masroor *et al.* 2015) [54]. The *Clostridium difficile* infections are developed either with the long term use of vancomycin antibiotic or via the root of nosocomial infections. These infections are, sometimes, proved to be fatal (Johnston *et al.* 2012) [42]. In such patients, fecal microbiota transplantations have been carried on by using healthy poop containing useful bacteria satisfactorily, giving good results. These patients have recovered well for a longer period of time (Masroor *et al.* 2015) [54].

Further, probiotics have been proven as the perfect antidote to the junk food (Guslandi *et al.* 2000) [28]. Oral and periodontal health also responded positively to probiotics (Tasli *et al.* 2006, Hatakka *et al.* 2007 and Keller *et al.* 2012) [31, 43, 83]. Probiotics have shown some very good results in biotherapeutics like lowering of cholesterol, blood pressure and the effects of vitamin B<sub>12</sub> deficiency. It has also been used in the quantification of folic acid in human faeces (Table 4) (Kiebling *et al.* 2002, Jauhainen *et al.* 2005, Strozzi and Mogna 2008, Molina 2009 and Kumar *et al.* 2012) [39, 45, 48, 60, 79].

However, there are some limitations reported with the use of these probiotics. Probiotic treatments could be harmful especially where the person consuming probiotics is critically ill (Kentaro *et al.* 2013) [44]. Similarly, in the therapeutic clinical trail it was found that the consumption of a mixture of probiotic bacteria increased the death rate of patients with predicted severe acute pancreatitis (Besselink *et al.* 2008 and Sun *et al.* 2009) [7, 80]. And, the people suffering from gastrointestinal illnesses like Crohn's disease or irritable bowel syndrome may upset their symptoms by taking probiotics. It's necessary to achieve internal harmony before it can be optimized (Guslandi *et al.* 2000 and Gugliemetti *et al.* 2011) [27, 28].

Further, it is worth mentioning that no claims about these probiotic researches have so far been accepted by the regulating agencies. They are of opinion that only preliminary studies exist for most of these probiotic researches claimed and even some of these probiotic products containing live microorganisms confer the health benefit by actually undergoing controlled evaluation to document health benefits in the target hosts (Reid 2008) [68]. Thus, it appears

that while most of these probiotic researches are experimentally proved others are yet to be confirmed (Masroor *et al.* 2018) [55].

#### 4. Conclusion

The review summarizes the efficacies of probiotic microorganisms in curing certain ailments and diseases developed due to altered microbiota causing dysbiosis in human. The various ailments and diseases have been cured with the consumption of different probiotic foods containing good bacteria. These probiotics have been reported to heal this altered microbiota without any harm and we always feel free to use them in our daily life. But, as these probiotic bacteria have continuously been using by the society to cure certain human diseases, we the authors felt the need of regulation in applying the pure probiotic bacteria, at least in cases of patients who are critically ill, quite old or immunocompromised. Similar is the case with patients having perforated guts. It may spoil the ecobalance of the normal flora of the human gut, if used in huge amounts orally. It would be rather better to apply these probiotic pure bacteria in such patients even under strict medical supervision. Here, the pure probiotics can only be prescribed if the potential benefits justify the potential risk to the patients. Finally, it appears that though, these probiotics have enormous potential to cure certain human ailments and diseases, more researches are required to prove them. And, they may only be applied as a supportive therapy.

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#### 6. Conflict of Interest

The authors have declared no conflict of interest. They have approved the final version of the manuscript contributing equally.

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