Journal of Probiotics & Health

Fang et al., J Prob Health 2018, 6:1
DOI: 10.4172/2329-8901.1000203

Research Article Open Access

A Pilot Study of the Influence of Probiotics on Hair Toxic Element Levels After Long-Term Supplement with Different Lactic Acid Bacteria Strains

Ssu Ting Fang[1], Da En Cheng[2], Yu Ting Huang[2], Ting Yuan Hsu[2*] and Henry Horng Shing Lu[3]

[1]*Institute of Biomedical Engineering, College of Electrical and Computer Engineering, National Chiao Tung University, Hsinchu City, Taiwan*

[2]*Department of Research and Development, Bio Ray Biotech Inc., Kaohsiung,Taiwan*

[3]*Institute of Statistics and Big Data Research Center, National Chiao Tung University, Hsinchu City, Taiwan*

***Corresponding author:** Ting Yuan Hsu, Department of Research and Development, Bio Ray Biotech Inc., Kaohsiung, Taiwan, Tel: +886928594562; E-mail: hsumd@bio-ray.com.tw

Received date: June 19, 2018; **Accepted date:** June 29, 2018; **Published date:** June 30, 2018

Abstract

There are toxic elements in different environments. As these toxic elements accumulate, they might compromise one's health. In past literatures, people are actively looking for appropriate functional food (probiotics) which is used in decreasing the concentration of toxic elements in environments, animals or human bodies. This retrospective study focuses on whether taking more specific probiotic strain for at least six months can help significantly decreasing the concentration of toxic elements in one's hair. There are in total 319 participants for five probiotic strains (*Lactobacillus paracasei* BRAP-01, *Bifidobacterium longum* BR022, *Lactobacillus acidophilus* AD300, *Lactobacillus reuteri* BR101, *Lactobacillus rhamnosus* AD500). A concentration of six toxic elements (Cadmium (Cd), Mercury (Hg), Lead (Pb), Beryllium (Be), Arsenic (As), and Aluminum (Al)) have been detected in all the participants before and after taking probiotics. The factors of this study include gender, age, and disease (cancer, diabetes, and hypertension). The statistical methods for the study are exact McNemar's test, (exact) Wilcoxon signed-rank test, and regression tree. The summary of the conclusions for this study are: 1. For those previously detecting an abnormal concentration of Hg and Be, a significant decrease in the number of patients has been observed after taking probiotics. 2. Taking probiotic for at least six months can significantly decreases the concentration of Hg and Be. 3. Since no literature indicates that taking probiotics can obviously decrease the concentration of Be in one's hair, thus this research might be the first to claim this fact. The result of the study will benefit relevant researches in the future.

Keywords: Probiotics; Toxic elements; Lactic acid bacteria

Introduction

Everyone may contact toxic elements in various ways, such as in air, food, drinking water, daily necessities, and soil. The toxic elements not only cause environmental pollution but also cause great damage to human bodies. Several diseases are related to the amount of toxic elements accumulated in one's body. For example, Cadmium (Cd), Beryllium (Be), and Arsenic (As), are reported as carcinogens.

Food supply quantity data 2013 released by Food Agriculture Organization of the United Nations (FAO) indicates that Taiwanese consume 35.41 kg seafood per capita per year. The average of sea food consumption in Taiwan is equivalent to double around the world. Thus, the more sea food a person consumes the more heavy metals a person accumulates, such as Cd and Hg. According to 2016 Environmental Performance Index (EPI) report launched at World Economic Forum (WEF), half of the world's population are exposed to unsafe air quality. Toxic elements are omnipresent in our life. Therefore, how to reduce the concentration of the toxic elements in one's body effectively becomes a very important issue.

Currently, the chelation therapy, including EDTA, DMSA, and DMPS, is the only way to excrete the toxic elements immediately from the body. However, it may have serious side effects, such as reducing the amounts of other essential minerals (Ca, Fe, and Zn, etc.) at the same time, dehydration, liver failure, renal failure, hypoglycaemia, and coagulation insufficiency. Hence, this treatment is not always suitable for patients. Recently, more and more researches have aimed at exploring other ways to eliminate toxic elements from the environments and animals. However, there are not such many studies to find the treatments in human bodies. Among the toxic elements, Cd, Hg, Pb, and Be are toxic heavy metals. Due to the different influence factors, such as different types of work, eating habits, and different location, the concentration of toxic elements in each individual varies.

The World Health Organization (WHO) has defined probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host". Probiotics are considered as a functional food. They can modulate the immune system functions, improvement of the barrier functions of the gut mucosa, and to suppress the growth of pathogenic bacteria [1]. The probiotics are highly used in clinical, including Diabetes, Hypertension, Urogenital health care, Lactose intolerance, Crohn's disease and ulcerative colitis, Colon cancer, Inflammation, Immune function and infections, Peptic ulcer, Liver diseases, Food allergy, Upper respiratory tract infection, Oral health, and so on [2]. In recent years, some research studied the function of LABs (lactic acid bacteria) that removes heavy metals (toxic elements) in culture medium, animals, and human bodies.

LABs, such as *Lactobacillus gasseri* and *Lactobacillus reuteri* (*L.reuteri*), etc. can bind with the toxic metals (e.g. Cd) *in vitro* [3]. *L. reuteri* Cd70-13 and Pb71-1could remove Cd (25%) and Pb (59%) from the MRS culture medium; therefore, they may adsorb the toxic heavy metals in the intestinal tract [4]. In the water, exopolysaccharide

(EPS) of *Lactobacillus rhamnosus* (*L. rhamnosus*) can remove Al^{+3} and Cd^{+2} [5]. *Bifidobacterium logum* (*B. Longum*) 46 is also able to remove Cd and Pb from the water [6].

In some animal studies, supplying *Lactobacillus plantarum* (*L. plantarum*) CCFM639 can reduce the damage of liver and kidney [7]. It can also reduce the absorption of Al in the intestines and the accumulation of Al in the tissues, and discharged them from the faeces [7]. *L. plantarum* CCFM8610 can prevent heavy metals' (Cd) acute poisoning [8,9]. *L. plantarum* and *Bacilus coagulans* (*B. coagulans*) can treat and prevent Hg poisoning in high-risk areas in rats [10]. Pb can be absorbed 90% in the *Lactobacillus acidipiscis* (*L. acidipiscis*) ITA44 and *Lactobaciilus pentosus* (*L. pentosus*) ITA23 culture medium. Feeding *L. acidipiscis* ITA44 and *L. pentosus* ITA23 to broiler chickens can decrease Pb accumulation for 48% in liver and 28% in serum samples [11]. It is reported that pregnant women taking probiotic yogurt (*L. rhamnosus* GR-1) are able to control the levels of Hg and As in blood [12]. Among all the research, different probiotic species or strains have different effects on toxic elements in different media. Based on the literature, the purpose of this study is to verify whether a specific toxic element can be excreted from the human body by taking some specific probiotic strain for at least six months.

Features of this study include probiotic strains of participant supplement, gender, age, disease, and twice detecting value of concentration of toxic elements in hair. In this study, we want to answer that probiotics can remove or not, and what will be the important factor in the toxic element elimination from the human body.

Materials and Methods

Participants

The data in this study was providing by Bio Ray Biotech Inc. including 319 participants. Figure 1 shows the way how the data be collected. In this study, every participant must meet the following requirements: (1) The age of the participant must exceed 20 years old. (2) The participant has no intensively taken probiotics before. (3) The participant is required to take 20 billion CFU of a specific probiotic strain per day for at least six months. (4) The concentration of toxic elements (Cd, Hg, Pb, Be, As, Al) is duplicate measured before and after probiotics supplement. The numbers of participants in each probiotic strain are randomly assigned as follows: *Lactobacillus paracasei* BRAP-01 (AP01, Bio-Ray, Kaohsiung, Taiwan): nLP=114; *Bifidobacterium longum* BR022 (Bio-Ray, Kaohsiung, Taiwan): nBL=25; *Lactobacillus acidophilus* AD300 (Biena, Quebec, Canada): nLA=66; *Lactobacillus reuteri* BR101 (Bio-Ray, Kaohsiung, Taiwan): nLRe=69; *Lactobacillus rhamnosus* AD500 (Biena, Quebec, Canada): nLRh=45. The data of gender, ages, and disease states were collected following the ethical principles of Declaration of Helsinki and approved by the Research Ethics Committee for Human Subject Protection of National Chiao Tung University. The average of age and the distribution of genders and diseases of the study population were shown in Table 1. Diseases of participants were simply classified as four groups including cancers, diabetes (DM), hypertension (HTN) and he others.

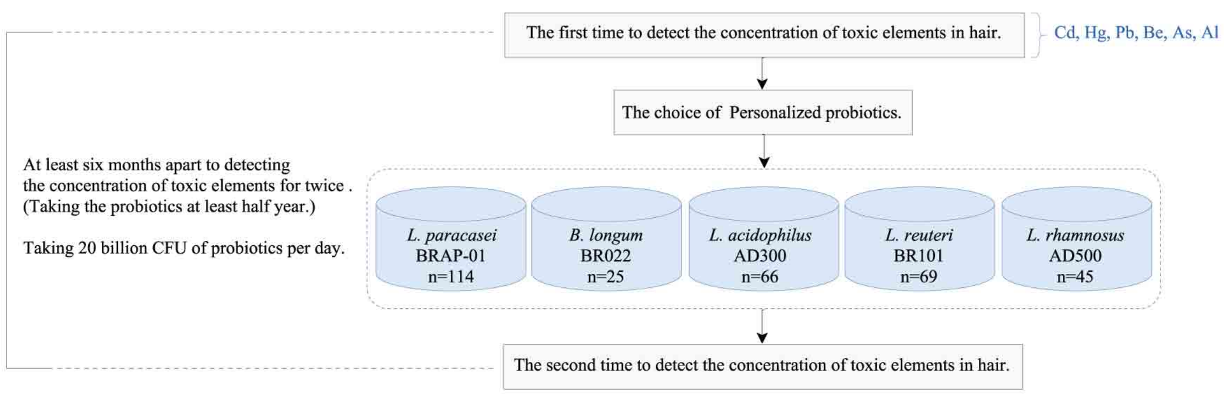

Figure 1: The flow chart of data collection.

Class	Type	Probiotics Strain					Total
		L. paracasei BRAP-01 n=114 (100%)	*B. longum* BR022 n=25 (100%)	*L. acidophilus* AD300 n=66 (100%)	*L. reuteri* BR101 n=69 (100%)	*L. rhamnosus* AD500 n=45 (100%)	n=319 (100%)
Gender	Male	71 (62.3%)	11 (44.0%)	39 (59.1%)	43 (62.3%)	33 (73.3%)	197 (61.8%)
	Female	43 (37.7%)	14 (56.0%)	27 (40.9%)	26 (37.7%)	12 (26.7%)	122 (38.2%)
Age	Mean ± SD	54.2 ± 10.7	56.6 ± 11.2	56.3 ± 11.9	56.1 ± 10.1	57.7 ± 12.7	55.7 ± 11.2
Disease	Cancer	28 (24.5%)	4 (16.0%)	14 (21.2%)	6 (8.7%)	7 (11.7%)	59 (18.5%)

	DM	23 (20.2%)	5 (20.0%)	12 (18.2%)	29 (42.0%)	14 (23.3%)	83 (26.0%)
	HTN	26 (22.8%)	5 (20.0%)	20 (30.3%)	24 (34.8%)	24 (40.0%)	99 (31.0%)
	Other	37 (32.5%)	11 (44.0%)	20 (30.3%)	10 (14.5%)	15 (25.0%)	78 (24.5%)

Table 1: Member of participants for each probiotic strain in different type.

Analysis of the toxic elements in hair

Each participant's hair is used as the sample to detect the concentration of toxic elements, and the experiment is conducted by La Belle Vie Inc. First, 75 mg hair sample is collected, and then cleaned by organic solvents and interacting agents. The hair sample is later dissolve into a solution and analysed by using ICP-MS to detect the concentration of toxic elements. The unit used in this study is ng/g hair (ppb).

Statistical methods

Exact McNemar's test, Wilcoxon signed-rank test, and regression tree are used in data analysis. In the following statistical analysis, significant level was set as 0.05. The statistical calculation was done in R version 3.2.4 (2016-03-10) and the related packages are "exact 2 × 2", "MASS", "exactRankTests", and "rpart".

Results

Number of people with an abnormal concentration of mercury and beryllium was significantly reduce after probiotics supplement

First at all, we analysed the concentration distribution of pre-supplement and post-supplement value for each toxic element. It showed only the median of Hg is decreased after probiotics supplement (Table 2 and Figure 2).

Toxic element	Pre-post	Median ± MAD[c]	Min[c]	Max[c]
Cd	pre[a]	8.59 ± 4.9	2.18	3532
	post[b]	9.14 ± 5.76	2.18	487
Hg	pre[a]	3767 ± 2376	16	33792
	post[b]	3106 ± 1873	110	37700
Pb	pre[a]	318 ± 194	17.3	2761000
	post[b]	359 ± 212	31.5	1011000
As	pre[a]	37.9 ± 26.5	3.58	3187
	post[b]	42.1 ± 26.8	3.58	895
Be	pre[a]	0.17 ± 0.1	0.07	159
	post[b]	0.17 ± 0.1	0.07	51
Al	pre[a]	4653 ± 2195	800	49940
	post[b]	4769 ± 2239	325	62040

Table 2: The concentration of toxic elements in hair for pro-post detection. [a]pre: the concentration of toxic element before taking probiotic. [b]post: the concentration of toxic element after taking probiotic. [c]The unit of Median, MAD (median absolute deviation), Min (Minimum), and Max (Maximum) are ppb.

To further investigate the changes of numbers from abnormal to normal ranges, we use the normal ranges suggested by La Belle Vie Inc. according to the investigation of hair elements evaluation in 5846 Japanese. Accordingly, the normal ranges of every element in hair were described as followed. (1) Cd is below 22 ppb. (2) Hg is below 6946 ppb. (3) Pb is below 1218 ppb. (4) As is below 89 ppb. (5) Be is below 0.74 ppb. (6) Al is below 7964 ppb. The number of concentration of toxic elements both in normal and abnormal cases were shown in Tables 3-8. The results demonstrate that the number of abnormal cases in Hg (p-value=0.001686) and Be (p-value=1.942×10^{-5}) decrease significantly after the participants have taken probiotics for at least six months. The intra-person difference showed that more than 50% participants who had decreased concentration of Hg, Pb, and As after taking probiotics for at least six months and 50% participants who is decreased the concentration of Be (Figure 3). Therefore, the intra-person decreasing effect of these toxic elements will be more attention.

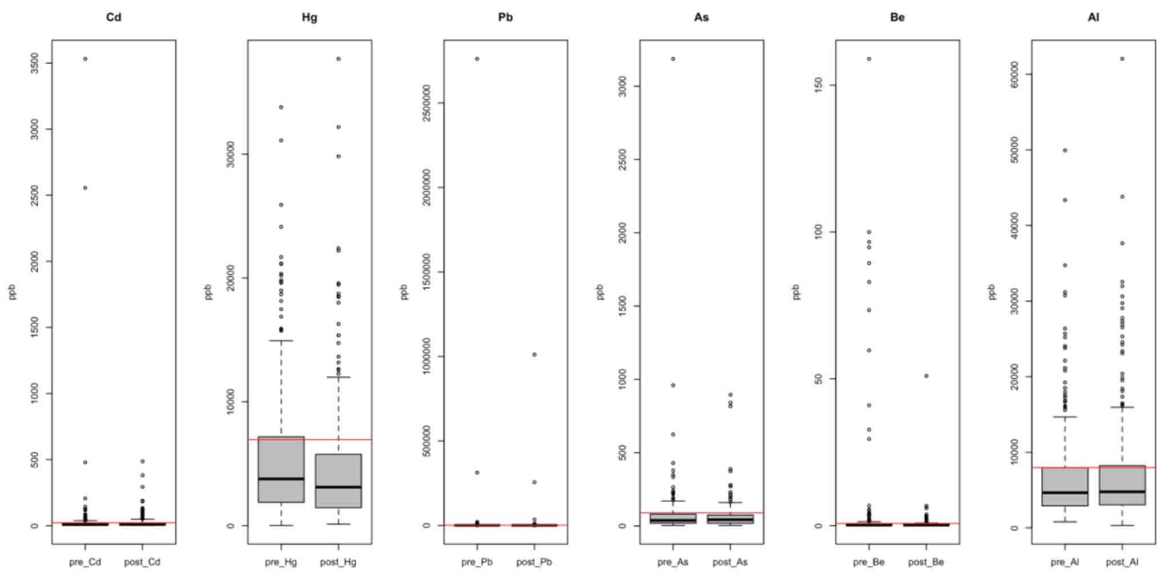

Figure 2: Boxplot for every toxic element pro-post supplement value. Red line: The normal ranges suggested by La Bella vie Inc.

Pre	Abn.	Norm.	Total
Post			
Abn.	39	27	66
Norm.	42	211	253
Total	81	238	319
p-value[a]=0.9734			

Table 3: Contingency table of cadmium (Cd). [a]Exact McNemar's Test.

Pre	Abn.	Norm.	Total
Post			
Abn.	35	50	85
Norm.	24	210	234
Total	59	260	319
p-value[a]=0.001686**			

Table 4: Contingency table of mercury (Hg). [a]Exact McNemar's Test, **p-value<0.01.

Pre	Abn.	Norm.	Total
Post			
Abn.	21	22	43
Norm.	18	258	276
Total	39	280	319
p-value[a]=0.3179			

Table 5: Contingency table of lead (Pb). [a]Exact McNemar's Test.

Pre	Abn.	Norm.	Total
Post			
Abn.	32	34	66
Norm.	24	229	253
Total	56	263	319
p-value[a]= 0.1185			

Table 6: Contingency table of arsenic (As). [a]Exact McNemar's Test.

Pre	Abn.	Norm.	Total
Post			
Abn.	18	53	71
Norm.	18	230	248
Total	38	283	319
p-value[a]=1.942×10^{-5}***			

Table 7: Contingency table of beryllium (Be). [a]Exact McNemar's Test, ***p-value<0.001.

Pre	Abn.	Norm.	Total
Post			

Abn.	49	31	80
Norm.	34	205	239
Total	83	236	319
p-value^a=0.6899			

Table 8: Contingency table of aluminum (Al). ^{a}Exact McNemar's Test.

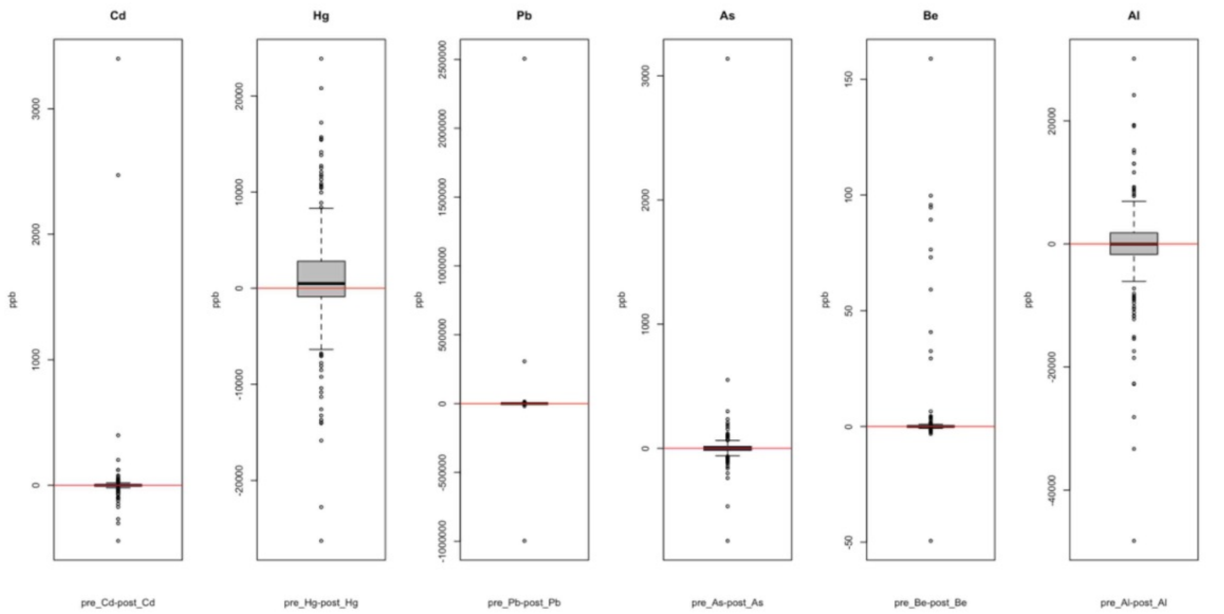

Figure 3: Boxplot for the difference between pro-post detecting values for every toxic element. Red line: No difference of the concentration in the toxic element after taking probiotic for at least six months.

Different probiotics strains exhibited different abilities in toxic element elimination

By analysing the difference of toxic element levels before and after supplement of probiotics in each participant, it showed that the concentration of Hg (p-value=1.846×10^{-5}) and Be (p-value=0.0275) are decreased significantly after taken probiotic for at least six months (Table 9). Especially, people who have taken *L. paracasei* BRAP-01(p-value=0.01964), *B. longum* BR022 (p-value=0.02938), and *L. reuteri* BR101 (p-value=6.195×10^{-6}). In addition, concentration of Be decrease significantly after the participants have taken *L. acidophilus* AD300 (p-value=0.006438) for at least six months.

Median ± MAD (p-value)^a	**Cd**	**Hg**	**Pb**	**Be**	**As**	**Al**
L. paracasei BRAP-01 (nLP=114)	0.21 ± 4.15	443 ± 1629	27.05 ± 133.5	0 ± 0.22	-1.72 ± 14.32	147 ± 1547
	-0.2281	(0.01964*)	-0.1835	-0.296	-0.6838	-0.4023
B. longum BR022 (nBL=25)	-5.16 ± 8.08	1073 ± 1871	-40 ± 184	0 ± 0.41	2.69 ± 17.01	-1702 ± 3972
	-0.9926	(0.02938*)	-0.8268	-0.3071	-0.3187	-0.9829
L. acidophilus AD300 (nLA=66)	-0.64 ± 5.35	433.5 ± 1897.5	26.55 ± 206	0.05 ± 0.3	1.98 ± 13.27	530 ± 1817.5
	-0.8305	-0.1161	-0.3893	(0.006438**)	-0.08498	-0.2936
L. reuteri BR101 (nLRe=69)	-0.48 ± 4.12	1394 ± 1613	-51 ± 178	0 ± 0.26	0.04 ± 17.24	104 ± 1593
	-0.9071	(6.195 × 10^{-8})	-0.7644	-0.2652	-0.5345	-0.2212

Citation: Fang ST, Cheng DE, Huang YT, Hsu TY, Lu HHS (2018) A Pilot Study of the Influence of Probiotics on Hair Toxic Element Levels After Long-Term Supplement with Different Lactic Acid Bacteria Strains. J Prob Health 6: 203. doi:10.4172/2329-8901.1000203

L. rhamnosus AD500 (nLRh=45)	0.55 ± 4.35	-508 ± 1349	95 ± 244	0 ± 0.14	-1.7 ± 31.9	-252 ± 1768
	-0.6605	-0.8436	-0.1104	-0.5618	-0.6473	-0.7082
Total (nTotal=319)	-0.2 ± 4.5	487 ± 1612	11 ± 168	0 ± 0.23	0.04 ± 1586	-15 ± 1808
	-0.9386	(1.846 × 10-***)	-0.3026	(0.0275*)	-0.4131	-0.6334

Table 9: Information about the difference of twice detection of the concentration of toxic elements in hair by taking each probiotic strain. [a]Wilcoxon signed-rank test. *p-value<0.05.**p-value<0.01. ***p-value<0.001.

The concentration decreasing effects in specific group of regression tree

Furthermore, we use the regression tree to determine the rank of factors in the database. Every regression tree is designed as the terminal nodes which contains at least ten samples and the maximum depth of regression tree is three. The regression tree is based on the difference between pre-detecting and post-detecting toxic element concentration value which factor include gender, age, disease (cancer, DM, and HTN) and five probiotics strains. After regression tree generating, do Wilcoxon signed-rank test for every node in regression tree. Then, find which specific group have significant decrease of concentration and observe whether there is any interaction for every toxic element.

Figure 4A demonstrated the regression tree for the difference between pre-detecting and post-detecting concentration of Hg. The most important factor of significant decreased of the concentration of Hg is cancer (yes or no). The second important factor is probiotics strain. The third important factor is age (age more than or equal to 54 years old or age less than 54 years old). Three important factors are interacting with each other. In the regression tree of Figure 4A, Node3 shows that having taken probiotics for at least six months, participants not suffering from cancer were significantly decreased the concentration of Hg (p-value=1.352 × 10^{-6}); Node4 shows that participants not suffering from cancer and having taken probiotics which are *L. paracasei* BRAP-01, *L. acidophilus* AD300 or *L. rhamnosus* AD500 for at least six months significantly decreased of the concentration of Hg (p-value=0.01225); Node5 shows that participants not suffering from cancer and having taken probiotics which are *B. longum* BR022 or *L. reuteri* BR101 for at least six months significantly decreased of the concentration of Hg (p-value=1.431 × 10^{-6}); Node6 shows that participants not suffering from cancer, having taken probiotics which are *B. longum* BR022 or *L. reuteri* BR101 for at least six months and aging greater than or equal to 54 years old significantly decreased of the concentration of Hg (p-value=0.005602); Node7 shows that participants not suffering from cancer, having taken probiotics which are *B. longum* BR022 or *L. reuteri* BR101 for at least six months and aging less than 54 years old significantly decreased of the concentration of Hg (p-value=4.951 × 10^{-6}).

Figure 4B is the regression tree for the difference between pre-detecting and post-detecting concentration of Be. The most important factor of significant decrease in concentration of Be is gender (male of female). The second important factor is age. The third important factor also is age. Those important factors are interacting with each other. In the regression tree of Figure 4B, Node3 shows that males having taken probiotics for at least six months significantly decreased of the concentration of Be (p-value=0.0372); Node5 shows that males having taken probiotics for at least six months and aging greater than 50 years old significantly decreased of the concentration of Be (p-value=0.003893); Node7 shows that males having taken probiotics for at least six months and aging greater than 50 years old and less than 58 years old significantly decreased of the concentration of Be (p-value=0.005324). In this study, only Hg and Be concentration decreased significantly whereas other toxic elements do not show any specific effect of decreasing in this study.

Figure 4: The regression tree for the differential concentration of mercury and beryllium in hair.

Discussion

The use of bacteria as bio sorbent in industrial and environment pollution has been studied for a long time. However, there are only few articles describing the use of probiotics as detoxification agent for heavy metal accumulation in animals. Present study is the first large scale investigation of the impact of probiotics on long term toxic accumulation. Also, it is the first time to compare the effect of different probiotics strain on the accumulation of different toxic element in human hair samples.

We found that the mercury accumulation is decreased in three of five different strains, including *L. paracasei* BRAP01, *B. longum* BR022 and *L. reuteri* BR101. Whereas the decision tree also showed that the supplement of *B. longum* BR022 and *L. reuteri* BR101 is also an important factor for the decreased mercury accumulation in the study population. The same result was also found in Bisanz's study in Tanzania which means mercury may be a major target of probiotics as bio sorbent. However, the *L. rhamnosus* strain we used did not show the same effect of *L. rhamnosus* GR-1 which means the effects may be strain restricted. The same phenomenon was also observed by Kirillova [13] and Bhakta [4] that different strains of the same species may have different toxic element absorption abilities. Unlike lead and cadmium, the mechanism of mercury to bacteria interaction has not been well identified. The only one studied of mercury binding protein in lactic acid bacteria was demonstrated by Kinoshida [3], but the mechanism is still not fully understood.

In the other hand, the bioremediation of lead and cadmium was not observed in all the five strains in this investigation. It also agree with the results of Bisanz's study in Tanzania that the same strain used in Bisanz's study even showed a good lead and cadmium binding abilities *in vitro* [14]. It suggests that the protection effects of probiotics to decrease toxic element accumulation in human hair may be different from the simple *in vitro* removing tests. The mercury metabolic enzyme, like methylmercury demethylase may also play an important. All above, the right strain that prevent accumulation of toxic element in human should be confirmed by clinical trial or other *in vitro* experiments.

Another interesting finding in this study is demonstrating that cancer may be an important factor in mercury excretion. One of the hypotheses is that the use of traditional Chinese medicine is very common in Eastern Asia to treat cancer patients. The heavy metal contamination, especially mercury and arsenic, are found either in commercial or unknown source of traditional Chinese medicine very often [15,16]. Another possible cause is the high consumption of selenium in cancers [17-19], and selenium is an important factor in mercury detoxification [20-22].

Up to date, the significant decrease in the beryllium after probiotics uptake is the first time being discovered in present study. Unlike other toxic element, the researches of interaction between beryllium and probiotics are relatively rare. However, there is lacking of strong evidence between beryllium and lung cancer, the long term exposure to beryllium still causes the damages of the body, including berylliosis and skin and eye irritation [23-25]. Our data demonstrated that the beryllium decrease could be observed in female, 50-58 years old after uptake *L. acidophilus* AD300. Considered of the residence, genders and habits of study population, we hypothesis that smoking is the most possible route of beryllium accumulation since tobacco often contains trace amount of beryllium [26-28]. Altogether, this study implies that the supplement of certified probiotics strains could be used in treatment of chronic accumulation of toxic elements, especially the mercury and beryllium, in human bodies and may prevent further damages and diseases.

References

1. Daliri EBM, Lee BH (2015) New perspectives on probiotics in health and disease. Food Sci Hum Wellness 1: 56-65.
2. Iqbal MZ, Qadir MI, Hussain T, Janbaz KH, Khan YH, et al. (2014) Review: Probiotics and their beneficial effects against various diseases. Pak J Pharm Sci 27: 405-415.
3. Kinoshita H, Sohma Y, Ohtake F, Ishida M, Kawai Y, et al. (2013) Biosorption of heavy metals by lactic acid bacteria and identification of mercury binding protein. Res Microbiol 164: 701-709.
4. Bhakta JN, Ohnishi K, Munekage Y, Iwasaki K, Wei MQ (2012) Characterization of lactic acid bacteria-based probiotics as potential heavy metal sorbents. J Appl Microbiol 112: 1193-1206.
5. Berecka MP, Szwajgier D, Waśko A (2014) Biosorption of Al(+3) and Cd(+2) by an exopolysaccharide from Lactobacillus rhamnosus. J Food Sci 79: T2404-T2408.
6. Halttunen T, Salminen S, Tahvonen R (2007) Rapid removal of lead and cadmium from water by specific lactic acid bacteria. Int J Food Microbiol 114: 30-35.
7. Yu L, Zhai Q, Yin R, Li P, Tian F, et al. (2017) Lactobacillus plantarum CCFM639 alleviate trace element imbalance-related oxidative stress in liver and kidney of chronic aluminum exposure mice. Biol Trace Elem Res 176: 342-349.
8. Zhai Q, Wang G, Zhao J, Liu X, Tian F, et al. (2013) Protective effects of Lactobacillus plantarum CCFM8610 against acute cadmium toxicity in mice. Appl Environ Microbiol 79: 1508-1515.
9. Zhai Q, Yu L, Li T, Zhu J, Zhang C, et al. (2017) Effect of dietary probiotic supplementation on intestinal microbiota and physiological conditions of Nile tilapia (Oreochromis niloticus) under waterborne cadmium exposure. Antonie Van Leeuwenhoek 110: 501-513.
10. Majlesi M, Shekarforoush SS, Ghaisari HR, Nazifi S, Sajedianfard J, et al. (2017) Effect of probiotic bacillus coagulans and lactobacillus plantarum on alleviation of mercury toxicity in rat. Probiotics Antimicrob Proteins 9: 300-309.
11. Jahromi MF, Liang JB, Ebrahimi R, Soleimani AF, Rezaeizadeh A, et al. (2017) Protective potential of Lactobacillus species in lead toxicity model in broiler chickens. Anim Int J Anim Biosci 11: 755-761.
12. Bisanz JE, Enos MK, Mwanga JR, Changalucha J, Burton JP, et al. (2014) Randomized open-label pilot study of the influence of probiotics and the gut microbiome on toxic metal levels in Tanzanian pregnant women and school children. mBio 5:e01580-e01514.
13. Kirillova AV, Danilushkina AA, Irisov DS, Bruslik NL, Fakhrullin RF, et al. (2017) Assessment of Resistance and Bioremediation Ability of Lactobacillus Strains to Lead and Cadmium. Int J Microbiol 2017: 9869145.
14. Reid JNS, Bisanz JE, Monachese M, Burton JP, Reid G (2013) The rationale for probiotics improving reproductive health and pregnancy outcome. Am J Reprod Immunol 69: 558-566.
15. Liu SH, Chuang WC, Lam W, Jiang Z, Cheng YC (2015) Safety surveillance of traditional Chinese medicine: Current and future. Drug Saf 38: 117-128.
16. Espinoza EO, Mann MJ, Bleasdell B (1995) Arsenic and mercury in traditional Chinese herbal balls. N Engl J Med 333: 803-804.
17. Kune G, Watson L (2006) Colorectal cancer protective effects and the dietary micronutrients folate, methionine, vitamins B6, B12, C, E, selenium, and lycopene. Nutr Cancer 56: 11-21.
18. Chen YC, Prabhu KS, Mastro AM (2013) Is selenium a potential treatment for cancer metastasis? Nutrients 5: 1149-1168.
19. Schrauzer GN, White DA, Schneider CJ (1997) Cancer mortality correlation studies-III: Statistical associations with dietary selenium intakes. Bioinorg Chem 7: 23-31.
20. Grandjean P, Weihe P, Jorgensen PJ, Clarkson T, Cernichiari E (1992) Impact of maternal seafood diet on fetal exposure to mercury, selenium, and lead. Arch Environ Health 47: 185-195.
21. Seppanen K, Kantola M, Laatikainen R, Nyyssonen K, Valkonen VP, et al. (2000) Effect of supplementation with organic selenium on mercury status as measured by mercury in pubic hair. J Trace Elem Med Biol Organ Soc Miner Trace Elem GMS 14: 84-87.
22. Ganther HE, Goudie C, Sunde ML, Kopecky MJ, Wagner P (1972) Selenium: Relation to decreased toxicity of methyl mercury added to diets containing tuna. Science 175: 1122-1124.

23. Van Ordstrand HS, Hughes R (1945) Beryllium poisoning. J Am Med Assoc 129: 1084-1090.
24. Nishimura M (1966) Clinical and experimental studies on acute beryllium disease. Nagoya J Med Sci 29: 17-44.
25. Epstein WL (1983) Commentary and update: beryllium granulomas of the skin: A small window to understanding. Cleve Clin Q 50: 73-75.
26. Fresquez MR, Pappas RS, Watson CH (2013) Establishment of toxic metal reference range in tobacco from US cigarettes. J Anal Toxicol 37: 298-304.
27. Pappas RS (2011) Toxic elements in tobacco and in cigarette smoke: Inflammation and sensitization. Met Integr Biometal Sci 3: 1181-1198.
28. Tso TC, Sorokin TP, Engelhaupt ME (1973) Effects of some rare elements on nicotine content of the tobacco plant. Plant Physiol 51: 805-806.