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Presence of heavy metals of some selected neutraceutical products and their quality control assessment

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Abstract

Neutraceutical is combination of two words nutrition and pharmaceutical. The right amount of Neutraceutical is taken for the optimal healing and with fewer side effects. A Neutraceutical is a substance can be used in necessity of vitamins required by the body in order to full fill the demand of food which can be a curative as well as therapeutically used. This research was conducted to check the percentage of trace elements of zinc, copper iron, and lead, in the seven Neutraceutical products by the help of atomic absorption spectrum which are frequently used by the public of Quetta city i-e capital of Province of Baluchistan. The Physio-chemical properties like thickness, diameter, weight variation, dissolution, friability, are also checked and compared to the specification given in USP and BP pharmacopeia to find out that during manufacturing SOPs are followed or not. The seven empty bottles were selected to make solution of Neutraceutical in different products we washed every tablet with methanol in order to protect these bottles from germs, dust or any other contamination. The results obtained by quality control tests indicate that there was much deviation in the weight variation and hardness among these tablets of same batch but no deviation between thickness and diameter of these tablets. The result obtained by atomic absorption showed that percentage of these trace elements was more or less than the recommended limits when compared to specification given in USP and BP pharmacopeia. The concentration of these elements has much concern with the therapeutic efficacy of the Neutraceutical. The high concentration of lead is very much toxic to the lungs, liver and kidney. As well as the high concentration of iron, copper, zinc also affect the normal physiology of human being. It was concluded from this research that SOPs were not followed during manufacturing. So manufacturer should take consideration in respect to these formulations, SOPs should be followed as well as pre formulation studies and quality control tests should performed during all development procedures.

Keywords: Nutraceuticals; Atomic absorption; Quality control; USP; BP

1. Introduction

Neutraceutical is combination of two words i-e nutrition and pharmaceutical. The part of our food which undergone the process of pharmaceutically designed procedures to convert these food into medicinal form is known as Neutraceutical (1). The Neutraceutical are the ingredients of food of our daily meal which uphold our health and can be utilized for the management and stoppage of disease. It is apprised that food available in the market is used by us without knowing that how it is prepared and what are the uses of this food, then this food is referred as functional food. Functional food consists of the required quantity of vitamins, proteins, fats, carbohydrates etc. which is utmost needed for our body and health (2). The right amount of Neutraceutical is taken for the optimal healing and with less side effects. 2000 years before Hippocrates stated that the food which is taken is your medicine and medicine which is taken is your food. Herbal natural medicines are strong tools in maintaining health and work very actively in the shape of nutrition against the

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acute and chronic illness and also improve health and quality of life (3) When functional food supports in the prevention and treatment of illness and or/disorders except anemia. It is termed as Neutraceutical. The functional foods usually act in one way or the other as antiemetic. However, if anemia is excluded then it is considered in two separate terms that is Neutraceutical and functional food (4). A Neutraceutical is a substance can be used in necessity of vitamins required by the body in order to full fill the demand of food which can be a curative as well as therapeutic. Neutraceutical includes all the special energy containing nutrient, dietary, supplement and genetically engineered food, herbal natural products, and food undergone by different chemical processes such as soup, cereals, and beverages. (5)

Natural drugs are mostly used for different chronic illness conditions. There are many elements which may be found in very less quantity. In natural drugs trace elements like Iron(Fe), Potassium(K), Cobalt(Co), Bromine(Br), Scandium(Sc), Rubidium(Rb), Samarium(Sm), Chromium(Cr), Aurum(Au), Zinc(Zn), Europium(Eu), are most common. Amongst these elements, the iron is found in a high quantity followed by zinc and rubidium. Samarium, europium and aurum are present in very minute quantity (6).

There is common perception amongst the masses that natural health products are beneficial for health and quite safe for human body, but it has been observed that plant possess many chemical ingredients. Out of these chemical ingredients some are potentially fatal such as cytotoxic anti-cancer products which are derived from plants, pyrozidine alkaloids, and digitalis etc. However, it has been assumed that side effects of natural products less harmful as compared to synthetic medicines. Clinical trials show that natural drugs exist without any doubt. A progressive improvement is the basic requirement in the process of manufacturing. The biotechnological studies and genetic improvements of medicinal plants over the cultivation of natural drugs in wild is required to ensure the efficacy and safety of natural drugs (7). It is comprehended that there is no trace elements or if present the quantity of traced elements is very less than the recommended limits, therefore it is assumed that these are less harmful for the human (8).

The common public has been taking herbal medicines/ natural drugs since long. This way of medication generally focuses on organ cure and their systems while the medication has an overall effect on the whole body (9). The ingredients which are used to make natural drugs are mostly highly contaminated therefore does not give the result up to the mark. When the final products are prepared these toxins and contaminations are mixed with the final products and hence cause numerous disorders (10). However when element lead is accidently contaminated the final dosage form therefore by taking this dosage it would cause severe health damage in a young age patient (11) it is believed to have led towards several disease symptoms in young patients and the chief reason of it being the usage of lead contaminated drugs (12).

2. Methodology

2.1. Chemicals

1. Deionizer (silex), **2**. Nitric Acid, **3**.Whatman's Filter Paper, **4**.PH Medium, **5**.Per Choleric acid

Table 1 Different Brand of Drugs (Nutraceuticals used)

S No	Name of the formulation	Ingredients	Manufacturers
1.	Sinofer	Iron, Folic acid with vitamin C	Sindhco Laboratories
2.	Vitowa	Vitamins and multivitamin	Feroza International pharmaceuticals
3.	Maltifar-F	Iron, Folic Acid	Sindhco Laboratories
4.	Sinovit	Multivitamin and Multimineral	Sindhco Laboratories
5	Sinocal	Vitamin D	Sindhco Laboratories
6.	Ginko-S	Ginkgo Biloba, Bacopa	Kamal Laboratories
7.	Velnaar	Multi Vitamin and Mineral	Green Health Nutraceuticals

2.2. Equipment's

1. Hot Plate, 2. Atomic Absorption Spectrometer, 3. Electric Balance, 4. PH Meter, 5. Friabilator 6. Hardness tester.;

2.3. Sample Selection and Collection

All the samples were taken from the market of Quetta City. These are collected from different Neutraceutical companies. These products are prescribed to the patient in all over Pakistan. All Neutraceutical are prescribed to cure the different serious illness. However, all these products were either mixed or in single preparation. I had selected different seven products of various brands. Selected sample of different drugs were analyzed for their percentage of the trace elements and also to check the quality control of these drugs. All these products were kept at normal temperature and it should be make sure that these products should be protected from humidity and any contamination (13).

2.4. Sample Preparation

In order to mask the identity of every tablet each tablet should be coded with different code numbers. Then seven empty bottles were selected to make solution of Neutraceutical in different products we washed every tablet with methanol in order to protect these bottles from germs, dust or any other contamination. The samples were separately crushed down into powder (empty, crush, motor pastel) and should keep in the dry glass bottles which are already coded and sealed air tightly (14).

2.5. Method of Determination

As per SOP (standard operating procedure) one gram of every sample were taken and pour it in a flask and incorporated it with 10ml of 67% nitric acid. Then after we took 4ml of per choleric acid and mix it with the same sample and this sample were kept into fume hood for 24 hours at room temperature. After that with the help of hotplate, the samples were concentrated up to 1m. These samples were concentrated with de ionized water which is 50ml. Now this de ionized water were mixed with the samples and then filtered with Whatt man's filter paper. Once the filtration is completed, we added de ionized water to make the overall volume of this solution as 100ml. Each of this solution was labeled as stock solution and these stock solutions were examined with the help of atomic absorption for the detection of percentage of trace elements (15).

2.6. Quality Control Tests

Following different Quality Control tests were performed and matched with BP and USP to check either the Neutraceutical manufacturers followed the standards of the Quality Control tests according to the specification (16).

2.6.1. Friability Test

This test was carried out to check the pressure bearing capacity of tablets during its manufacturing, coating, packaging and transport. Where we checked the cracking and chopping of the tablets and that should not be differentiate than the normal values as per Pharmacopeia specification.

2.6.2. Hardness and Thickness Tests

We took 20 tablets and weighed them individually and find out the average hardness after that compared the hardness of individual tablet with average hardness. The checked hardness and thickness were compared with the standards specified in USP and BP to find out either the Neutraceutical fallow the standards or not.

2.6.3. Weight Variation

20 tablets were selected for this test and weighed them individually with the help of electronic balance after weighing calculated the average weight and then compare the individual weight with the average weight and standards specified in USP and BP.

3. Results

3.1. Physical Characterization of selected Nutraceuticals

The results confirmed the findings of (13).

The thickness of all the different brands of Neutraceutical were done according to the USP and BP specification as Neutraceutical have no specifications to check or compare the physical parameters. That is why it was preferred to check the all the physical characteristics according to the USP and BP specifications and it was found that there is huge difference between all these formulations when compared with each other.

The diameter of all the different brands of Neutraceutical were done according to the USP and BP, it was found that there is slight difference between all these formulations when compared with each other.

The weight variation of different brands of the Neutraceutical was done according to the USP and BP specification. It was found that there is slight difference between all these formulations when compared with each other.

The hardness of all the different brands of Neutraceutical were done according to the USP and BP specification, it was found that there is slight difference between all these formulations when compared with each other.

The friability of two products is within the specification given by USP and BP i-e less than 1%. The friability tests are not performed for rest of the Neutraceutical products because these were coated.

Table 2 Physical Characteristics

Code of Formulation	Thickness	Diameter	Weight Variation	Hardness	Friability
NPU-15	0.68cm	1.39cm	440mg	15.2kg/cm	Coated not performed
NPU-25	0.68cm	2.09cm	450mg	13.6kg/cm	Coated, not performed
NPU-35	0.57cm	2.2cm	610mg	16.41kg/cm	Coated not performed
NPU-45	0.57cm	2.14cm	680mg	19.4kg/cm	Coated not performed
NPU-55	0.55cm	2.14cm	610mg	21.51kg/cm	0.56%
NPU-65	2.04cm	1.38cm	450mg	9.24kg/cm	Coated, not performed
NPU-75	0.6cm	2.03cm	550mg	19.7kg/cm	0.44%

3.2. NPU-15 Trace Elements

The results confirmed the findings of (13).

The presence of heavy metals in the Neutraceutical product of NPU-15 tablets was done with the help of atomic absorption. All values are calculated as ±SEM.

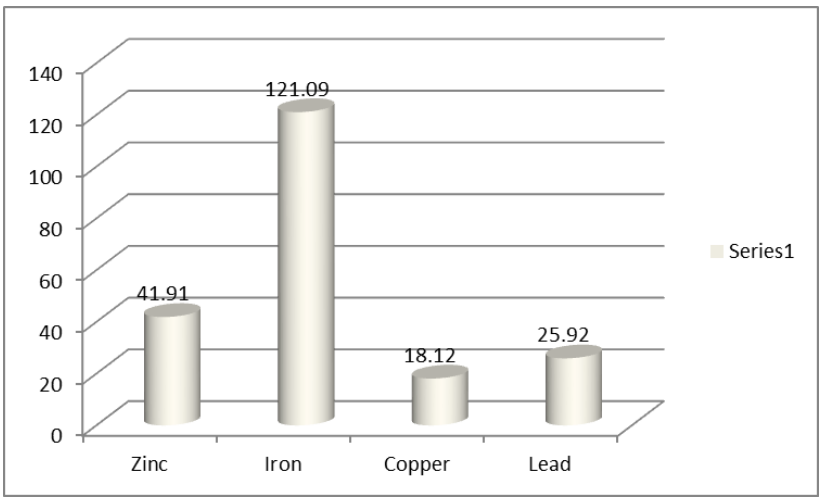

Figure 1 NPU-15 Trace Elements

The results of NPU-15 showed that the value of zinc calculated by atomic absorption was 41.19 ±SEM 0.44 and the recommended limits allowed by USP and BP specification is 27.4 ppm. These results showed that the quantity of zinc in the Product NPU-15 was much higher than the recommended limits.

The results of NPU-15 showed that the value of iron calculated by atomic absorption was 121.09 ±SEM 0.31 and recommended limits allowed by USP and BP specification is 20 ppm. These results showed that the quantity of iron in the products NPU-15 was much higher than the recommended limits.

The result of NPU-15 showed that the value of copper calculated by atomic absorption was 18.02 ±SEM 1.21 and the recommended limits allowed by USP and BP specification was 100 ppm. These results indicate that the value of copper was much less than the recommended limits.

The result of NPU-15 showed that the value of lead calculated by atomic absorption was 25.92 ± SEM 1.11 and USP and BP specification recommended limits is 10 ppm. These results indicate that the value of lead was much higher than the recommended limits.

Table 3 NPU-15 TRACE ELEMENTS

Elements Found	Zinc	Iron	Copper	Lead
Concentration (PPM)	41.19±0.44	121.09±0.31	18.02±1.21	25.92±1.11
Recommended Limits (PPM)	27.4	20	100	10

(The values given in the table were mean ± SEM)

3.3. NPU-25 trace elements

The results confirmed the findings of (13).

The presence of heavy metals in the Neutraceutical products of NPU-25 tablets was detected by the help of atomic absorption. All values are calculated as ± SEM.

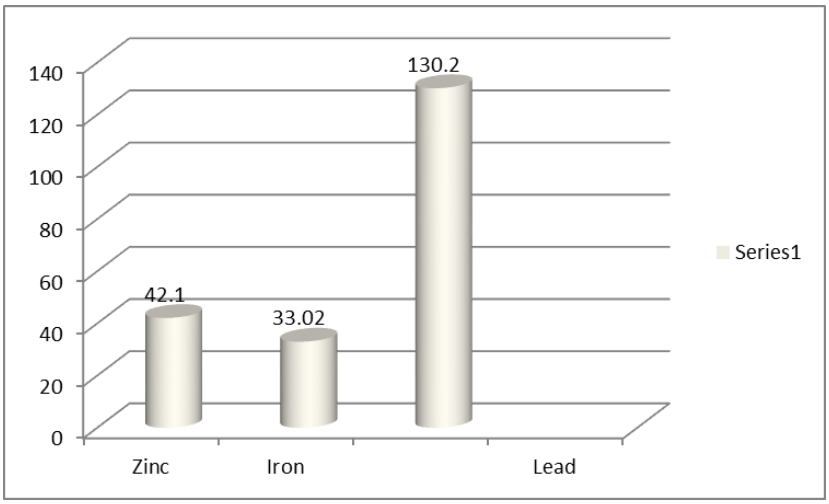

Figure 2 Trace Elements of NPU-25

The results of NPU-25 showed that the value of zinc calculated by atomic absorption was 42.10

±SEM 0.45 and the recommended limits allowed by USP and BP specification is 20ppm. These results indicate that the value of zinc was higher than the recommended limits.

The results of NPU-25 showed that the value of iron calculated by atomic absorption was 33.02 ±SEM 0.20 and the recommended limits allowed by USP and BP specification is 20 ppm. These results indicate that the value of iron was slightly higher than the recommended limits.

The results of NPU-25 showed that the value of copper calculated by atomic absorption was 130.20 ±SEM 0.63 and the recommended limits allowed by USP and BP specification is 100ppm. These results indicate that the value of copper was higher than the recommended limits.

The results of NPU-25 showed that the value of lead calculated by atomic absorption was 15.32 ±SEM 1.15 and the recommended limits allowed by USP and BP specification is 10ppm. These results indicate that value of lead was slightly higher than the recommended limits.

Table 4 NPU-25 Trace Elements

Elements Found	Zinc	Iron	Copper	Lead
Concentration (PPM)	42.10±0.45	33.02±0.20	130.20±0.63	15.32±1.15
Recommended Limits (PPM)	27.4	20	100	10

(The values given in the table were mean ± SEM)

3.4. NPU-35 Trace Elements

The results confirmed the findings of (13).

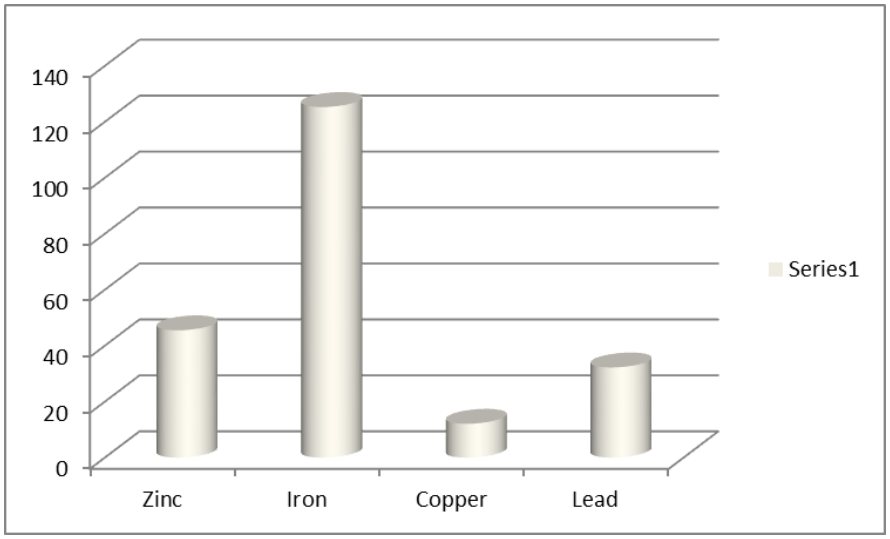

Figure 3 Trace Elements of NPU-35

The presence of heavy metals in the Neutraceutical product of NPU-35 tablets was detected by the help of atomic absorption. All values are calculated as ±SEM.

The results of NPU-35 showed that the value of zinc calculated by atomic absorption was 45.50 ±SEM 0.11 and the recommended limits allowed by USP and BP specification is 27.4 ppm. These results indicate that the value of zinc was higher than the recommended limits.

The results of NPU-35 showed that the value of iron calculated by atomic absorption was 125.30 ±SEM 1.12 and the recommended limits allowed by USP specification is 20 ppm. These results indicate that the value of iron was much higher than the recommended limits.

Table 5 NPU-35 Trace Elements

Elements Found	Zinc	Iron	Copper	Lead
Concentration (PPM)	45.50±0.11	125.30±1.12	12.10±0.13	32.21±0.28
Recommended Limits (PPM)	27.4	20	100	10

(The values given in the table were mean ± SEM)

The results of NPU-35 showed that the value of copper calculated by atomic absorption was 12.10 ±SEM 0.13 and the recommended limits allowed by USP and BP specification is 100 ppm. These results indicate that the value of copper was much less than the recommended limits.

The results of NPU-35 showed that the value of lead calculated by atomic absorption was 32.21 ±SEM 0.28 and the recommended limits allowed by USP and BP specification is 10 ppm. These results indicate that value of lead was higher than the recommended limits.

3.5. NPU-45 Trace Elements

The results confirmed the findings of (13).

The presence of heavy metals in the Neutraceutical product of NPU-45 tablets was detected by the help of atomic absorption. All values are calculated as ±SEM

The results of NPU-45 showed that the value of zinc calculated by atomic absorption was 28.50 ±SEM 1.06 and the recommended limits allowed by USP and BP specification is 27.4 ppm. These results showed that the quantity of zinc in the Product NPU-45 was much higher than the recommended limits.

The results of NPU-45 showed that the value of iron calculated by atomic absorption was 15.02 ±SEM 0.33 and recommended limits allowed by USP and BP specification is 20 ppm. These results showed that the quantity of iron in the products NPU-45 was slightly less than the recommended limits.

The result of NPU-45 showed that the value of copper calculated by atomic absorption was 85.25 ±SEM 1.21 and the recommended limits allowed by USP and BP specification is 100 ppm. These results indicate that the value of copper was slightly less than the recommended limits.

The result of NPU-45 showed that the value lead calculated by atomic absorption was 12.15 ±SEM 2.16 and recommended limits followed by USP and BP specification is 10 ppm. These results indicate that the value of lead was slightly deviated from the recommended limits.

Table 6 NPU-45 Trace Elements

Elements Found	Zinc	Iron	Copper	Lead
Concentration (PPM)	28.50±1.06	15.02±0.33	85.25±1.21	12.15±2.16
Recommended Limits (PPM)	27.4	20	100	10

(The values given in the table were mean ± SEM)

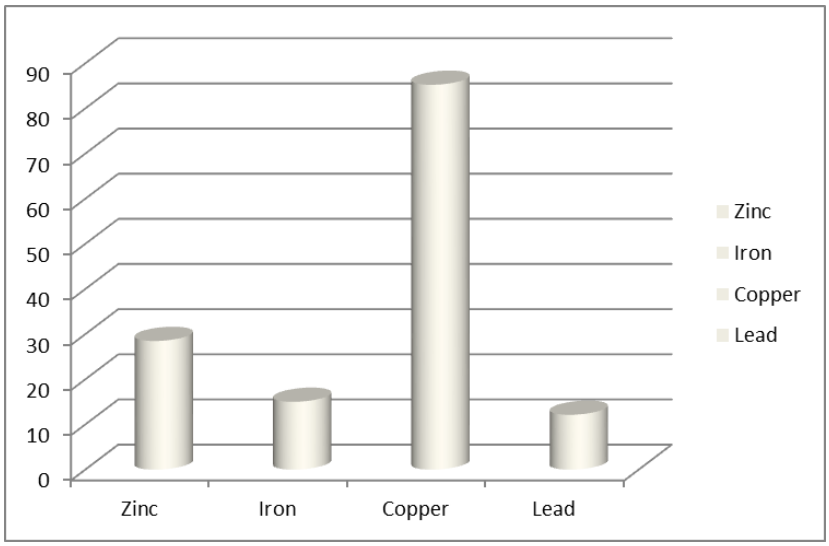

Figure 4 Trace Elements of NPU-45

3.6. NPU-55 Trace Elements

The results confirmed the findings of (13).

The presence of heavy metals in the Neutraceutical product of NPU-55 tablets was detected by the help of atomic absorption. All values are calculated as + SEM

The results of NPU-55 showed that the value of zinc calculated by atomic absorption was 16.06 ±SEM 1.10 and the recommended limits allowed by USP and BP specification is 27.4 ppm. These results showed that the quantity of zinc in the Product NPU-45 was much less than the recommended limits.

The results of NPU-55 showed that the value of iron calculated by atomic absorption was 112.25 ±SEM1.21 and recommended limits allowed by USP and BP specification is 20 ppm. These results showed that the quantity of iron in the products NPU-55 was much higher than the recommended limits.

The result of NPU-55 showed that the value of copper calculated by atomic absorption was 90.12 ±SEM1.14 and the recommended limits allowed by USP and BP specification was 100 ppm. These results indicate that the value of copper was slightly less than the recommended limits.

The result of NPU-55 showed that the value of lead calculated by atomic absorption was 13.12 ±SEM 0.32 and USP and BP specification recommended limits is 10 ppm. These results indicate that the value of lead was slightly higher than the recommended limits.

Table 7 NPU-55 Trace Elements

Elements Found	Zinc	Iron	Copper	Lead
Concentration (PPM)	16.06±1.10	112.25±1.21	90.12±1.14	13.12±0.32
Recommended Limits (PPM)	27.4	20	100	10

(The values given in the table were mean ± SEM)

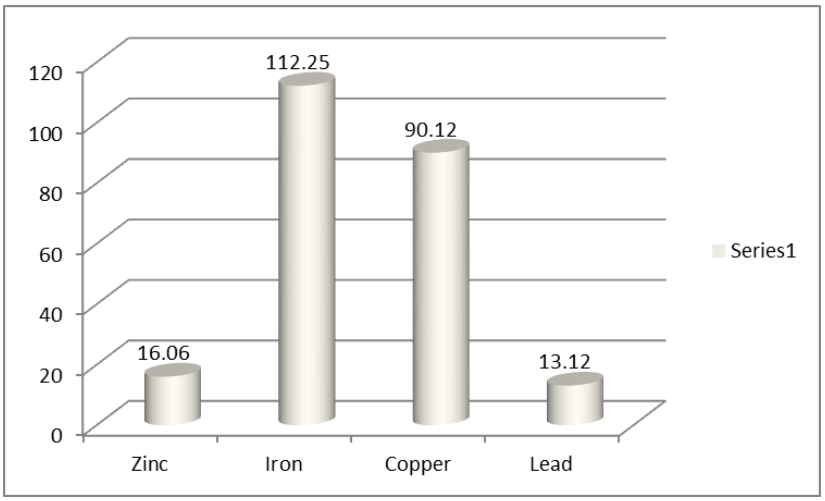

Figure 5 Trace Elements of NPU-5

3.7. NPU-65 Trace Elements

The results confirmed the findings of (13).

The presence of heavy metals in the Neutraceutical product of NPU-65 tablets was detected by the help of atomic absorption. All values are calculated as ±SEM

The results of NPU-65 showed that the value of zinc calculated by atomic absorption was 26.15 ±SEM 0.59 and the recommended limits allowed by USP and BP specification is 27.4 ppm. These results showed that the quantity of zinc in the Product NPU-65 was according to the recommended limits.

The results of NPU-65 showed that the value of iron calculated by atomic absorption was 163.21 ±SEM 1.51 and recommended limits allowed by USP and BP specification is 20 ppm. These results showed that the quantity of iron in the products NPU-65 was much higher than the recommended limits.

The result of NPU-65 showed that the value of copper calculated by atomic absorption was 85.27 ±SEM 2.11 and the recommended limits allowed by USP and BP specification was 100 ppm. These results indicate that the value of copper was slightly less than the recommended limits.

The result of NPU-65 showed that the value of lead calculated by atomic absorption was 38.19 ± SEM 1.61 and recommended limits followed by USP and BP specification is 10 ppm. These results indicate that the value of lead was much higher than the recommended limits.

Table 8 NPU-65 Trace Elements

Elements Found	Zinc	Iron	Copper	Lead
Concentration (PPM)	26.15±0.59	163.21±1.51	85.27±2.11	38.19±1.61
Recommended Limits (PPM)	27.4	20	100	10

(The values given in the table were mean ± SEM)

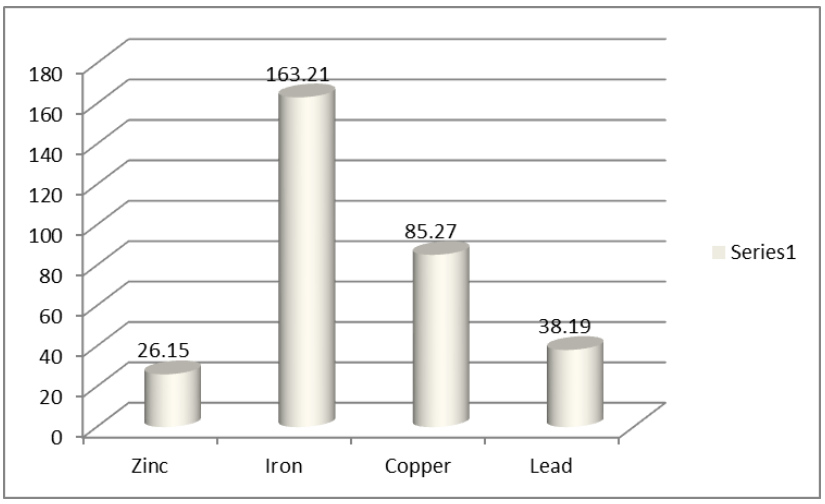

Figure 6 Trace Elements of NPU-65

3.8. NPU-75 Trace Elements

The results confirmed the findings of (13).

The presence of heavy metals in the Neutraceutical product of NPU-75 tablets was detected by the help of atomic absorption. All values are calculated as ±SEM.

The results of NPU-75 showed that the value of zinc calculated by atomic absorption was 12.15 ±SEM 0.59 and the recommended limits allowed by USP and BP specification is 27.4 ppm. These results showed that the quantity of zinc in the Product NPU-75 was much less than the recommended limits.

The results of NPU-75 showed that the value of iron calculated by atomic absorption was 132.11 ±SEM 0.43 and recommended limits allowed by USP and BP specification is 20 ppm. These results showed that the quantity of iron in the products NPU-75 was much higher than the recommended limits.

The result of NPU-75 showed that the value of copper calculated by atomic absorption was 63.11 ±SEM 1.12 and the recommended limits allowed by USP and BP specification was 100 ppm. These results indicate that the value of copper was much less than the recommended limits.

The result of NPU-75 showed that the value of lead calculated by atomic absorption was 12.18 ±SEM 1.21 and USP and BP specification recommended limits is 10 ppm. These results indicate that the value of lead was slightly higher than the recommended limits.

Table 9 NPU-75 Trace Elements

Elements Found	Zinc	Iron	Copper	Lead
Concentration (PPM)	12.15±0.59	132.11±0.43	63.11±1.12	12.18±1.21
Recommended Limits (PPM)	27.4	20	100	10

(The values given in the table were mean ± SEM)

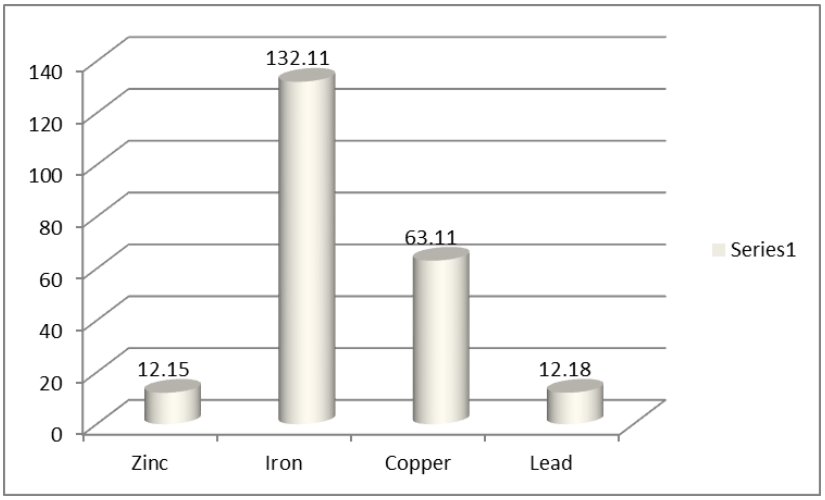

Figure 7 Trace Elements of NPU-7

4. Conclusion

It is concluded from this study that nutraceuticals when compared there Quality control tests with officials standards of USP and BP, it was observed deviations in the weight variation and hardness among these tablets of same batch but no deviation observed between thickness and diameter. The percentage of trace elements of zinc, iron, copper, and lead was also analyzed by the help of atomic absorption. The results showed that percentage of trace elements were much higher and few were less than the recommended limits. The concentration of these elements has much concern with the therapeutic efficacy of the Neutraceutical. The high concentration of lead is very much toxic to the lungs, liver and kidney. As well as the high concentration of iron, copper, zinc also affect the normal physiology of human being.

It was concluded from this research that SOPs were not followed during manufacturing. So manufacturer should take consideration in respect to these formulations, SOPs should be followed as well as pre formulation studies and quality control tests must performed before the formulation.

Compliance with ethical standards

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Disclosure of conflict of interest

All the authors have no conflict of interest in this research article and all of them have contributed to support and help for the compilation of this research work.

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