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# Toxicological concern of heavy metals in multivitamins by analytical studies

Pragati .K. Shinde, Dr.S.D.Sonawane, Sanjay.K.Bais sir
*Fabtech college of Pharmacy Sangola, Dist-solapur, Maharashtra - 413307*

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**ABSTRACT**
The worldwide rise in the use of nutritional supplements, especially multivitamins, has created a pressing need for dependable analytical approaches to identify harmful contaminants such as heavy metals. In contrast to pharmaceutical medicines, dietary supplements are subject to less stringent regulation despite their extensive consumption, raising ongoing concerns about their quality and safety. Toxic metals like lead (Pb), cadmium (Cd), chromium (Cr), and iron (Fe) can be introduced into supplement formulations through impurities in raw materials or during the production process, posing health risks even at minute concentrations. Atomic Absorption Spectrophotometry (AAS) continues to serve as an accurate, sensitive, and economical technique for measuring these metals in food and pharmaceutical products. This review outlines current progress in analytical procedures for detecting heavy metals in multivitamin and dietary supplement formulations, emphasizing the central role of AAS in trace-metal evaluation. The discussion also addresses essential trace minerals such as nickel, zinc, copper, manganese, and cobalt, which are vital for normal physiological processes but may become toxic at elevated concentrations. Ultimately, ensuring the safety and therapeutic reliability of multivitamin supplements requires ongoing surveillance, compliance with international quality regulations, and rigorous validation of analytical techniques.

**KEYWORDS:-**Multivitamins, Heavy metals, Atomic Absorption Spectrophotometry (AAS), Dietary supplements, Toxicity, Quality control.

## I. INTRODUCTION

The development of reliable analytical techniques for detecting harmful substances in food and pharmaceutical products has become increasingly important, especially for nutritional supplements that must comply with national and international safety regulations. Unlike pharmaceutical drugs, which undergo strict regulatory scrutiny, nutritional supplements often receive comparatively limited oversight despite their widespread use and therapeutic claims. These products commonly contain bioactive constituents such as vitamins, minerals, herbal extracts, and enzyme-derived compounds. [1].

A diverse array of dietary supplements—particularly multivitamin preparations—is marketed to meet human nutritional requirements. Vitamins are organic substances needed in small quantities to support normal physiological processes. They are classified as vitamins when the human body cannot synthesize them in adequate amounts and must therefore obtain them from external dietary sources. Vitamin needs vary among species; for example, humans depend on dietary intake of ascorbic acid (vitamin C), whereas many other animals can produce it endogenously. Similarly, nutrients such as biotin and vitamin D are considered essential for humans only under certain physiological or environmental conditions. The term "vitamin" generally excludes other essential nutrients, including minerals, amino acids, and fatty acids, which are required in larger quantities, along with other bioactive substances that contribute to overall health [2].

In countries like Pakistan, the use of multivitamin supplements is highly prevalent. Their widespread acceptance is largely influenced by low cost, easy availability, and aggressive marketing, which often presents these products as entirely safe due to adherence to Good Manufacturing Practices (GMP). However, unregulated or excessive consumption can pose risks. Long-term or unnecessary use may result in the buildup of heavy metals to toxic levels. Even trace amounts of metals such as lead (Pb), cadmium (Cd), and chromium (Cr) can pose serious health threats. Therefore, rigorous testing of multivitamin products for heavy metal contamination is essential before they reach consumers [3]. The current study aims to quantify heavy metal levels in commercially available multivitamin brands in Pakistan using Atomic Absorption Spectrophotometry (AAS). To the best of available knowledge, this is the first study in the country

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employing AAS to analyze heavy metal contamination in multivitamin supplements [4].

- "Nutrient compensation: Multivitamins are developed to correct or prevent deficiencies in essential macro- and micro-nutrients.
- Preventive and therapeutic role: Such supplements are widely used to manage or prevent conditions associated with nutrient inadequacy.
- Growing demand: Global consumption of multivitamins has risen substantially over the past few decades.
- Regulatory accountability: As per European Regulation No. 178/2002, manufacturers and distributors are responsible for ensuring that all dietary supplements meet required safety and labeling standards.
- Product safety: These supplements should contain only the declared ingredients and must be free from toxic contaminants such as heavy metals.
- Determinants of safety: The ultimate quality and safety of dietary supplements depend largely on the purity of raw materials and the manufacturing process used [5].

Iron is an indispensable trace element naturally found in both surface and groundwater [6]. It serves critical biological functions, particularly in oxygen transport, energy metabolism, and enzymatic activity. However, elevated concentrations of iron can exert toxic effects, potentially damaging key organs such as the heart, liver, kidneys, pancreas, and muscles [7]. Adequate iron intake is essential to prevent anemia, yet supplementation must be carefully controlled. Over the last two decades, the use of multivitamin and mineral preparations has significantly increased, especially in developed nations such as the United States, Canada, and those of Northern Europe [8]. In the U.S., the FDA monitors vitamins and dietary supplements under DSHEA (1994) [9], and current Good Manufacturing Practice (CGMP) regulations stipulate that manufacturers must ensure their products contain only the labeled ingredients and remain free of hazardous contaminants, including heavy metals and pesticide residues [10].

Prior to elemental analysis, multivitamin samples often undergo preliminary digestion or pre-treatment to make the matrix compatible with analytical detection. Common approaches include dry ashing or wet acid digestion using mineral acids [11]. These methods, though effective, can be time-consuming and unnecessary for easily soluble samples where organic matter does not interfere with metal analysis [12]. A related study aimed to develop and validate a rapid and straightforward procedure for determining magnesium in a water-soluble multivitamin formulation using Flame Atomic Absorption Spectrometry (FAAS) [13].

According to the United States Pharmacopeia (USP), metals such as Pb, Hg, Bi, As, Sb, Sn, Cd, Ag, Cu, and Mo are routinely monitored during pharmaceutical quality testing without diferentiation between Individual elements [14]. Among these, lead and cadmium are of greatest toxicological concern due to Their potential to cause severe health efects even at very low exposure levels [15]. Chronic exposure to Lead has been associated with neurological, cognitive, and behavioral impairments [16]. Historically, blood Lead concentrations below 10 mg/dL were considered safe in children, but newer studies have shown that Even lower levels can cause adverse developmental efects [17]. Regular ingestion of as little as 0.06 mg Of lead per day for a month may induce chronic toxicity, leading to renal dysfunction, bone disorders, and Pulmonary complications [18]. These fndings reinforce the need for continuous monitoring and strict Control of lead exposure from all sources [19]. Despite its widespread industrial use, lead remains one of The most hazardous environmental toxins, entering the human body through contaminated soil, air, water, Food, cosmetics, and even pharmaceuticals [20]. Children are particularly at risk due to their heightened Absorption rates and developing biological systems, which make them more susceptible to neurotoxic Damage [21]. The Centers for Disease Control and Prevention (CDC) has reported that even low blood lead Concentrations (~100 µg/L) can result in cognitive delays, attention defcits, and behavioral issues in Children [22].

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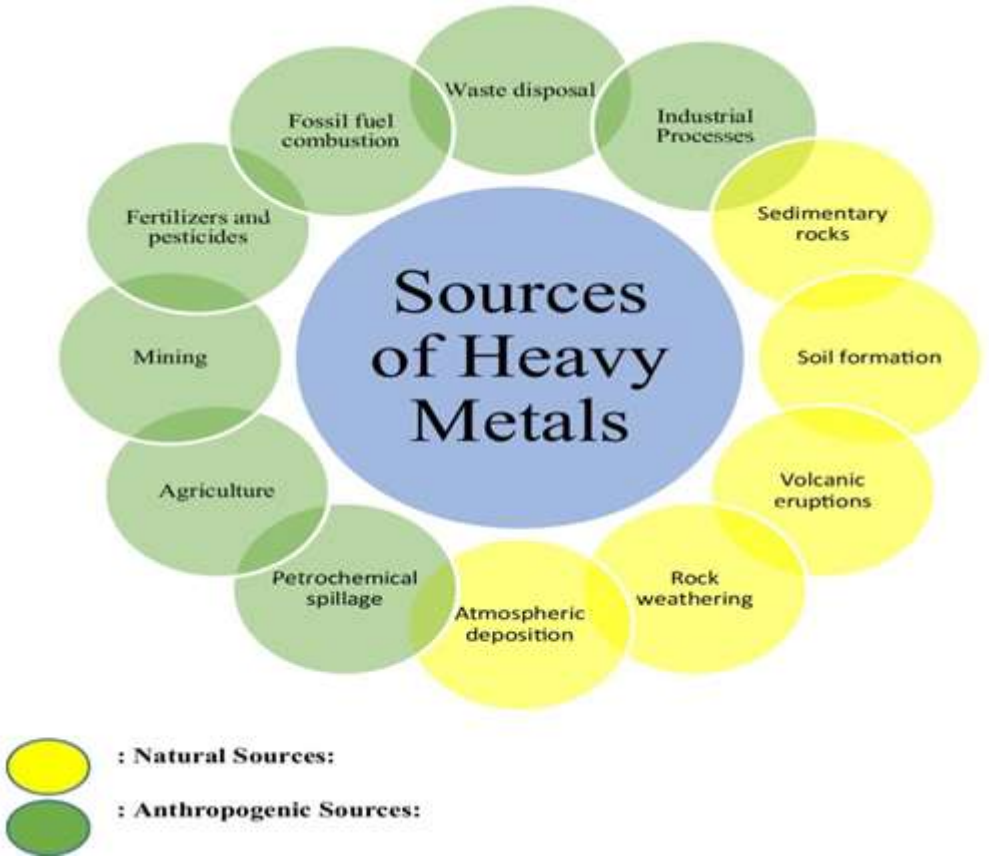


❖ **Significance of Heavy Metals Analysis in Multivitamins Using AAS.**

1. Health and Safety Assessment:

Heavy metals are toxic even at low concentrations and can cause neurological, renal, and developmental disorders upon long-term exposure. AAS helps in determining whether their levels are within permissible limits set by regulatory bodies like the FDA and WHO.

2. Quality Control:

Regular monitoring of heavy metals ensures that the multivitamin formulation maintains purity and safety standards, preventing adulteration or contamination.

3. Regulatory Compliance:

The results from AAS confirm compliance with pharmacopoeial standards and international safety guidelines, which is mandatory for product approval and marketing.

4. High Sensitivity and Accuracy:

AAS provides precise quantitative data for trace levels (µg/L or µg/g) of metals, making it a reliable analytical tool for detecting even minute contamination.

5. Consumer Protection:

Ensuring heavy metals are within safe limits safeguards consumers from chronic metal toxicity and builds trust in the product's safety.[23]

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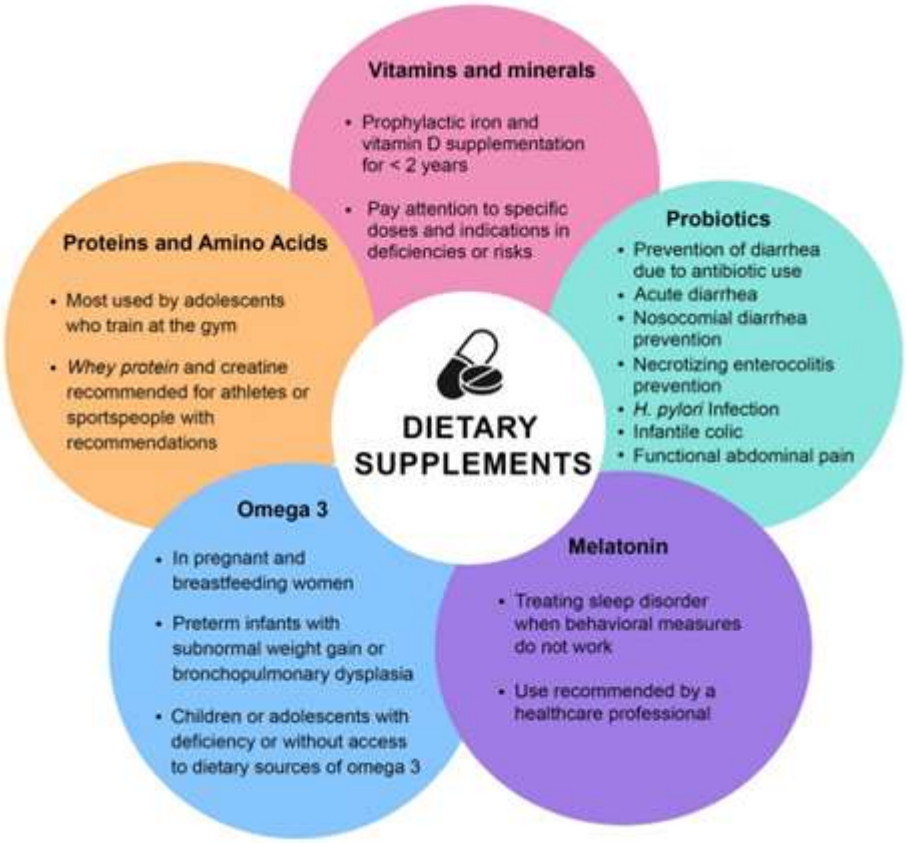


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❖ **Harmful effects to taking multivitamin In dietary supplement:-**

Consuming an excessive amount of multivitamins can be harmful, leading to side effects such as digestive discomfort, a higher risk of kidney stones, and toxicity from fat-soluble vitamins like A, D, E, and K. Overdosing may also interfere with certain medications and cause specific health issues — for instance, too much vitamin $B_6$ can result in nerve damage, while excessive vitamin E may increase the risk of bleeding. Therefore, it's essential to stick to the recommended dosage and seek medical advice, particularly if you also eat fortified foods or take additional supplements.[24]

❖ **Risks of Excessive Intake:-**

**1.Fat-soluble vitamin toxicity: -**

Vitamins A, D, E, and K accumulate in the body, and consuming them in large amounts can lead to toxicity. For instance, too much vitamin A may cause headaches, nausea, and dizziness, while excessive vitamin D can elevate calcium levels in the blood.[25]

**2.Mineral overload: -**

Overconsumption of minerals can be dangerous. High iron intake may result in nausea, vomiting, and, in extreme cases, liver damage or even death. Too much calcium can cause kidney stones, and excessive zinc may weaken the immune system and hinder copper absorption.

**3.Water-soluble vitamin concerns: -**

Although the body generally eliminates excess water-soluble vitamins, very high doses can still be harmful. Large amounts of vitamin $B_6$ can lead to nerve damage, while excessive vitamin C may cause diarrhea, nausea, and increase the risk of kidney stones.[26]

**4.Medication interactions:-**

High doses of certain vitamins can alter nutrient absorption or affect how medications function. For example, vitamin K can decrease the effectiveness of blood-thinning drugs, and too much vitamin C can interfere with certain laboratory tests.

**5.Group-specific risks :-**

Pregnant women should avoid taking large amounts of preformed vitamin A, as it can increase the likelihood of birth defects. Similarly, smokers should be cautious with supplements containing high levels of beta-carotene and vitamin A, which may raise the risk of lung cancer.[27]

Table 1. Heavy metal concentration (microgram/gram) in commercial multivitamin tablet samples

| Multivitamin Sample | Ni | Cu | Zn | Fe | Cr | Co | Mn |
|---|---|---|---|---|---|---|---|
| Daylets (Tab) | 23.89 | 453.95 | 182.45 | N/D | N/D | N/D | 7.65 |
| Megacit. (Tab). | 50.67 | N/D | 21.37 | N/D | 131.19 | N/D | 126.87 |
| Biovit-M (Tab) | N/D | N/D | N/D | 26.82 | 104.94 | 55.27 | N/D |
| Optilets-M (Tab) | 89.79 | N/D | N/D | N/D | N/D | 62.00 | 27.97 |
| Centural Gold (Tab). | 39.17 | 23.78 | 36.46 | N/D | N/D | N/D | N/D |
| Nutrifer (Tab). | 41.54 | N/D | 33.46 | 13.83 | 161.67 | N/D | 33.40 |
| ADE- (Tab) | N/D | 1697.4 | 514.59 | N/D | N/D | N/D | N/D |
| Diabetone (Cap) | N/D | N/D | N/D | N/D | N/D | N/D | 9.41 |
| Geritol (Cap). | 8.06 | 18.90 | 23.64 | 43.49 | 51.56 | N/D | 10.31 |
| Divasas (Tab) | N/D | N/D | N/D | 58.45 | 42.12 | N/D | 661.40 |

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- **Brand name of selected tablets and capsules :-**

| Sr. No | Tablets / Capsules | Brand Name |
|---|---|---|
| 1 | Daylets(Tab) | Abbott |
| 2 | Megacit(Tab). | Megestrol acetate |
| 3 | Biovit-M (Tab) | Biovit M |
| 4 | Optilets-M (Tab) | Optilets-M |
| 5 | Visionance | Vizylac |
| 6 | Nutrifer (Tab). | Nutrifer |
| 7 | ADE- (Tab) | Heptral (Abbott) |
| 8 | Diabetone (Cap) | Diabetone |
| 9 | Geritol (Cap). | Geritol |
| 10 | Divasas (Tab) | Divasas |

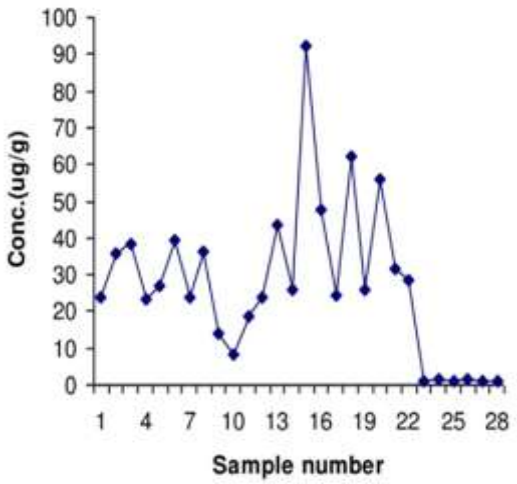
❖ **Essential elements which are used in multivitamin tablets:-**

**1. Nickel –**

Prolonged exposure to nickel can trigger allergic conditions, particularly skin rashes visible on the skin's surface. Animal studies indicate that excessive nickel intake may lead to disorders of the kidneys, blood, and stomach [28]. The average dietary intake of nickel is estimated to be 25–35 µg [29]. In the tested products, nickel concentrations varied between 0.8–92.28 µg/g, as presented in Tables 1 and 2.

The highest level was detected in Vidaylin-T (tablet) at 92.28 µg/g, produced by Abbott Laboratories, Karachi, Pakistan, while the lowest was in Becotin syrup (0.8 µg/g), manufactured by Life Pharmaceutical Company, Multan, Pakistan. Currently, there is limited information regarding the exact toxic threshold of nickel. Table 3 summarizes the estimated daily intake of nickel based on the manufacturers' recommended doses.

Among the analyzed samples, five products exceeded the recommended daily intake: Once a Day (tablet) by CCL Pharmaceuticals, Kot Lakhpat, Pakistan; ADE (tablet) by Image Pharma, Lahore, Pakistan; Engran (tablet) by Bristol Myers Squibb, Karachi, Pakistan; Skinvite (tablet) by Zeb Laboratories (Pvt.) Ltd., Lahore, Pakistan; and Hemolif syrup by Life Pharmaceutical Company, Multan, Pakistan. Consequently, the use of these products may pose a potential risk of nickel toxicity.




**2. Copper :-**

Copper is an essential trace element for human metabolism, participating in numerous biological processes such as energy production, connective tissue formation, and neurotransmitter synthesis[30] . However, excessive copper intake can lead to adverse effects including vomiting, nausea, diarrhea, and damage to the liver and kidneys . The recommended daily intake is 340–440 µg for children and 890–900 µg for adults[31] .

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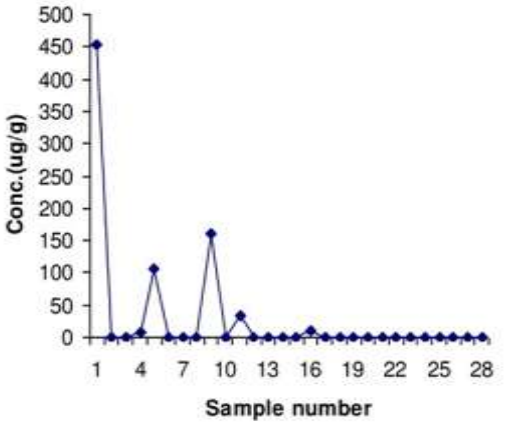
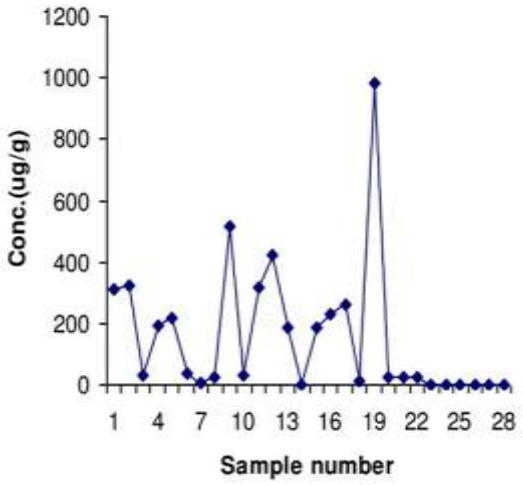
Copper concentrations (µg/g) detected in multivitamin tablets and syrups are summarized in with estimated daily intake values provided in Table 3. Among the tested products, only Daylets (tablet) manufactured by Abbott Laboratories, Karachi, Pakistan, exceeded the children's recommended limit (522.5 µg/day), though this dosage aligns with adult requirements and is not considered harmful for them.



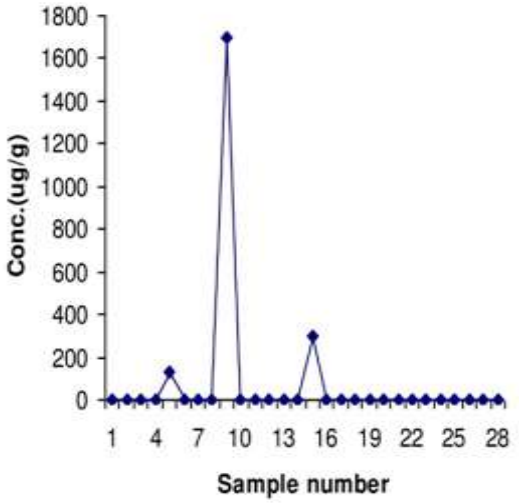

**3. Zinc:-**

Zinc is a vital trace element necessary for numerous physiological processes in humans and animals. It functions as a cofactor for nearly 100 enzymes and contributes to the structural stability of proteins and cell membranes. Additionally, zinc plays a role in cellular signaling, hormone secretion, and apoptosis [32]. Acute zinc ingestion of 225–450 mg can induce gastrointestinal distress including abdominal pain, nausea, vomiting, and diarrhea, while chronic exposure may lead to copper deficiency . Recommended dietary allowances are 4000–5000 µg/day for children, 13,000–19,000 µg/day for men, and 9000–13,000 µg/day for women [33]. The analyzed samples contained zinc concentrations between 0.37 and 980.93 µg/g. Calculations based on manufacturer-recommended doses indicated that none of the products exceeded permissible intake levels for any age or sex group.




**4.Iron:–**

The estimated daily intake of iron, based on the manufacturer's recommended dosage, is presented in Table 3. The iron content in the analyzed samples was found to be as high as 1697.39 µg/g . In most multivitamin products, iron was not detected at the ppm level, except in Optilets-M tablets (123.8 µg/g), Diabitone capsules (1697.4 µg/g), and Vidaylin-T tablets (293.81 µg/g). The recommended dietary allowance (RDA) for iron is 7000–10,000 µg/day for children, 8000 µg/day for adults, and 27,000 µg/day for pregnant women [34]. Thus, the iron levels observed in the tested samples were below the established RDA values.




**5.Manganese**:-

Manganese (Mn) plays a vital role in supporting human health. As indicated in Table 3, the daily intake recommended by manufacturers

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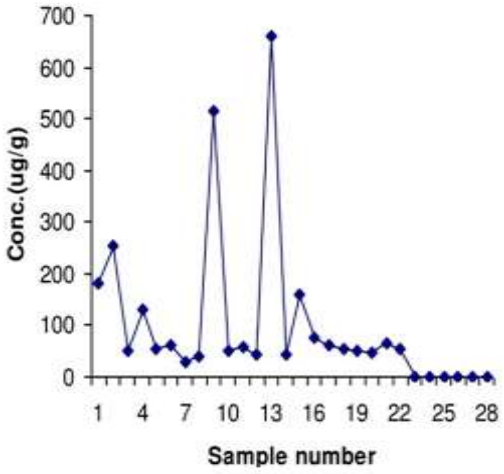
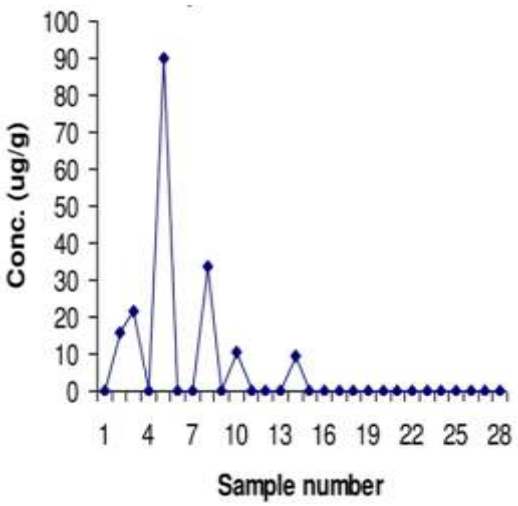
was evaluated, and Mn was detected in every tested multivitamin sample, with concentrations ranging between 1.47 and 661.40 µg/g (Tables 1 and 2). The maximum concentration (661.40 µg/g) appeared in Visionance capsules from Vitabiotics Ltd., London, while the minimum (1.47 µg/g) was recorded in Multibionta syrup from Merck (Pvt) Ltd., Quetta, Pakistan. the permissible dietary intake of Mn is 1200–1500 µg/day for children, 2300 µg/day for men, and 1800–2000 µg/day for women[35]. The results show that all the analyzed multivitamin products contained manganese levels below the recommended daily requirements for all age and gender groups.




**6.Cobalt**:-

The element cobalt serves as an indispensable minor nutrient, as well as a core part of cobalamin ($B_{12}$).Insufficient cobalt intake may result in anemia, a serious hematological disorder. The manufacturer-recommended daily dose of cobalt is presented , while the ordinarydietaryconsumption is typically approximated to range between 20 and 40 µg [36]. In the current analysis, Cobalt remained below detection limits in all multivitamin preparations tested. formulations; however, it was identified in six out of twenty-two multivitamin tablet samples, as shown in Tables 1 and 2. Notably, only one tablet formulation (Optilet-M) exhibited a cobalt concentration (89.79 µg) exceeding the recommended daily intake, which could potentially pose health risks. In contrast, the remaining multivitamin samples demonstrated cobalt concentrations below the permissible daily limit, indicating compliance with recommended safety standards.[37]




**7.Chromium:-**

Chromium exists in two ionic forms—trivalent ($Cr^{3+}$ ) and hexavalent ($Cr^{6+}$ ). Among these, trivalent chromium is the biologically active form utilized by humans and naturally occurs in food sources. It plays a vital role in regulating glucose metabolism. Although precise data regarding the minimum permissible limit of chromium intake are limited, the Food and Nutrition Board has proposed an adequate intake level of 11–25 µg/day for children and 30–35 µg/day for adults. Excessive exposure to chromium, particularly at high concentrations, has been associated with dermatitis and lung cancer [38]. Table 3 presents the estimated daily intake of all analyzed products based on their manufacturer's recommended dosage. The analysis revealed that chromium was not detected at the ppm level in any of the tested multivitamin formulations.[39]

- **Some Toxic elements which are used in multivitamin :-**

1. **Lead**
2. **Cadmium**
3. **Mercury**
4. **Arsenic**

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**1.Lead :-**

| Sr. no | Parameters | Information |
|---|---|---|
| **1** | Symbol | Lead (Pb) |
| **2** | Role in body | Non toxic |
| **3** | Common source | Contaminated minerals, herbs, equipment |
| **4** | Toxic effects | Neurotoxicity, anemia, kidney damage |
| **5** | Permissible limit (FDA) | <0.5-1 microgram/day in supplements |
| **6** | Detection method | AAS , ICP – MS |
| | | |

❖

❖ **Applications of AAS for Lead in Multivitamins:**

- Detection of Trace Lead Contamination:-

AAS identifies and measures even minute concentrations of lead that mayenter the product through raw materials or processing equipment.

- Quality Control and Safety Assessment:-

It ensures that the lead content remains below the permissible limit (usually < 10 ppm or 0.01 mg/g depending on regulations).

- Regulatory Compliance:-

Data obtained from AAS testing is used to demonstrate compliance with national and international safety standards.

- Environmental and Source Monitoring:-

Helps trace the origin of contamination (such as soil, water, or excipient sources).[ 40]

**2.Cadmium:-**

| Sr. No | Parameters | Information |
|---|---|---|
| **1** | Symbol | Cadmium (cd) |
| **2** | Biological role | None (toxic) heavy metal |
| **3** | Common source | Contamination from raw materials, soil, water, or manufacturing equipment |
| **4** | Toxic effects | Kidney dysfunction, skeletal damage, bioaccumulation in organs |
| **5** | Detection method | Atomic Absorption Spectroscopy (AAS), ICP-MS |
| **6** | Permissible limit | 0.3–1.0 µg/g (ppm), depending on regulatory standards (WHO, FDA) |

❖ **Applications of AAS for Cadmium in Multivitamins**

- **Detection of Trace Cadmium Contamination:-**

AAS allows sensitive and accurate measurement of even very low cadmium concentrations in multivitamin tablets.

- **Quality Control:-**

Ensures that cadmium levels remain below permissible regulatory limits, safeguarding product safety.

- **Regulatory Compliance:-**

Provides documented evidence that cadmium content complies with standards set by WHO, FDA, and other health authorities.

- **Source and Process Monitoring:-**

Helps identify contamination sources such as raw materials, processing equipment, or packaging materials.

- **Toxicological Assessment:-**

Enables evaluation of potential health risks associated with cadmium exposure through dietary supplements.[41]

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**3. Mercury :-**

| Sr. No | Parameters | Information |
|---|---|---|
| **1** | Symbol | Mercury (Hg) |
| **2** | Biological role | None (highly toxic) |
| **3** | Common source | Contamination from raw materials, processing equipment, or environment |
| **4** | Toxic effect | Neurotoxicity, kidney damage, developmental toxicity, bioaccumulation |
| **5** | Detection method | Atomic Absorption Spectroscopy (AAS), often with cold vapor technique |
| **6** | Permissible limit | Typically <0.1 µg/g (ppm) in dietary supplements (WHO/FDA guidelines) |

❖ **Applications of AAS for Mercury in Multivitamins**

- **Sensitive Detection:**

AAS, particularly cold vapor AAS, allows precise detection of trace mercury levels in multivitamin tablets.

- **Quality Control:**

Ensures that mercury contamination is below permissible limits, protectingconsumer health.

- **Regulatory Compliance:**

Confirms adherence to safety standards set by WHO, FDA, and other authorities.

- **Source Monitoring:**

Helps identify and minimize mercury contamination from raw materials or processing.

- **Toxicological Assessment:**

Evaluates potential health risks due to mercury exposure from dietary supplements.[42]

**4.Arsenic :-**

| Sr. No | Parameters | Information |
|---|---|---|
| **1** | Symbol | Arsenic (As) |
| **2** | Biological role | None (toxic) |
| **3** | Common source | Contamination from raw materials (minerals, herbs), water, or processing equipment |
| **4** | Toxic effect | Skin lesions, cancer, cardiovascular and neurological effects, organ toxicity |
| **5** | Detection method | Atomic Absorption Spectroscopy (AAS), often hydride generation AAS (HG-AAS) |
| **6** | Permissible limit | Typically ≤1 µg/g (ppm) in dietary supplements (WHO/FDA guidelines) |

❖ **Applications of AAS for Arsenic in Multivitamins**

- **Trace Detection:**

AAS allows precise quantification of arsenic even at very low concentrations.

- **Quality Control:**

Ensures arsenic contamination is within permissible limits, protecting consumer safety.

- **Regulatory Compliance:**

Confirms adherence to safety standards established by WHO, FDA, and other authorities.

- **Source and Process Monitoring:**

Identifies potential sources of contamination in raw materials or manufacturing processes.

- **Toxicological Assessment:**

Evaluates the risk of arsenic exposure through multivitamin consumption.[43]

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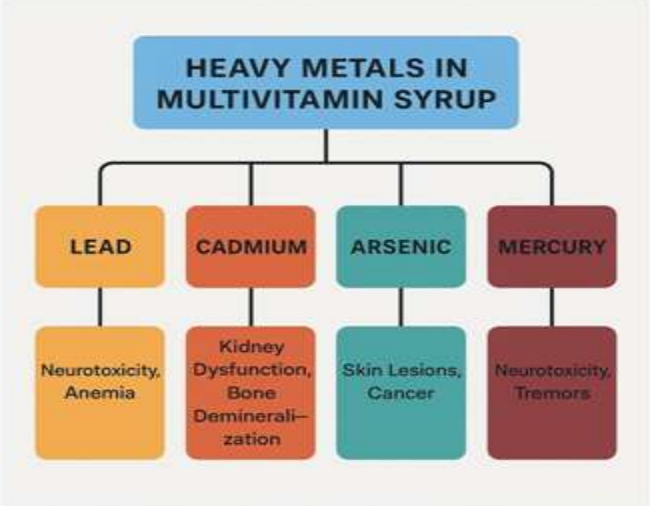


## II. DISCUSSION

Using atomic absorption spectrophotometry, the study quantified the concentrations of selected heavy metals—nickel, manganese, zinc, chromium, copper, and iron—in multivitamin formulations purchased from local markets. The analytical findings are detailed in Tables 1 and 2 [44].

Trace levels of heavy metals were detected in every sample assessed. Among the contaminants, lead and cadmium were the most prevalent, followed by arsenic and chromium. While the measured values typically fell within established safety limits, noticeable differences among brands point to inconsistent quality assurance during manufacturing. Long-term intake of these products may still contribute to gradual metal buildup in the body. The results reaffirm the effectiveness of AAS as a precise and dependable tool for heavy-metal analysis and highlight the necessity for routine monitoring of both raw materials and finished supplement products.

## III. CONCLUSION

Heavy metal contamination in multivitamin supplements persists as a significant quality and safety concern worldwide. Among reported contaminants, lead and cadmium are most prevalent, followed by arsenic and chromium. Although their concentrations typically fall within permissible regulatory limits, prolonged consumption may lead to cumulative toxicity. Ensuring consumer safety requires strict adherence to Good Manufacturing Practices (GMP), regular raw material screening, and sensitive analytical monitoring through AAS or ICP–MS. Strengthened regulatory oversight, standardized testing protocols, and greater public awareness are essential to reduce contamination risks and maintain the therapeutic integrity of multivitamin formulations.

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