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Determination of two heavy metals (Zn and Cu) in Anti-diabetic and Iron supplements by using Atomic Absorption Spectroscopy

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Abstract: This research aimed to quantify two heavy metals (zinc and copper) in 2 Anti-diabetic drugs and 3 iron supplement samples. The chosen samples were manufactured from different countries (Denmark, Poland, India, Egypt, and Belgium) at Bani Waleed City. The determination of selected elements was accomplished by atomic absorption spectroscopy (AAS) after wet digestion with concentrated acid HNO_3: H_2O_2 in a ratio of 3:1. From the obtained result, it was clear that heavy metals present in insulin samples were within an acceptable concentration range 1.21 µg/ml in Mixtard 30 and 1.31 µg/ml in Gensulin M30 for the zinc while the copper content was 0.137 µg/ml in Mixtard 30 and 0.423 µg/ml in Gensulin sample. The iron supplement samples contained Cu and Zn in µg/g (1.708 and 0.108 for the Irofix cap, 1.472 and 0.245 for the Feroxyl cap while the Iron velvet tab contained 1.984 and 0.256 respectively). All results were lower than the maximum limits and safe to use. Quality control of medicinal products especially drugs is highly recommended.

Keywords: anemia, atomic absorption spectroscopy, heavy metals, Pharmaceutical products.

Introduction

More than 450 million have Diabetes a prolonged disease that results when the insulin is not enough to regulate blood glucose leading to severe harm to nerves and blood vessels. People with type 1 diabetes need insulin injections for survival. [1] Another health issue is Anemia, a problem of hemoglobin carrying oxygen from the lungs to the body's tissues. Anemia has many forms and it can be short-term or long-term. Taking Pharmaceutical products such as iron supplements can treat anemia. [2]

Pharmaceutical products are consumed daily as a treatment, analgesic, or food supplement, making them an alternative to crude herbal preparations [3]. Most pharmaceutical products are synthesized chemically from organic or inorganic materials, especially those based on metals. Although Pharmaceutical products are used for the diagnosis, treatment, and prevention of diseases and ailments, continual use of pharmaceutical products will cause an accumulation of metals in our body causing nutritional deficiencies, hormonal differences, and cancer [4]. Besides interaction with other pharmaceutical drugs altering the biological effectiveness of the former, the toxicity of heavy metals (free radicals) might be the reason for several health sicknesses, such as lipid destruction or DNA mutation [5]. The human body needs different amounts of 'heavy metals such as iron, manganese, copper, zinc, etc. High levels can cause health issues. On the other hand, mercury, lead, and arsenic are toxic metals that have no vital role in our bodies [6, 7].

Zinc is an important element for the body in a minor amount and can obtained in food. As zinc quantity gets higher than 40 mg/day, it becomes a toxic element instead of essential which causes stomach cramps, nausea, and anemia in the long term. Likewise, copper is a metal that works as a nutritional supplement because it helps the red blood cells absorb iron which plays a functional role in hemoglobin formation [8]. Nevertheless, heavy metals are being added to pharmaceutical products where they are not estimated to play any therapeutic role, the high quantity of the former may be regarded as a contaminant [9, 10]. This work aimed to quantify the amount of two heavy metals: Cu and Zn in some selected Drug samples by using AAS and comparing the result with WHO limits.

Chemicals and Instruments

Concentrated nitric acid, grinder, Anti-diabetic (Mixtard 30 and Gensulin M30), iron supplements (Feroxyl cap, Irofix cap and Iron Velvet tab), hydrogen peroxide, distilled water, hot plate, electronic balance and atomic absorption spectroscopy model varian spectra 220Z at **D**elta **s**cientific **l**aboratory.

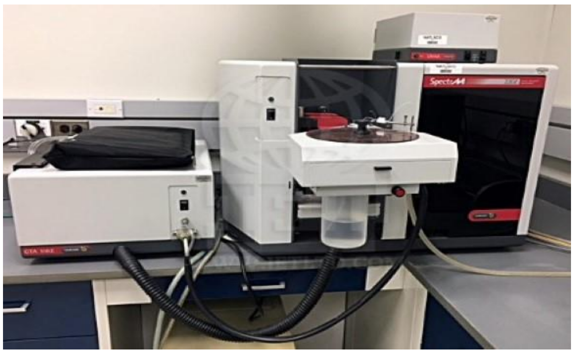

Fig. 1 shows the atomic absorption spectroscopy model varian spectra 220Z

Procedure

1 g of each iron supplement sample was accurately weighed and ground well while 1 ml of each anti-diabetic sample was measured by micropipette and then transferred separately into a 50 ml Flask. 1.5 ml of hydrogen peroxide and 5 ml of concentrated nitric acid were added into each flask of the five. Each mixture was heated on a hot plate for 40 minutes and then cooled to room temperature. After filtration, the volume continued with distilled water to obtain a clear solution. Finally, 0.7 ml of each prepared sample was injected into AAS to be analyzed.

RESULTS AND DISCUSSION

1- **Anti-diabetic samples**

Table 1: The content of zinc and copper (µg/ml) in Anti-diabetic samples by using AAS instrument.

Table 1

Replicates	Drugs	Concentration (µg/ml) Cu	Concentration (µg/ml) Zn	Average (µg/ml) Cu	Average (µg/ml) Zn	Standard deviation Cu	Standard deviation Zn
1	Mixtard 30	**0.140**	**1.12**	**0.137**	**1.21**	**0.015**	**0.158**
2		**0.120**	**1.13**				
3		**0.150**	**1.40**				
1	Gensulin M30	**0.450**	**1.32**	**0.423**	**1.31**	**0.025**	**0.015**
2		**0.420**	**1.29**				
3		**0.400**	**1.31**				

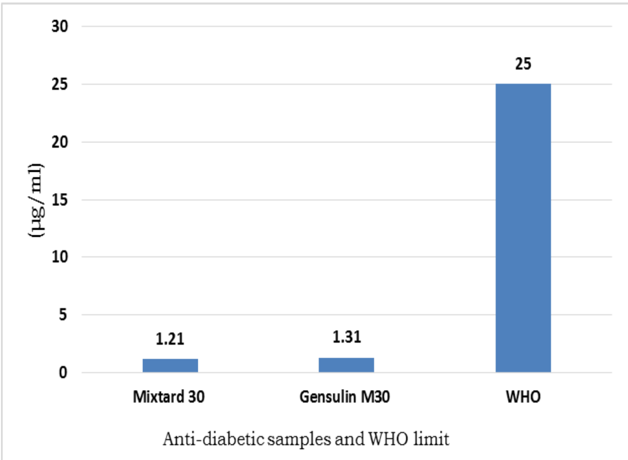

Fig. 2 Illustrates zinc concentration (µg/ml) in Anti-diabetic samples and WHO maximum limit.

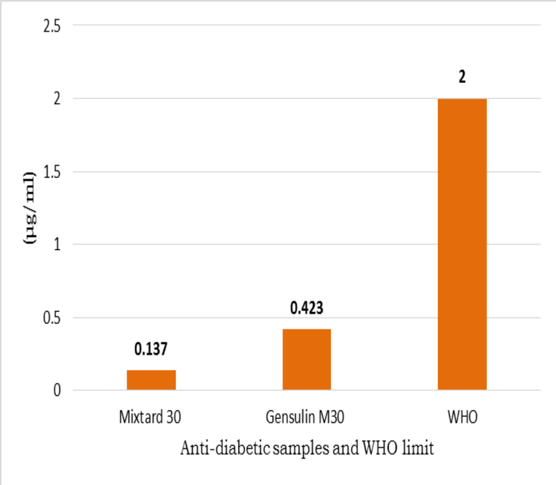

Fig. 3 Demonstrates copper concentration (µg/ml) in Anti-diabetic samples and WHO maximum limit.

Among different types of anti-diabetic medicine, Mixtard 30 and Gensulin M30 are the most used. The bar chart in Fig. 3 demonstrates the zinc content in these two drugs, where the X axis shows the average concentration of the zinc (µg/g), and The Y axis represents the types of anti-diabetic samples and the maximum level according to the World Health Organization. From the chart above in Fig. 2, it can be seen that Gensulin M30 has a higher zinc concentration than the Mixtard type with 1.31 (µg/ml) for the former and 1.21 (µg/ml) for the latter. Both samples of the anti-diabetic medicine were significantly smaller than the maximum level of zinc additive to anti-diabetic medicine according to WHO (25 µg/ml). The daily use of these drugs (Mixtard 30 and Gensulin M30) can not cause any accumulation of zinc due to the lower content of the latter. T-test was used to test for the difference within the anti-diabetic samples where P-value = 0.43 which means there is no significant difference between the means of zinc concentration in the two anti-diabetic samples.

On the other hand, copper was quantified as zinc with the same procedure and the obtained result was found to be dramatically less than the WHO limit as shown in Fig. 4. The copper content in Mixtard 30 was 0.137 µg/ml while for the Gensulin M30 was quite higher with 0.423 µg/ml. from Fig. 3 it can be seen that both anti-diabetic samples contained a lower amount of copper compared with the standard of WHO (2 µg/ml).

2- Iron supplement samples

Table 2: The content of zinc and copper (µg/g) in Iron supplement samples by using AAS instrument.

Replicates	Drugs	Concentration (µg/ml)		Average (µg/ml)		Standard deviation	
		Cu	Zn	Cu	Zn	Cu	Zn
1	Irofix cap	0.140	1.12	0.137	1.21	0.015	0.158
2		0.120	1.13				
3		0.150	1.40				
1	Feroxyl cap	0.450	1.32	0.423	1.31	0.025	0.015
2		0.420	1.29				
3		0.400	1.31				
1	Iron velvet tab	1.96	0.257	1.98	0.256	0.017	0.003
2		1.99	0.252				
3		1.99	0.255				

Table 2

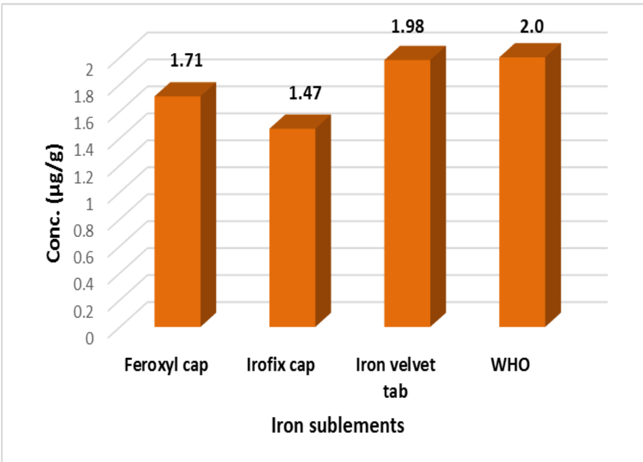

Fig. 4 illustrates copper concentration (µg/g) in Iron supplement samples and WHO maximum limit.

It can be seen from **Fig. 4** that the Iron velvet tab has the highest average value of copper

1.98 µg/g among the three Iron supplement samples whereas the Feroxyl cap has the lowest mean value of 1.47 µg/g while the Irofix cap has 1.71 µg/g. By comparing the content of copper in these three samples with the WHO standard we have found all three samples are within acceptable limits (2.0 µg/g).

Adding copper to iron supplements increases iron absorption because Copper-dependent enzymes transport iron in the body, and the absence of copper leads to iron deficiency.

Analysis of variance (ANOVA) was used to test for the difference within the iron supplement samples where P-value = 3.44 $\times 10^{-05}$ which means there is a difference between the means of copper concentration in the three iron supplement samples.

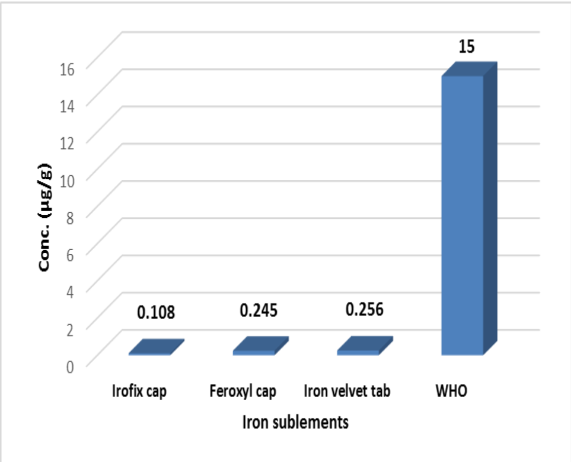

Fig. 5 illustrates zinc conc (µg/g) in Iron supplement samples and WHO maximum limit..

In contrast, the amount of zinc was meager in the three samples by comparing with the allowed value of zinc additive to iron supplement medicine by WHO (15 µg/g) as shown in Fig. 5 where the Irofix cap has the lowest content with 0.108 µg/g. In comparison, the Feroxyl cap contains 0.245 µg/g even though the iron velvet tab has the highest amount among the three samples with 0.256 µg/g. There is no difference in iron absorption in the human body with or without zinc, which explains the low zinc content in iron supplements.

CONCLUSION

Exposure to heavy metals can cause health issues in the long term especially the consumption of pharmaceutical samples which contain metal additives. The current study was carried out for the determination of two heavy metals (copper (Cu) and zinc (Zn)) in 2 anti-diabetic and 3 iron supplement samples by using atomic absorption spectroscopy (AAS). In all samples, concentrations of heavy metals were lower than the maximum level according to WHO. In addition, the concentration of zinc was 1.21 (µg/ml) in Mixtard 30, 1.31 (µg/ml) in Gensulin M30, 0.108(µg/g) in the Irofix cap, 0.245 (µg/g) in the Feroxyl cap and 0.256 (µg/g) in the Iron velvet tab. Nevertheless, the copper content was 0.137 (µg/ml) in Mixtard 30, 0.423 (µg/ml) in Gensulin M30, 1.708 (µg/g) in the Irofix cap, 1.472 (µg/g) in the Feroxyl cap and 1.984 (µg/g). All the results were within the acceptable limits.

Arabic section:

تقدير اثنين من المعادن (الخارصين و النحاس) في عينة من مكملات الحديد و ادوية السكر باستخدام جهاز طيف الامتصاص الذري.

المؤلفون: خميس علي ابراهيم، غيث محمد غيث، دنيا محمد خالد، اية محمد منصور، الاء ناصر فرج

يهدف هذا البحث إلى تحديد كمية اثنين من المعادن الثقيلة (الزنك والنحاس) في اثنين من الأدوية المضادة للسكري و3 عينات من مكملات الحديد. تم تصنيع العينات المختارة من دول مختلفة (الدنمارك، بولندا، الهند، مصر، وبلجيكا) و الموجودة في صيدليات مدينة بني وليد. تم تحديد العناصر المختارة بواسطة مطيافية الامتصاص الذري (AAS) وذلك بطريقة الهضم الرطب مع حمض النيتريك المركز و فوق اكسيد الهيدروجين بنسبة 3:1. من خلال النتيجة التي تم الحصول عليها، تبين أن المعادن الثقيلة الموجودة في عينات الأنسولين كانت ضمن نطاق تركيز مقبول 1.21 ميكروغرام/مل في ميكستارد 30 و 1.31 ميكروغرام/مل في جينسولين M30 بالنسبة للزنك بينما كان محتوى النحاس 0.137 ميكروغرام/مل في ميكستارد 30 و 0.423 ميكروجرام/مل في عينة جينسولين.

احتوت عينات مكملات الحديد على النحاس والزنك بالميكروجرام/جم فكانت علي النحو التالي (1.708 و0.108 في عينة ايرونفكس، و1.472 و0.245 لعينة فيروكسيل بينما احتوت بينما احتوت عينة ايرون فلفت على 1.984 نحاس و0.256 خارصين). كانت جميع النتائج أقل من الحدود القصوى وآمنة للاستخدام. يوصى بشدة بمراقبة جودة المنتجات الطبية وخاصة الأدوية.

الكلمات المفتاحية: فقر الدم، طيف الامتصاص الذري، المعادن الثقيلة، منتجات صيدلانية

Abbreviations and acronyms

Zn: zinc

Cu: copper

AAS: atomic absorption spectroscopy

Conc: concentration

WHO: world health organization

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