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DETERMINATION OF TRACE LEVELS OF NICKEL(II) BY CYCLIC VOLTAMMETRY WITH SPEs FROM FOOD PRODUCTS

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Abstract: *Detectable nickel ion levels are found in many foods, including cocoa beans, legumes, grains, nuts and seeds, crustaceans, saltwater fishes, and fruits. Itis known that approximately 15% of the human population suffers from an allergy to dietary nickel. In addition to digestive problems, dietary nickel intolerance may lead to diffuse dermatitis and itching, fever, rhinitis, and headaches. Increased nickel levels can affect liver function leading to hepatic failure. Due to the harmful effects that nickel can have on human health, it is necessary to accurately measure nickel levels in foods and develop efficient detection protocols. The aim of this paper was to develop a chemosensor for the detection of nickel(II) ions in food products and in this case bismuth oxide –SPEs (screen-printed electrodes) and graphene modified SPEs were used with very small amount of dimethylglyoxime and amino acid L-histidine which were deposited. A potentiostat was used to study the electrochemical properties of nickel standard solution with different concentration. The results obtained with AAS (Atomic Absorption Spectrometry) reference method for food samples were compared with the results obtained with the developed chemosensor. Based on the results, the developed chemosensor that used bismuth oxide –SPEs with dimethylglyoxime was found efficient, having a linear response over a wide range (1–10 ppm) of nickel concentrations.*

Keywords*: electrochemical method, nickel allergy, screen printed electrodes.*

1. Introduction

Nickel (Ni) is the fifth most abundant element on Earth [1,2]. It is a silvery white hard, ductile, and malleable metal, with a density of 8.9 g/mL and a melting point of 1453 °C. Nickel (II) is the dominant inorganic species and has a wide pH and redox potential range (Eh) [4-6]. Elemental nickel is a group 10 transition metal, which is most commonly found in either the 0 or +2 oxidation states in biological materials, and less commonly in the -1 to +4 oxidation states. It is an indispensable metal for a number of industrial and clinical applications [3], and because nickel is abundant in the environment, it is commonly found in living tissues and many other kinds of organic matter. Nickel performs many essential functions as a microtrace nutrient in many organisms, and specifically in the human body it is involved in the activation of urease, a metalloenzyme that catalyzes the hydrolysis of urea to carbon dioxide and ammonia [7]. Nickel is moderately toxic to the human metabolism when compared to other transition metals. However, higher levels of nickel ions in the human body can be toxic, affecting the lungs, brain and

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kidney, and may lead to other complications such as allergies, muscular damage, neurological disorders, and respiratory cancer. Dietary intake of nickel is generally the main path of bioaccumulation [8-14].

The U.S. Agency for Toxic Substance and Disease Registry estimates that the daily tolerable dietary intake of nickel for a 70 kg adult is 0.001–0.0024 mg/kg. About 5-40% of nickel present in foods and beverages is absorbed in the digestive tract, while ambient air when inhaled, absorption oscillates from around 20-35% [11]. The nickel content in most commercial vegetables is usually 10 mg/kg but in nickel-rich soils it can reach 100 mg/kg [15]. The greatest natural sources of dietary nickel are cocoa products, legumes, baking soda, nuts, and drinking water, with some of the highest mean concentrations of nickel measured in wild edible mushrooms (containing >10 mg/kg dry weight) [16-19].

Daily consumption of these foods in high amounts can increase nickel intake up to 900 mg. The level of nickel ions in these foods depends on where and how they are cultivated, specifically application of herbicides, pesticides and fertilizers, as well as nickel levels occurring in soil and air (natural or due to pollution), food processing methods, transport and storage conditions [20-24]. The link between dietary nickel bioaccumulation and human health is well-established [25-29], and therefore, it prompts the need for the development of efficient detection methods. Biosensors hold great value because they can be selective to the analysis of interest, are both cost-effective and time-efficient, and can produce reliable data that benefits human health, namely that nickel detection is a preventative health care measure [30].

Considering its toxic effects, precise quantification of nickel in our food supply is of great importance.

The importance of determining the concentration of nickel ions in food products arises from its toxicity for human health. It is estimated that approximately 8–15% of women and 1–2% of men are sensitive to nickel [31-38].

Total nickel content analysis is performed using flame atomic absorption spectrometry, graphite furnace atomic absorption spectrometry, inductively coupled plasma optical emission spectrometry, or mass spectrometry. These methods used to detect nickel in food and water samples, can be with or without preconcentration or separation steps [39-41]. To streamline the sample preparation process, save time and materials, biosensors are increasingly used in the last years. Biosensors are integrated devices capable of providing specific quantitative analyses by using a biological receptor in direct contact with a transducer [42-46]. A chemosensor is not a sensor, strictly speaking, as it is not a device, but it can be the active part of the device [47]. Development of biosensors is largely to the success in glucose measurement for diabetics, where it dramatically improved patient care by providing a convenient, hygienic, compact method of self-monitoring [48-51]. Currently, biosensors applications have greatly expanded in detection of certain pathogens or even markers of cancer, cardiovascular disease and hormones.

Similar to its design in other fields, biosensors used in analyzing food compounds consist of a biologically active receiver, a transducer, and an electronic system for amplifying, processing and displaying data that provides specific analytical information that allows the recognition of a particular biological or chemical species. Biosensors in the food industry are used to identify microorganisms, antibodies, heavy metals, alcohols, carbohydrates, vitamins and allergens [52, 53].

Biosensor's technology has evolved greatly from in vitro studies based on the biosensitivity of organic beings to the highly sophisticated world of nanofabricated biosensors [54-56].
The application of this chemosensor solves the problem of the determination of nickel ions from foods which nowadays is difficult, expensive, requires specialized personnel and is limited to detection in a laboratory because there are no efficient *in situ* methods.

2. Materials and methods

Reagents

For the experimental part of developing and testing of chemosensor, nickel sulphate, dimethylglyoxime (DMG) (1%), amino acid L-histidine (1%), nitric acid, and ammonium buffer were purchased from Sigma-Aldrich (Steinheim, Germany). Graphene and bismuth modified screen-printed electrodes were purchased from Dropsens. All solutions were made using deionized water with a resistivity of 18.2 MΩ×cm (Millipore, Direct-Q 3 UV).

Electrochemical Measurements

A Metrohm Autolab bipotentiostat µStat 300 controlled by DropView 8400 software was used for the electrochemical measurements. The testing conditions were: starting potential -0.1 V, switching potential 0.9 V, and scanning rate 0.1 V/s. A drop of sample was placed on the SPE, then the potential was applied, and as a result, the Ni-DMG complex was formed. Response time was 60 seconds.

Immobilization of ligand on SPE and development of chemosensor

The ligand, dimethylglyoxime 1% and 1 µL amino acid L-histidine solution 1% were pipetted and immobilized on the surface of the working electrode of the SPE.

Then the miniaturized electrode was used for nickel ions analyses by cyclic voltammetry. The development and testing of chemosensor were caried out according Anchidin-Norocel et al. (2021) [60].

Testing the chemosensor on food products

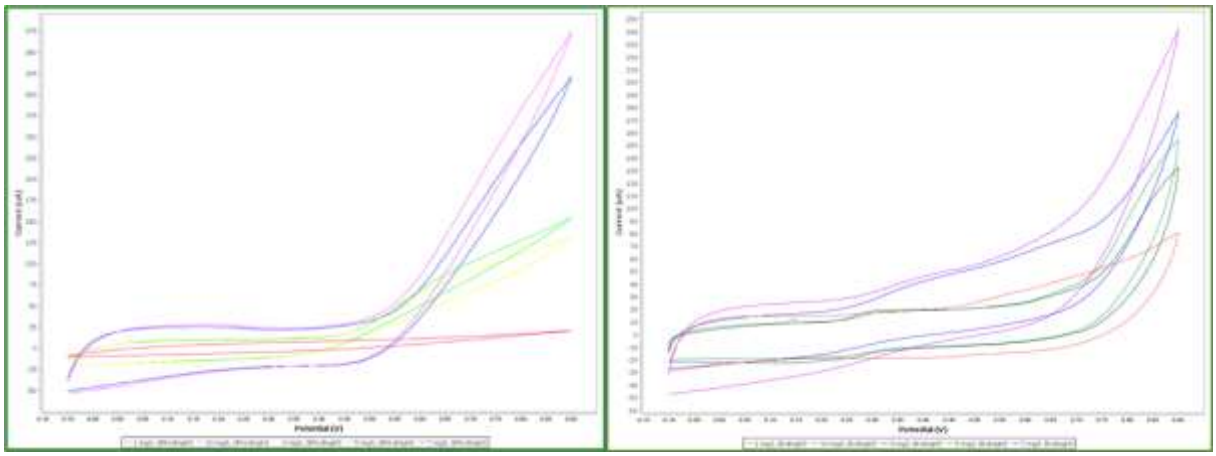
In this study, cocoa, cabbage, wine, and spinach samples were analyzed by the voltammetric method. The results obtained were compared with the Atomic Adsorption Spectrometry (AAS) values of the same samples.

Atomic Adsorption Spectrometry method

Nickel determination by AAS was made using the method presented by Salazar et al. (2011) [11] to prepare samples via acid digestion and calcination.

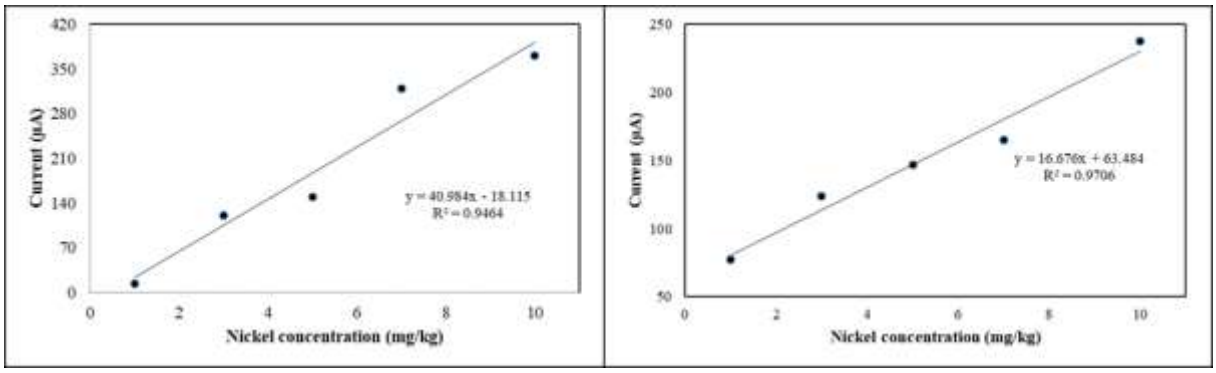
3. Results and discussion

The chemosensor development process had several stages, the first of which was to make a calibration curve with standard solution, to identify a linear regression higher and to use the most performant chemosensor for food samples. The concentration was reported at the maximum current density for each solution because the anodic and cathodic peaks are extremely small (Figure 1). So, in order to obtain a calibration curve from the cyclic voltammograms, nickel solutions (1, 3, 5, 7, and 10 mg/L) were used (Figure 2).
Following the analysis of the nickel solution, higher linear regression value (0.97) was obtained for SPE- Bi_2O_3/C - $dmgH_2$ and lower value (0.94) for cyclic voltammograms performed with SPE-GPH-$dmgH_2$. Because these results turned out to be better for SPE- Bi_2O_3/C - $dmgH_2$, analysis of food samples were made only for this chemosensor. By comparing the developed method with the reference method (AAS) similar values were observed.



a) **b)**

Fig. 1. The cyclic voltammogram obtained for nickel standard solutions with a) SPE-GPH-dmgH_2 and b) SPE-Bi_2O_3/C - dmgH_2



c) **d)**

Fig. 2. Calibration curve obtained for nickel standard solutions with a) SPE-GPH-dmgH_2 and b) SPE- Bi_2O_3/C - dmgH_2

Figure 3 shows that the results obtained for two samples of cocoa, wine, spinach and cabbage analyzed with the developed chemosensor, had higher values than the AAS method, suggesting that this biologic element may select from the matrix of food samples compounds another ion that interferes with nickel. So, we had to analyze the interferences that appear in the food sample matrices. This analitycal performance characteristic in this case can be called selectivity and is made in same condition (for an intermediary concentration of standard solution) for a lot of minerals standard solution (Fe, Na, Ca, Al, Zn, Cd, Cu, K, Pb). The results of this evaluation are presented in Figure 4.

The analytical performances of the chemosensor were evaluated also by sensitivity calculated according to Norocel & Gutt [58, 59].

$$\text{Sensitivity} = m/A$$

where *m*-slope of calibration curve (µA Mm^{-1}), *A*-area of active surface (cm^2).

The results obtained for sensitivity were 3.25 for SPE-GPH-dmgH_2 and 1.32 for SPE- Bi_2O_3/C - dmgH_2. Both the voltamogram and the calibration curve had shown that the values extracted can provide good results and can be used to calculate the nickel concentration of the standard solution.

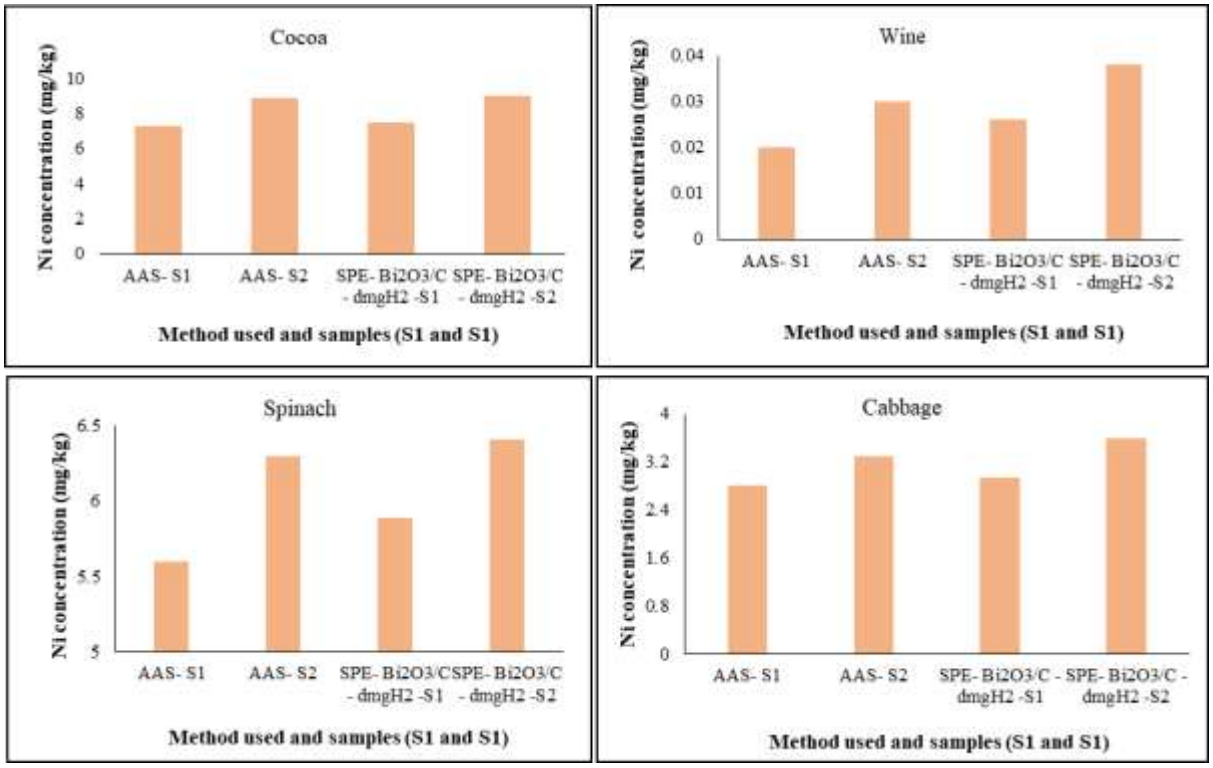


Fig. 3. Concentrations of nickel in food samples -S1, -S2 from final name of method used means samples 1 and samples 2

Chemosensor reproducibility was analyzed by measuring the nickel-generated current of 5 mg/L in 10 mL deionized water. The chemosensor was tested on three different days with a triple analysis (n = 3). The total mean value was calculated and the relative standard deviation (RSD) provided analytical precision, and, the resulted reproducibility was 96.2% for SPE-GPH-$dmgH_2$ and 94.4% for SPE- Bi_2O_3/C - $dmgH_2$.

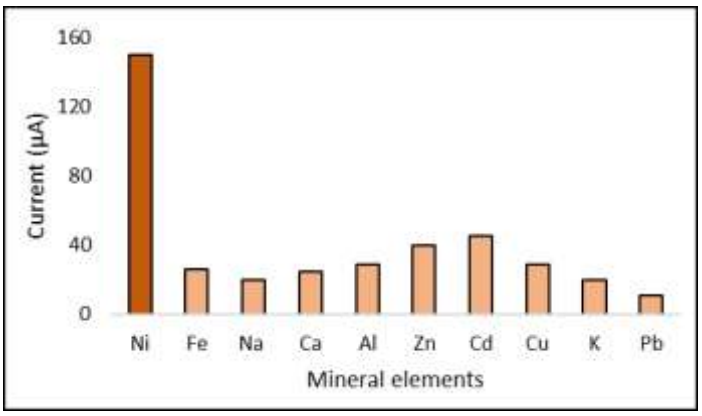


Fig. 4. Selectivity evaluation of the developed chemosensor against the interference of mineral elements

Even if there are already many chemosensors for the determination of nickel ions, the difference between them is made by the analytical performance characteristics, respectively the detection limit, the sensitivity but also the dynamic range.

4. Conclusion

Clearly, from a public safety perspective, nickel needs to be measured in the food supply and used for environmental health assessments (e.g., air, soil, and water quality). Chemosensors are ideal tools for the task of detecting analytes like nickel because they can be synthesized to have very high specificity and can be adapted for high-throughput processing. Chemosensors are generally of lower cost and portable, which makes them valuable for small-scale and mobile/remote applications. Most chemosensors used in the analysis of nickel ions found in the literature have no application data in certain industries and if both existing chemosensors and other new chemosensors were tried in identifying these ions in food, it would be very beneficial for people suffering from these allergies. The results obtained with the proposed chemosensor for determining nickel ion concentration in foods have proven to be effective both for the performance characteristics and for comparing the results with the reference method. The ligand used showed good sensitivity for the target analyte, thus recommending it as a possible mean for the quantification of nickel ions in the food samples analyzed.

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6. References

[1]. MATTISON, R. L., BOWYER, A. A., & NEW, E. J. Small molecule optical sensors for nickel: The quest for a universal nickel receptor. *Coord. Chem. Rev*, (2020). 425, 213522.

[2]. GOPALAPILLAI, Y., FASFOUS, I. I., MURIMBOH, J. D., YAPICI, T., CHAKRABORTY, P., & CHAKRABARTI, C. L. Determination of free nickel ion concentrations using the ion exchange technique: application to aqueous mining and municipal effluents. *Aquat Geochem*., 14(2), (2008), 99-116.

[3]. LI, J. J., HOU, C. J., HUO, D. Q., SHEN, C. H., LUO, X. G., FA, H. B., ... & ZHOU, J. Detection of trace nickel ions with a colorimetric sensor based on indicator displacement mechanism. *Sens Actuators B Chem*, 241, (2017), 1294-1302.

[4]. MATTISON, R. L. Fluorescent sensors to monitor Ni (II) in complex environments (Doctoral dissertation, University of Sydney), (2020).

[5]. ADEGOKE AV, ALIYU DH, AKEFE IO, NYAN SE. A Review on the Metal Complex of Nickel (II) Salicylhydroxamic Acid and its Aniline Adduct. *J Transl Sci Res*, (2019) 2: 006.

[6]. HUANG, D., & LIU, J. Functions and toxicity of nickel in plants: recent advances and future prospects. *Clean–soil, air, water*, (2009), 37(4-5), 304-313.

[7]. MUTHUSELVI, R. Determination of nickel (II) by spectrophotometry in micellar media. *Pharm Anal Chem*, 3(3), (2017).

[8]. D'ALCAMO, A., MANSUETO, P., SORESI, M., IACOBUCCI, R., BLASCA, F., GERACI, G., ... & IACONO, G. Contact Dermatitis Due to Nickel Allergy in Patients Suffering from Non-Celiac Wheat Sensitivity. *Nutrients*, 9(2), 103, (2017).

[9]. DUDA-CHODAK, A., & BLASZCZYK, U. The impact of nickel on human health. *Journal of Elementology*, 13(4), (2008), 685-693.

[10]. KRUSZEWSKI, B., OBIEDZIŃSKI, M. W., & KOWALSKA, J. Nickel, cadmium and lead levels in raw cocoa and processed chocolate mass materials from three different manufacturers. J *Food Compost Anal.*, 66, (2018), 127-135.

[11]. SALAZAR, R. F. D. S., ALCÂNTARA, M. A. K. D., & IZÁRIO FILHO, H. J. Evaluation of sample preparation methods and optimization of nickel determination in vegetable tissues. *Revista brasileira de Ciência do Solo*, 35(1), (2011). 241-248.

[12]. VERMA, N., & SINGH, M. A Bacillus sphaericus based biosensor for monitoring nickel ions in industrial effluents and foods. *J Autom Methods Manag Chem.*, (2006).

[13]. ALMAQUER, F. E. P., RICACHO, J. S. Y., & RONQUILLO, R. L. G. Simple and rapid colorimetric sensing of Ni (II) ions in tap water based on aggregation of citrate-stabilized silver nanoparticles. *Sustain. Environ. Res*, 29(1), (2019), 1-10.

[14]. ANTICO, A., & SOANA, R. Nickel sensitization and dietary nickel are a substantial cause of symptoms provocation in patients with chronic allergic-like dermatitis syndromes. *Allergy & Rhinology*, 6(1), 2015.
[15]. KUMARI, S., CHANDRAWAL, A., KUMAR, M., & KUMAR, A. Toxicity of cadmium and nickel in soil and vegetables. Inter-national Int *J Curr Microbiol Appl Sci*, 7(10), (2018), 2341-2352.
[16]. SMART, G. A., & SHERLOCK, J. C. Nickel in foods and the diet. *Food Addit Contam*, 4(1), (1987), 61-71.
[17]. ONIANWA, P. C., LAWAL, J. A., OGUNKEYE, A. A., & OREJIMI, B. M. Cadmium and nickel composition of Nigerian foods. *Food Compost Anal.*, 13(6), (2000), 961-969.
[18]. REILLY, C. Metal contamination of food (pp. 40-60). London: Applied science publishers. (1980).
[19]. BRAGA, M., QUECCHIA, C., PEROTTA, C., TIMPINI, A., MACCARINELLI, K., DI TOMMASO, L., & DI GIOACCHINO, M. Systemic nickel allergy syndrome: nosologic framework and usefulness of diet regimen for diagnosis. *Int J Immunopathol Pharmacol.*, 26(3), (2013), 707-716.
[20]. PEETERS, K., ZULIANI, T., ŽIGON, D., MILAČIČ, R., & ŠČANČAR, J. Nickel speciation in cocoa infusions using monolithic chromatography –Post-column ID-ICP-MS and Q-TOF-MS. *Food Chem*, 230, (2017), 327-335.
[21]. DOHNALOVA, L., BUCEK, P., VOBORNIK, P., & DOHNAL, V. Determination of nickel in hydrogenated fats and selected choc-olate bars in Czech Republic. *Food chem.*, 217, (2017), 456-460.
[22]. SAITO, M., ARAKAKI, R., YAMADA, A., TSUNEMATSU, T., KUDO, Y., & ISHIMARU, N. Molecular mechanisms of nickel allergy. *Int. J. Mol. Sci*., 17(2), 202, (2016).
[23]. FEYZULLAH TOKAY, Development of UV-Vis Spectrophotometric Method for Rapid Nickel Determination in Original Oil Matrix, *J. Nat. Appl. Sci*, Volume 21, Issue 2, 332-337, 2017, DOI: 10.19113/sdufbed.67183
[24]. GIDEON RAMTAHAL, IVAN CHANG YEN, ET AL., Cost-effective Method of Analysis for the Determination of Cadmium, Copper, Nickel and Zinc in Cocoa Beans and Chocolates, *J. Food Res.*, Vol. 4, No. 1, 2015.
[25]. AHLSTRÖM, M. G., THYSSEN, J. P., MENNÉ, T., & JOHANSEN, J. D. Consumer Behaviour Among Nickel-allergic Patients. *Acta Derm Venereol*, 97(8-9), (2017), 1247-1248.
[26]. ALIZADEH, K., & RAD, N. A new optical sensor for selective monitoring of nickel ion based on a hydrazone derivative immobilized on the triacetyl cellulose membrane. *J Anal Bioanal Tech*, (2016), 7(2).
[27]. Brandão, M. H. T., & Gontijo, B. (2012). Contact sensitivity to metals (chromium, cobalt and nickel) in childhood. *An Bras Dermatol*, 87(2), 269-276.
[28]. BABAEE, S., PAKDEHI, S. G., & NABAVI, A. S. An Optical Chemical Sensor for Determination of Nickel in Water and Hydrogen Peroxide Samples. *Journal of New Developments in Chemistry*, 1(2), 58, (2016).
[29]. CHEN, B., XIA, G., CAO, X. M., WANG, J., XU, B. Y., HUANG, P., ... & JIANG, Q. W. Urinary levels of nickel and chromium associated with dental restoration by nickel–chromium based alloys. *International journal of oral science*, 5(1), 44, (2013).
[30]. EFSA Panel on Contaminants in the Food Chain (CONTAM). Scientific Opinion on the risks to public health related to the presence of nickel in food and drinking water. *EFSA Journal*, 13(2), 4002, (2015).
[31]. LUSI, E. A., DI CIOMMO, V. M., PATRISSI, T., & GUARASCIO, P. High prevalence of nickel allergy in an overweight female Mansouri population: a pilot observational analysis. *PloS one*, 10(3), e0123265. (2015).
[32]. VENTER, C. Food hypersensitivity: diagnosing and managing food allergies and intolerances. *Journal of allergy*, (2012).
[33]. VALENTA, R., HOCHWALLNER, H., LINHART, B., & PAHR, S. Food allergies: the basics. *Gastroenterology*, 148(6), (2015), 1120-1131.
[34]. STRINNHOLM, Å. Food hypersensitivity among schoolchildren: prevalence, Health Related Quality of Life and experiences of double-blind placebo-controlled food challenges (Doctoral dissertation, Umeå universitet). (2017).
[35]. CHAKRABARTY K., CHAKRABARTY A.S. Food Hypersensitivity. *In: Textbook of Nutrition in Health and Disease. Springer*, Singapore, (2019). https://doi.org/10.1007/978-981-15-0962-9_6
[36]. NASR, I. H. HUMAID AL WAHSHI Food Intolerance versus Food Allergy, 2. (2017). https://scientonline.org/open-access/food-intolerance-versus-food-allergy.pdf
[37]. KUMAR, R. V., RAJVIKRAM, N., RAJAKUMAR, P., SARAVANAN, R., DEEPAK, V. A., & VIJAYKUMAR, V. An Accurate Method-ology to detect Leaching of Nickel and Chromium Ions in the Initial Phase of Orthodontic Treatment: An in vivo Study. *J. Contemp. Dent. Pract.*, 17(3), (2016), 205-210.
[38]. MANSOURI M. Food Allergy: A Review, *Arch Pediatr Infect Dis.* (2015); 3(3):e22470. doi: 10.5812/pedinfect.22470.

[39]. FORZANI, E. S., ZHANG, H., CHEN, W., & TAO, N. Detection of heavy metal ions in drinking water using a high-resolution differential surface plasmon resonance sensor. *Environ Sci Technol*, 39(5), (2005), 1257-1262.
[40]. GAO, P. F., ZHANG, X. W., KUANG, H. Z., LI, Q. Q., & LI, Y. Study on simultaneous determination of Ni, Pb and Cd by ion chromatography. In *IOP Conference Series: Earth and Environmental Science* (Vol. 146, No. 1, p. 012068). (2018). IOP Pub-lishing.
[41]. KUMAR, B. N., KANCHI, S., SABELA, M. I., BISETTY, K., & JYOTHI, N. V. V. Spectrophotometric determination of nickel (II) in waters and soils: Novel chelating agents and their biological applications supported by DFT method. *Karbala International Journal of Modern Science*, 2(4), (2016), 239-250.
[42]. SOLEYMANI, L., & LI, F. Mechanistic challenges and advantages of biosensor miniaturization into the nanoscale. *ACS Sensors*, 2(4), (2017), 458-467.
[43]. PATEL, S., NANDA, R., SAHOO, S., & MOHAPATRA, E. Biosensors in health care: the milestones achieved in their development towards lab-on-chip-analysis. *Biochem. Res. Int*, (2016).
[44]. HASAN, ANWARUL., Review Article - Recent Advances in Application of Biosensors in Tissue Engineering, *Biomed Res Int* Volume (2014), Article ID 307519, 18 pages http://dx.doi.org/10.1155/2014/307519
[45]. ODOBASIC, A., SESTAN, I., & BEGIC, S. Biosensors for Determination of Heavy Metals in Waters. In Biosensors for Envi-ronmental Monitoring. *IntechOpen*. Chapters. (2019).
[46].*https://www.intechopen.com/books/biosensors-for-environmental-monitoring/biosensors-for-determination-of-heavy-metals-in-waters*
[47]. RANI, P. Chemosensor and its applications. *IRJRR*, 3, (2015), 1-10.
[48]. BHATT, G., & BHATTACHARYA, S. Biosensors on chip: a critical review from an aspect of micro/nanoscales. *Journal of Micromanufacturing*, 2(2), (2019), 198-219.
[49]. TURDEAN, G. L., Review Article, Design and Development of Biosensors for the Detection of HeavyMetal Toxicity, SAGE-Hindawi Access to *Research International Journal of Electrochemistry*, Volume 2011.
[50]. MOHANTY, S. P., KOUGIANOS, E., Biosensors: A tutorial review, 0278-6648/06, *IEEE, Potentials*, (2006).
[51]. STAMATIN, I., Nanomateriale aplicații în biosenzori, surse de energie, medicină, biologie, Elemente de Nanotehnologie, *Editura Universității din București*, (2008).
[52]. CASTILLO-HENRÍQUEZ, L., BRENES-ACUÑA, M., CASTRO-ROJAS, A., CORDERO-SALMERÓN, R., LOPRETTI-CORREA, M., & VE-GA-BAUDRIT, J. R. Biosensors for the Detection of Bacterial and Viral Clinical Pathogens. *Sensors*, 20(23), 6926, (2020).
[53]. BAHADIR, E. B., MUSTAFA KEMAL SEZGINTURK, Applications of commercial biosensors in clinical, food, environmental, and bio-threat/biowarfare analyses, 0003-2697, *Elsevier, Anal Biochem*, (2015).
[54]. BHATTARAI, P., & HAMEED, S. Basics of Biosensors and Nanobiosensors. Nanobiosensors: From Design to Applications, 1-22, https://doi.org/10.1002/9783527345137.ch1 (2020).
[55]. BANERJEE, A., MAITY, S., & MASTRANGELO, C. H. Nanotechnology for biosensors: *A Review. arXiv preprint* arXiv:2101.02430, (2021).
[56]. CHAMBERS, J. P., ET AL, Biosensor Recognition Elements, *Horizon Scientific Press, (*2008).
[57]. ARORA, R.K., AND SAINI, R.P., Biosensors: Way Of Diagnosis, Int. J. Pharm. Sci. Res, *IJPSR*, (2013); Vol. 4(7): 2517-2527.
[58]. NOROCEL, L., & GUTT, G. Screen-Printed Voltammetric Biosensors for the Determination of Copper in Wine. *Sensors*, 19(21), 4618, (2019).
[59]. NOROCEL, L., & GUTT, G. Development and performance testing of an electrochemical sensor for determination of iron ions in wine. *Australian journal of grape and wine research*, 25(2), (2019), 161-164.
[60]. ANCHIDIN-NOROCEL, L., AMARIEI, S., & GUTT, G. Sensing of Nickel (II) Ions by Immobilizing Ligands and Using Different SPEs. *Engineering Proceedings*, 6(1), 2, (2021).