### Accepted Manuscript

A new and highly selective turn-on fluorescent sensor with fast response time for the monitoring of cadmium ions in cosmetic, and health product samples

Rouhollah Khani, Ebrahim Ghiamati, Ramin Boroujerdi, Abdolreza Rezaeifard, Mohadeseh Hosseinpour Zaryabi

 PII:
 \$1386-1425(16)30113-5

 DOI:
 doi: 10.1016/j.saa.2016.03.011

 Reference:
 \$AA 14324

To appear in:

Received date:23 November 2015Revised date:9 March 2016Accepted date:11 March 2016

Please cite this article as: Rouhollah Khani, Ebrahim Ghiamati, Ramin Boroujerdi, Abdolreza Rezaeifard, Mohadeseh Hosseinpour Zaryabi, A new and highly selective turnon fluorescent sensor with fast response time for the monitoring of cadmium ions in cosmetic, and health product samples, (2016), doi: 10.1016/j.saa.2016.03.011

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



### A new and highly selective turn-on fluorescent sensor with fast response time for the monitoring of cadmium ions in cosmetic, and health product samples

Rouhollah Khani, Ebrahim Ghiamati\*, Ramin Boroujerdi, Abdolreza Rezaeifard,

Mohadeseh Hosseinpour Zaryabi

Department of Chemistry, Faculty of Science, University of Birjand, P.O. Box 414, Birjand, Iran

#### Abstract

Cadmium (Cd) which is an extremely toxic could be found in many products like plastics, fossil fuel combustion, cosmetics, water resources, and wastewaters. It is capable of causing serious environmental and health problems such as lung, prostate, renal cancers and the other disorders. So, the development of a sensor to continually monitor cadmium is considerably demanding. Tetrakis(4-nitrophenyl) porphyrin, T(4-NO<sub>2</sub>-P)P, was synthesized and used as new and highly selective fluorescent probe for monitoring cadmium ions in the "turn-on" mode. There was a linear relationship between fluorescence intensity and the concentration of Cd(II) in the range of  $1.0 \times 10^{-6}$  to  $1.0 \times 10^{-5}$  mol L<sup>-1</sup> with a detection limit of 0.276 µM. To examine the most important parameters involved and their interactions in the sensor optimization procedure, a four-factor central composite design (CCD) combined with response surface modeling (RSM) was implemented. The practical applicability of the developed sensor was investigated using real cosmetic, and personal care samples.

*Keywords:* Turn-on sensor; Fluorescent probe; Porphyrin; Multivariate optimization; Cadmium; Cosmetic samples.

\*Corresponding author. Tel: +985632202065, ext. 336

E-mail address: eghiamati@birjand.ac.ir

#### **1. Introduction**

Heavy metals, are one of the main sources of pollution in environment, especially because of their significant effects on biological systems. The importance of heavy metals determination at trace levels is due to their rapid diffusion as environmental contaminants [1,2], to the surroundings. Cadmium is toxic even at low levels and has influence on various biological processes [3-7]. Cadmium is a naturally occurring non-essential trace element and has a tendency to bioaccumulates in living organisms, raising environmental concerns [8,9]. Cadmium is ranked seventh in priority list of top 275 hazardous material on Comprehensive Environmental Response, Compensation, and Liability Act in USA [10,11]. Furthermore, the accumulation of cadmium in the human body can damage important internal organs like liver, lung, kidneys, central nervous system and bones [12,13]. Epidemiological studies conducted in general human populations have shown that Cd increases the risk of developing breast, prostate, and endometrial cancers [14-17].

Many attempts have been made during the last two decades to develop different methods for detecting cadmium, including electrochemical methods such as differential pulse anodic stripping voltammetry [18,19], optical spectroscopic methods like flame atomic absorption spectrometry [7,20], and inductively coupled plasma mass spectrometry [21]. The problems with these techniques are the requirements for expensive instrumentation, specialized operator, and long analysis time. Spectrofluorometric and spectrophotometric methods, like Dual-Signaling Fluorescent (DSF) [22] were used to detect trace amount of metal ions, too. Fluorescent and colorimetric-based chemosensors are widely utilized for measuring the amount of cadmium ions in solutions [23-36].

Due to unique properties of fluorescence techniques, many detection methods have been emerged for speciation of analytes, such as heavy metal ions, mostly by studying the emission spectra like peak shifting [37], quenching [38,39], or enhancement [40-42]. The development of optical sensing approaches in designing sensors and biosensors for the detection of environmentally and biologically important species, such as toxic heavy metal ions, has been an inevitable task. A fluorescence-based optical sensor is one of the most practical application of these endeavors, because of its intrinsic sensitivity, high selectivity, specificity, real-time monitoring with fast response time and undamaging effects on the analytes [43-45].

On the other hand, the porphyrins are macrocyclic compounds constituting 1:1 complexes almost with all the metal ions. Mg(II), Cd(II) and Zn(II) in their porphyrin complexes, readily combine with one more ligand to form pentacoordinated complexes with square-pyramidal structure [46]. Porphyrins reactions with large metal ions like Cd(II), are relatively fast, because they cannot fit into the porphyrin nucleus and just sit on top of the molecule [47]. Porphyrin based sensory methods were widely used during the past decade because of their ability to interact with metal ions. Many of the newly developed Cd turn-on sensors capable of detecting Cd and Zn are unable to function selectively only for cadmium [48-52]. In this work T(4-NO<sub>2</sub>-P)P was employed as a specific turn-on fluorescent probe to quantify cadmium ions in real samples. The influence of important variables such as temperature, time of response, the amount of the reagent and the concentration of zinc on function of the sensor were investigated. The optimization was carried out via a  $2^4$  full factorial central composite design (CCD) combined with response surface methodology (RSM) to maximize sensor efficiency of the target analyte. In this methodology, the interactions of two or more variables could be studied simultaneously, resulting in higher percentage yields, reduced process variability, closer confirmation of the output response to nominal and target achievement, and less treatment time with minimum costs [53].

#### 2. Experimental

#### 2.1 Reagents

#### 2.1.1. Chemicals

All chemicals were purchased from Merck (Darmstadt, Germany) and were of analytical reagent grade. Absolute ethanol (Merck) was used for preparing the respective solutions. The metal ions stock solutions were made up of their nitrate and chloride salts. The Hg (II) ions were of its acetate salt. Double distilled deionized water was used for solutions dilution.

#### 2.1.2. Real Samples

Three real samples were chosen, i) A Kiss Beauty pink-purple lipstick; ii) An Atusa brown hair color from Sabzgolsar Co. under the supervision of Jos. H. Lowenstein, USA; and iii) My Lang Anhaltendes liquid foundation make up cream manufactured by ACT Cosmetics Co. (under the license of Kahl & Co, Germany).

#### 2.2. Instrumentation and software

Photoluminescence (PL) spectra were obtained using a Shimadzu RF-5301PC spectrofluorometer (Japan) at room temperature ( $298 \pm 2$  K). UV-Visible spectra were acquired by A-160 Shimadzu UV-Vis equipped with a photomultiplier tube (PMT) detector. AA-6300 Shimadzu (Japan) atomic absorption spectrometer (AAS) equipped with a deuterium lamp background correction and cadmium hollow cathode lamp was used as a source for determination of cadmium. The lamp was operated at optimum condition expressed by the manufacture. For centrifugation, Hettich Zentrifugen Model EBA 200 was used. Wisettir model MSH-20D was utilized for magnetic stirring of the solutions.

#### 2.3. Software

The Design-Expert, a statistical package software version 9.0 (Stat-Ease Inc., Minneapolis, MN, USA) was used for experimental design analysis and subsequent regression analysis of the experimental data. The proposed three dimensional molecular structure was drawn using Chem & BioDraw Ultra version 11.0 of Cambridge Soft products.

#### 2.4. Central composite design

The central composite design (CCD) was used to signify the effects of involved parameters including temperature, time of response, amount of the T (4-NO<sub>2</sub>-P)P and the concentration of zinc. Due to the similarity between the structure of  $Zn^{2+}$  and  $Cd^{2+}$  metal ions and the low fluorescence response of the proposed sensor to the zinc ions, the concentration of zinc plus three of above mentioned factors was examined using Design-Expert 9.0. A five-level CCD was implemented to evaluate the influence of the quantities on fluorescence intensity (Table 1) leading to 30 runs for the optimization process. Table 2 shows the experimental design points consist of  $2^n$  factorial points with 2n axial points along N<sub>c</sub> central points and the test results for the response variables. The center points are used to estimate the experimental errors and the reproducibility of the data.

Fulfilling the response surface methodology (RSM) role, followed by the implementation of optimization and performing distinct experiments allow us to determine the relative significance of parameters on the process even in systems with complex interactions. The modeling was conducted to derive the first or second-order polynomial equations. Then the analysis of

variances (ANOVA) were plotted in a three dimensional graphs. The outcome leads to a surface response, corresponding to a response function which is always used for the prediction of real optimum points.

#### 2.5. Preparation of real samples

To validate the proposed method, it was applied to determination of cadmium in three real samples, one a lipstick; the other, a brown hair coloring, and the last, the liquid foundation makeup cream. One g of a real sample was taken (lipsticks were sliced to tiny pieces) and was placed in a beaker. Then 8.0 mL of HNO<sub>3</sub> (65%) and 2.0 mL of acetone were added to it. The solution left intact for 24 h. After that, it was filtered. The filtrate was centrifuged in speed of 4000 rounds per minute (rpm) for 30 minutes to remove the colloidal fine particles. The upper solution was separated from the solid and dried. The dried material was added to a beaker containing absolute ethanol, stirred with stirring rod at 1500 rmp for 2 h till Cd (II) was dissolved. The solid material was removed by centrifugation, and the solution was repeated for the other two samples.

#### 3. Results and discussion

#### 3.1. Synthesis of T(4-NO<sub>2</sub>-P)P

Tetrakis(4-nitrophenyl)porphyrin was synthesized by using A. Bettelheim et al. method[54], with some changes for increasing the yield of the reaction, which briefly explained here. An 11.03 g (73 mmol) 4-nitrobenzaldehyde and 127 mmol of acetic anhydride were added to 300 mL of stirring propionic acid. After the solution was brought to reflux, 5.06 mL (73 mmol) of freshly distilled pyrrole in 10 mL of propionic acid was added. The dark solid was collected by filtration, washed three times with water, and finally dried. The extracted solid material was dissolved into 80 mL of pyridine, and refluxed for an hour. After cooling, the final product was washed with acetone. Fig. 1 shows the UV-Vis spectrum of the synthesized T(4-NO2-P)P. Our method produced 19-22% yield which was five times improvement in comparing to ref. 54 method. The molecular structure of the synthesized porphyrin ring has been shown in Fig. 2.

#### 3.2. Fluorescence measurements

A solution with concentration of  $1.0 \times 10^{-4}$  mol L<sup>-1</sup> of the T(4-NO<sub>2</sub>-P)P was prepared in chloroform. Scanning the spectrum in UV-Visible region showed a sharp peak at 420 nm. Therefore, 420 nm was selected for further studies.

Eighteen stock solutions of  $1.0 \times 10^{-3}$  mol L<sup>-1</sup> from different metal ions (Mg<sup>2+</sup>, Na<sup>+</sup>, Zn<sup>2+</sup>, Al<sup>3+</sup>, Mn<sup>2+</sup>, K<sup>+</sup>, Cd<sup>2+</sup>, Hg<sup>2+</sup>, Ag<sup>+</sup>, Co<sup>2+</sup>, Ni<sup>2+</sup>, Ca<sup>2+</sup>, Pb<sup>2+</sup>, Cu<sup>2+</sup>, Cr<sup>2+</sup>, Ce<sup>3+</sup>, Fe<sup>2+</sup>, Fe<sup>3+</sup>) were made in ethanol. Another stock solution of  $1.0 \times 10^{-4}$  mol L<sup>-1</sup> T(4-NO<sub>2</sub>-P)P in chloroform was also prepared. From first series of the stock solutions, a solution of  $8.0 \times 10^{-5}$  mol L<sup>-1</sup> of each metal ions of was mixed with  $1.0 \times 10^{-5}$  mol L<sup>-1</sup> of the T(4-NO<sub>2</sub>-P)P and diluted to the mark with ethanol. Fluorescence spectra for these were recorded at 608 nm ( $\lambda_{exc}$ : 420 nm).

As can be seen in Fig. 3, no obvious changes in emission spectra were observed upon the addition of different metal ions except for  $Zn^{2+}$  and  $Cd^{2+}$  solutions, which leads to appearance of a peak at 608 nm ( $\lambda_{exc}$ : 420 nm). The intensity of this peak in the presence of Cd ions was dramatically greater with respect to  $Zn^{2+}$  ions. The highly selective response of the T(4-NO<sub>2</sub>-P)P to Cd<sup>2+</sup> ions make it suitable for sensory usage (Fig. 4).

#### 3.3. Mechanism of fluorescence

The change in the fluorescence spectrum of T(4-NO<sub>2</sub>-P)P in the presence of different cations is due to the interactions of the four non-core nitro groups of the porphyrin with the cation (Fig. 5). According to literatures, the porphyrin core of meso-tetra(aryl)porphyrins with no steric hindrance at the meso positions is planar or nearly planar[55], and therefore the non-bonding electrons of the central nitrogen atoms cannot coordinate to the metal ion. On the other hand, these interactions cause deviation from planar configuration, leading to color change. No color change was observed confirming our proposed mechanism, i.e., interaction of NO<sub>2</sub> with Cd (II) which causes fluorescence turn-on is correct. Substituents attached to the meso aryl groups such as terpyridine [56], or functional groups such as carboxylate [56-58], may form coordinative bonds with metal cations such as Cd(II). The formation of such complexes were reported for Cd(II) in reaction with the functional groups of different aromatic ligands and nitrate anion [59].

# 3.4. Optimization of sensor efficiency using response surface methodology (RSM) approach 3.4.1. Interpretation of the regression analysis

Analysis of variance (ANOVA) using Design-Expert 9.0 (Table 3) produces useful information about the significance and magnitude of the effect on the main variables and their interactions. A p-value of less than 0.05 indicates the statistical significance of an effect at 95% confidence level. The "Lack of Fit" (LOF) p-value is 0.0645 which simultaneously confirms the suitability of the model for well-fitting of the experimental data, and demonstrates the insignificance LOF meaning that the other interactions are not significant with respect to the pure error. F-test was used to estimate the statistical significance of all terms in the polynomial equation within 95% confidence interval. Based on the data analysis the expression for evaluation of fluorescence intensity was obtained as follows:

Flu. Intensity = +207.49 - 125.34\*A - 7.37\*B - 0.43\*C - 18.79\*D - 20.74\*AB + 1.60\*AC + 14.43\*AD +0.92\*BC +19.05\*BD +3.77\*CD +33.04\*A<sup>2</sup> +20.33\*B<sup>2</sup> +2.17\*C<sup>2</sup> -2.03\*D<sup>2</sup> (1)

ANOVA results imparting this quadratic model could be utilized to navigate through the design space. As can be seen in Table 3 the P-value for fluorescence intensity of Cd (II) (p-value <0.0001) is lower than 0.05 conveying that quadratic model is significant. High value of  $R^2$  (94.0%) and  $R^2$  (adjusted) (90.0%) signifies a high dependency and correlation between the observed and the predicted values of response.

#### 3.4.2. Interpretation of residual graphs and 3D plots

The normal probability plot (NPP) is a graphical technique for assessing whether or not a data set is approximately normally distributed [60]. The residual is the difference between the observed and the predicted value (or the fitted value) from the regression. If the points on the plot fall fairly close to the straight line then the data are normally distributed. Fig. 6 illustrates NPP of residual values. It could be seen that the experimental points were reasonably aligned suggesting normal distribution was happened.

RSM application following CCD assists researchers to optimize the critical factors and to provide useful information about response nature. Fig. 7 represents the relevant fitted response surfaces for the design and depicts the response surface plots of fluorescence intensity versus respective variables, while their curvatures illustrate the presence of interactions among

variables. The response surface plots (Fig. 7 a–c) indicate the dependency of fluorescence intensity on variables such as temperature, time of reaction and concentration of the  $T(4-NO_2-P)P$ . In addition to, Fig. 7a confirms that maximum Cd(II) fluorescence intensity could occur at a temperature 298 K or at room temperature. According to Fig. 7b, it was found that Cd(II) has maximum fluorescence intensity in the first 25 min of reaction time. Fig. 7c illustrate that the temperature and time of reaction have negative correlation with the Cd(II) fluorescence intensity. It is noteworthy to mention that there is no significant interaction between these factors.

#### 3.4.3. Optimization of CCD by desirability function (DF) for Cd(II) sensor performance

The profile for predicted values and desirability option in the Design-Expert, Stat-Ease Inc. 9.0 software was used for the optimization process. This procedure involves specifying the DF for the dependent variable (fluorescence intensity) by assigning predicted values. The scale in the range of 0.0 (undesirable) to 1.0 (very desirable) was used to obtain a global function (D) that should be maximized according to efficient selection of variables. The CCD design matrix results in Table 2 show the maximum (561.936) and minimum (110.308) fluorescence intensity for Cd(II). On the basis of desirability score of 0.92, maximum fluorescence intensity of 432 A.U. was obtained at optimized conditions, so the parameters set as follows: reaction time 25 min, concentration of T(4-NO<sub>2</sub>-P)P and Zn(II)  $8.0 \times 10^{-6}$  mol L<sup>-1</sup> and  $5.0 \times 10^{-5}$  mol L<sup>-1</sup> respectively and 298 K for temperature. The performance of three replicates at specified optimum conditions showed a good agreement with predicted results and supported high applicability of CCD for prediction of real behavior of Cd(II) sensor.

#### 3.5 Fluorescence intensity of probe against different Concentrations of $Cd^{2+}$

Concentration of  $Cd^{2+}$  shows prominent effect on emission intensity of the probe, accompanying an increase in the concentration of  $Cd^{+2}$  in optimum conditions, with the peak intensity of the maximum emission at 608 nm. As it has been shown in Fig. 8, there are a linear change in fluorescence intensity with the addition of appropriate concentration of Cd (II). The inset demonstrates that fluorescence intensity is proportional to the concentration of Cd(II) in the range of  $1.0 \times 10^{-6}$ - $1.0 \times 10^{-5}$  mol L<sup>-1</sup>.

#### 3.6. Analytical figures of merit

To evaluate practical applicability of the proposed cadmium turn-on sensor, linearity, limit of detection, and relative standard deviation (RSD) were investigated. The calibration curve for cadmium was linear from  $1.0 \times 10^{-6}$  to  $1.0 \times 10^{-5}$  mol L<sup>-1</sup> with the coefficient of determination (R<sup>2</sup>) of 0.994. The limit of detection (LOD) based on 3S<sub>b</sub>/m definition (where m is the slope of the calibration curve and S<sub>b</sub> is the standard deviation of five blank measurements) was  $2.76 \times 10^{-7}$  mol L<sup>-1</sup>. Relative standard deviation (RSD %) of the method for determination of cadmium was 1.9% (n = 5).

#### 3.7. Application of the proposed turn-on sensor to real samples

In order to evaluate the reliability and analytical applicability of the proposed turn-on sensor for analysis of different matrices, the optimized method was applied for the determination of cadmium in cosmetic, and personal care samples. Sample preparations of real samples were performed as described in Section 2.3. For verification of the accuracy of the method, cadmium was also determined in all the samples by FAAS, not presenting statistical difference between results obtained. All these results are presented in Table 4. The nearness results of the two methods (i.e. FAAS and spectrofluorometry) proves the well working of the synthesized probe as a selective and sensitive sensor even in complex matrices and show that the sensing system has great potential for quantitative determination of cadmium in different cosmetic, and personal care samples.

#### 4. Conclusion

Prevention of the effects of toxic elements, like cadmium, requires a complete monitoring in real samples. Cosmetic and health products are one of widespread consumed products globally and improper amount of cadmium in any product makes a big health related problems. We have developed a new, highly sensitive and selective spectrofluorometric sensor for measuring the amount of Cd ions over a wide range of foreign ions in various real samples with complex matrices. For this purpose T(4-NO<sub>2</sub>-P)P was synthesized in higher yield than before, and used as a turn-on sensor for the fast detection of trace amounts of the cadmium ions in organic media. Optimum operating conditions that yield the maximum efficiency, determined by using response surface methodologies (RSM). Central composite design was utilized to reveal quadratic and

interaction terms, enabling us to choose more precisely the best experimental conditions for the effective involved factors with minimal experimental trials. The practical ability of the proposed turn-on sensor for the detection of cadmium ions in different cosmetic and health products samples with complex matrices was tested and the satisfactorily results were obtained.

#### Acknowledgements

We are grateful to the research council of the University of Birjand for financial support.

#### References

[1] E. Merian, Metals and their compounds in the environment: occurrence, analysis and biological relevance, VCH, Verlagsgesellschaft, mbH, 1991.

[2] S. Rauch, G. Morrison, L. Ebdon, L. Pitts, R. Cornelis, H. Crews, O. Donard, P.

Quevauviller, Trace Element Speciation for Environment, Food and Health, L. Ebdon, L. Pitts,

R. Cornelis, H. Crews, OFX Donard, Ph. Quevauviller (Eds.), The Royal Society of Chemistry Pub., Cambridge, 2001, 176-187.

[3] B. Debelius, J.M. Forja, Á. DelValls, L.M. Lubián, Ecotox. Environ. Safe. 72 (2009) 1503-1513.

[4] G. Liu, X. Chai, Y. Shao, L. Hu, Q. Xie, H. Wu, J. Environ. Sci. 23 (2011) 330-335.

[5] M.M. Junior, L.O. Silva, D.J. Leão, S.L. Ferreira, Food Chem. 160 (2014) 209-213.

[6] M. Behbahani, N.A.G. Tapeh, M. Mahyari, A.R. Pourali, B.G. Amin, A. Shaabani, Environ. Monit. Assess. 186 (2014) 7245-7257.

[7] T. Daşbaşı, Ş. Saçmacı, A. Ülgen, Ş. Kartal, Food Chem. 174 (2015) 591-596.

[8] J. Kalman, I. Riba, T.A. DelValls, J. Blasco, Ecotox. Environ. Safe. 73 (2010) 306-311.

[9] C. M. Liao, Y. R. Ju, W. Y. Chen, B. C. Chen, Sci. Total Environ. 409 (2011) 503-513.

[10] T. Jennings, "Cadmium environmental concerns". PVC handbook, Munich, Germany, Hanser Verlag, 2005.

[11] M. Mench, Agr. Ecosyst. Environ. 67 (1998) 175-187.

[12] G. Xiang, S. Wen, X. Wu, X. Jiang, L. He, Y. Liu, Food Chem. 132 (2012) 532-536.

[13] A. Afkhami, H. Ghaedi, T. Madrakian, M. Rezaeivala, Electrochim. Acta 89 (2013) 377-386.

[14] A. Åkesson, B. Julin, A. Wolk, Cancer Res. 68 (2008) 6435-6441.

- [15] B. Julin, A. Wolk, L. Bergkvist, M. Bottai, A. Åkesson, Cancer Res. 72 (2012) 1459-1466.
- [16] B. Julin, A. Wolk, J. E. Johansson, S. O. Andersson, O. Andrén, A. Åkesson, Brit. J. Cancer 107 (2012) 895-900.
- [17] I. Ali, P. Damdimopoulou, U. Stenius, K. Halldin, Chem-Biol. Interact. 231 (2015) 44-52.
- [18] H. Xu, L. Zeng, D. Huang, Y. Xian, L. Jin, Food Chem. 109 (2008) 834-839.
- [19] N. Serrano, A. González-Calabuig, M. del Valle, Talanta 138 (2015) 130-137.
- [20] Ö. Dalman, A. Demirak, A. Balcı, Food Chem. 95 (2006) 157-162.
- [21] B. Chen, Y. Zeng, B. Hu, Talanta 81 (2010) 180-186.
- [22] Y. Wang, L. Xiong, F. Geng, F. Zhang, M. Xu, Analyst 136 (2011) 4809-4814.
- [23] L. Wang, X.-t. Tao, J.-h. Shi, X.-q. Yu, M.-h. Jiang, J. Phys. Chem. B 110 (2006) 19711-19716.
- [24] R. McRae, P. Bagchi, S. Sumalekshmy, C.J. Fahrni, Chem. Rev. 109 (2009) 4780-4827.

[25] M. Choi, M. Kim, K.D. Lee, K.-N. Han, I.-A. Yoon, H.-J. Chung, J. Yoon, Org. Lett. 3 (2001) 3455-3457.

- [26] S.K. Kim, J.H. Lee, J. Yoon, Bull. Korean Chem. Soc. 24 (2003) 1032-1034.
- [27] T. Gunnlaugsson, T.C. Lee, R. Parkesh, Org. Lett. 5 (2003) 4065-4068.
- [28] L. Prodi, M. Montalti, N. Zaccheroni, J.S. Bradshaw, R.M. Izatt, P.B. Savage, Tetrahedron Lett. 42 (2001) 2941-2944.
- [29] R.T. Bronson, D.J. Michaelis, R.D. Lamb, G.A. Husseini, P.B. Farnsworth, M.R. Linford,
- R.M. Izatt, J.S. Bradshaw, P.B. Savage, Org. Lett. 7 (2005) 1105-1108.
- [30] C. Lu, Z. Xu, J. Cui, R. Zhang, X. Qian, J. Org. Chem. 72 (2007) 3554-3557.
- [31] X.-L. Tang, X.-H. Peng, W. Dou, J. Mao, J.-R. Zheng, W.-W. Qin, W.-S. Liu, J. Chang, X.-J. Yao, Org. Lett. 10 (2008) 3653-3656.
- [32] M. Soibinet, V. Souchon, I. Leray, B. Valeur, J. Fluoresc. 18 (2008) 1077-1082.
- [33] G.M. Cockrell, G. Zhang, D.G. VanDerveer, R.P. Thummel, R.D. Hancock, J. Amer. Chem. Soc. 130 (2008) 1420-1430.
- [34] Y. Zhou, Y. Xiao, X. Qian, Tetrahedron Lett. 49 (2008) 3380-3384.
- [35] Y. M. Zhang, Y. Chen, Z. Q. Li, N. Li, Y. Liu, Bioorg. Med. Chem. 18 (2010) 1415-1420.
  [36] L. Xue, G. Li, Q. Liu, H. Wang, C. Liu, X. Ding, S. He, H. Jiang, Inorg. Chem. 50 (2011) 3680-3690.
- [37] G. Grynkiewicz, M. Poenie, R.Y. Tsien, J. Biol. Chem. 260 (1985) 3440-3450.

- [38] M. Shamsipur, M. Sadeghi, M.H. Beyzavi, H. Sharghi, Mater. Sci. Eng. C 48 (2015) 424-433.
- [39] B.A. Makwana, D.J. Vyas, K.D. Bhatt, V.K. Jain, Y.K. Agrawal, Spectrochim. Acta, Part A 134 (2015) 73-80.
- [40] R. Manjunath, E. Hrishikesan, P. Kannan, Spectrochim. Acta, Part A 140 (2015) 509-515.
- [41] F. Huo, J. Kang, C. Yin, J. Chao, Y. Zhang, Sens. Actuators, B 215 (2015) 93-98.
- [42] L. Dong, C. Deng, C. He, L. Shi, Y. Fu, D. Zhu, H. Cao, Q. He, J. Cheng, Sens. Actuators, B 180 (2013) 28-34.
- [43] N. Shao, Y. Zhang, S. Cheung, R. Yang, W. Chan, T. Mo, K. Li, F. Liu, Anal. Chem. 77 (2005) 7294-7303.

[44] J.R. Lakowicz, Principles of fluorescence spectroscopy, Springer Science & Business Media, 2007.

- [45] A.M. Powe, S. Das, M. Lowry, B. El-Zahab, S.O. Fakayode, M.L. Geng, G.A. Baker, L. Wang, M.E. McCarroll, G. Patonay, Anal. Chem. 82 (2010) 4865-4894.
- [46] M. Biesaga, K. Pyrzyńska, M. Trojanowicz, Talanta 51 (2000) 209-224.
- [47] M. Tanaka, Pure Appl. Chem. 55 (1983) 151-158.
- [48] X. Liu, N. Zhang, J. Zhou, T. Chang, C. Fang, D. Shangguan, Analyst 138 (2013) 901-906.
- [49] H. Xu, R. Miao, Z. Fang, X. Zhong, Anal. Chim. Acta 687 (2011) 82-88.
- [50] X. Luo, W. Wu, F. Deng, D. Chen, S. Luo, C. Au, Microchim. Acta 181 (2014) 1361-1367.
- [51] Y. Pourghaz, P. Dongare, D.W. Thompson, Y. Zhao, Chem. Commun. 47 (2011) 11014-11016.
- [52] M. Li, H. Y. Lu, R. L. Liu, J. D. Chen, C. F. Chen, J. Org. Chem. 77 (2012) 3670-3673.
- [53] Y. Lv, L. Wu, W. Shen, J. Wang, G. Xuan, X. Sun, J. Porphyrins Phthalocyanines 19 (2015) 769-774.
- [54] R. Khani, J.B. Ghasemi, F. Shemirani, Spectrochim. Acta, Part A 122 (2014) 295–303.
- [55] A. K. Wertsching, A. S. Koch, S. G. DiMagno, J. Am. Chem. Soc. 123 (2001) 3932-3939.
- [56] H. Y. Luo, J.H. Jiang, X.B. Zhang, C.Y. Li, G.L. Shen, R.Q. Yu, Talanta 72 (2007) 575– 581.
- [57] L. Li, J.Q. Tao, Acta Cryst. C 70 (2014) 1138–1142.
- [58] S. Roy, A. Bauza, A. Frontera, R. Banik, A. Purkayastha, M. G. B. Drew, B.M. Reddy, B. Sridhar, S. Kr. Dasa, Subrata Das, Cryst. Eng. Comm. 17 (2015) 3912-3916.

- [59] Z. Shariatinia, R. Shajareh Tuba, J. Sol. Energ., 137 (2015) in Press.
- [60] K. Yetilmezsoy, S. Demirel, R.J. Vanderbei, J. Hazard. Mater. 171 (2009) 551-562.

. h

#### List of figures captions:

**Fig. 1**. UV-Vis spectrum of synthesized T(4-NO<sub>2</sub>-P)P,  $[T(4-NO_2-P)P]=1 \times 10^{-4} \text{ mol } L^{-1}$  in chloroform.

Fig. 2. The molecular structure of the T(4-NO2-P)P.

**Fig. 3**. Fluorescence emission spectra of  $1.0 \times 10^{-5}$  mol L<sup>-1</sup> of the T(4-NO2-P)P at  $\lambda_{emi} = 608$  nm in the presence of  $8 \times 10^{-5}$  mol L<sup>-1</sup> solutions of various metal ions at  $25^{\circ}$ C and in ethanol. Excitation was done at  $\lambda_{exc} = 420$  nm.

Fig. 4. Fluorescence response profile changes of  $1.0 \times 10^{-5}$  mol L<sup>-1</sup> of T(4-NO2-P)P in the presence of  $8 \times 10^{-5}$  mol L<sup>-1</sup> solutions of various metal ions at  $25^{0}$ C and in ethanol, at  $\lambda_{exc} = 420$  nm.

Fig. 5. The proposed structure for the interaction of  $T(4-NO_2-P)P$  with Cd(II); Sol. = solvent molecule.

Fig. 6. Normal probability plot (NPP) for residuals.

Fig. 7. The 3D response surface plots for fluorescence intensity vs. a) concentration of the T(4-

NO<sub>2</sub>-P)P and temperature, (b) concentration of the T(4-NO<sub>2</sub>-P)P and time of reaction and (c) temperature and time of response.

**Fig. 8**. Fluorescence intensity of probe against different concentrations of  $Cd^{2+}$  in optimum conditions.





SCR SCR



















Fig. 8

Table 1           Experimental factors	s and levels	s in the c	central compo	site design.	5		
Factors	Unit	Notat	ion	Range and Levels			
			-α	-1	0	+1	+α
Conc. T(4- NO <sub>2</sub> -P)P	mol L <sup>-1</sup>	А	$4.5 \times 10^{-6}$	$8.0 \times 10^{-6}$	$1.15 \times 10^{-5}$	$1.5 \times 10^{-5}$	$1.85 \times 10^{-5}$
Temperature	K	В	288	298	308	318	328
Time	min	С	15	25	35	45	55
Conc.Zn(II)	mol L <sup>-1</sup>	D	$2.5  imes 10^{-5}$	$5.0  imes 10^{-5}$	$7.5  imes 10^{-5}$	$1.0  imes 10^{-4}$	$1.25  imes 10^{-4}$
	400						

Design	main and the re	esuits of the centra	u compos	site full factorial c	lesign.
Run	Α	B	С	D	Flu. intensity
1	$1.50 \times 10^{-5}$	318	25	$5.00  imes 10^{-5}$	118.977
2	$8.00  imes 10^{-6}$	298	25	$1.00  imes 10^{-4}$	285.082
3	$1.50  imes 10^{-5}$	318	45	$1.00  imes 10^{-4}$	113.6
4	$1.50  imes 10^{-5}$	318	45	$5.00  imes 10^{-5}$	128.227
5	$1.15 \times 10^{-5}$	308	35	$7.50  imes 10^{-5}$	171.294
6	$8.00 imes10^{-6}$	298	45	$5.00 imes10^{-5}$	414.188
7	$8.00 imes10^{-6}$	298	25	$5.00 imes10^{-5}$	442.174
8	$8.00 imes10^{-6}$	298	45	$1.00 imes10^{-4}$	292.779
9	$8.00 imes10^{-6}$	318	25	$1.00 imes10^{-4}$	408.215
10	$8.00 imes10^{-6}$	318	45	$1.00 imes10^{-4}$	420.925
11	$1.15  imes 10^{-5}$	308	35	$7.50 imes10^{-5}$	180.963
12	$8.00 imes10^{-6}$	318	45	$5.00 imes10^{-5}$	430.758
13	$1.15  imes 10^{-5}$	308	35	$7.50 imes10^{-5}$	230.978
14	$1.50  imes 10^{-5}$	298	45	$5.00 imes10^{-5}$	154.016
15	$1.50  imes 10^{-5}$	298	25	$1.00 imes10^{-4}$	110.308
16	$1.50  imes 10^{-5}$	298	25	$5.00 imes10^{-5}$	160.232
17	$8.00 imes10^{-6}$	318	25	$5.00 imes10^{-5}$	446.408
18	$1.50  imes 10^{-5}$	298	45	$1.00 imes10^{-4}$	118.992
19	$1.50  imes 10^{-5}$	318	25	$1.00 imes10^{-4}$	122.971
20	$1.15  imes 10^{-5}$	308	35	$7.50 imes10^{-5}$	206.156
21	$1.15 \times 10^{-5}$	308	15	$7.50 imes10^{-5}$	212.131
22	$1.15  imes 10^{-5}$	308	35	$2.50 imes10^{-5}$	205.16
23	$1.15  imes 10^{-5}$	308	35	$1.25  imes 10^{-4}$	190.786
24	$4.50 imes10^{-6}$	308	35	$7.50 imes10^{-5}$	561.963
25	$1.85  imes 10^{-5}$	308	35	$7.50 imes10^{-5}$	114.496
26	$1.15 imes10^{-5}$	308	35	$7.50 imes10^{-5}$	220.285
27	$1.15  imes 10^{-5}$	308	55	$7.50 imes10^{-5}$	217.414
28	$1.15  imes 10^{-5}$	288	35	$7.50\times10^{\text{-5}}$	384.688
29	$1.15  imes 10^{-5}$	328	35	$7.50\times10^{\text{-5}}$	190.079
30	$1.15  imes 10^{-5}$	308	35	$7.50\times10^{\text{-5}}$	230.409

Table	2
-------	---

Design matrix and the results of the central composite full factorial design.

Source	Sum of Squares	DF <sup>a</sup>	Mean Square	F -value	p-value	
			•		Prob > F	
Model	$4.424 \times 10^{-5}$	14	31599.13	14.50	< 0.0001	Significant
А	$3.770 \times 10^{5}$	1	$3.770 \times 10^{5}$	172.98	< 0.0001	
В	1304.02	1	1304.02	0.60	0.4521	
С	4.43	1	4.43	$2.034 \times 10^{-3}$	0.9647	
D	8469.63	1	8469.63	3.89	0.0688	
AB	6883.03	1	6883.03	3.16	0.0973	
AC	40.88	1	40.88	0.019	0.8930	
AD	3333.50	1	3333.50	1.53	0.2366	
BC	13.62	1	13.62	$6.247 \times 10^{-3}$	0.9381	
BD	5806.06	1	5806.06	2.66	0.1249	
CD	227.42	1	227.42	0.10	0.7515	
A^2	29937.37	1	29937.37	13.73	0.0023	
B^2	11331.85	1	11331.85	5.20	0.0388	
C^2	129.53	1	129.53	0.059	0.8109	
D^2	112.67	1	112.67	0.052	0.8234	
Residual	30515.13	14	2179.65			
Lack of fit	28308.04	10	2830.80	5.13	0.0645	Not significant
Pure error	2207.08	4	551.77			
Cor Total <sup>b</sup>	$4.731 \times 10^{5}$	29				

Table 3 The ANOVA results of CCD for fluorometric detection of Cd(II).

<sup>a</sup> Degree of freedom. <sup>b</sup>Totals of all information corrected for the mean.

402

 Table 4

 Determination of Cd(II) in cosmetic, and personal care samples by proposed fluorometric and FAAS methods.

<b>D</b> ool comple	Amount of $Cd(\Pi)$ (mol L <sup>-</sup> )							
Keal sample —	Fluorometric	6	FAAS					
Lipstick	$3.06 \times 10^{-6}$		$2.92  imes 10^{-6}$					
Hair Color	$1.46 imes10^{-6}$		$1.41 imes10^{-6}$					
Makeup Cream	$0.80 imes10^{-6}$		$0.73 imes10^{-6}$					

#### **Graphical Abstract**



#### Graphical Abstract Synopsis

In this study for the first time, a porphyrin ring which bounded to four deactivating  $NO_2$  groups was used as a "turn-on" fluorescence sensor. The developed sensor showed high selectivity, giving sensitive response toward cadmium metal ion and detecting micro-molar concentrations. This fluorescent probe could be used to measure the amount of cadmium ions in cosmetic and health product samples.

#### Highlights

- $\checkmark$  A new T(4-NO<sub>2</sub>P)P has been synthesized and used as a turn-on fluorescence sensor.
- ✓ Turn-on fluorescence sensor showed very high selectivity to Cd(II) ions.
- $\checkmark$  The proposed sensor was applied for the detection of Cd(II) in cosmetic samples.
- ✓ Fluorescent probe optimization was conducted by multivariate chemometrics method.

A CER MAN