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A luminescent metal-organic framework composite as a turn-on sensor for the selective determination of monosodium glutamate in instant noodles

--Manuscript Draft--

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Abstract:	This work reports the development and application of a new fluorescent nanoprobe sensor depending on using luminescent metal organic framework (LMOF). The developed sensor composed of hybridized Ca 1,3,5-benzenetricarboxylic acid metal organic framework with microcrystalline cellulose (Ca-BTC/MCC MOF) as a fluorescent probe for the determination of the monosodium glutamate (MSG), a non-chromophoric food additive. The developed sensor was characterized using a high-resolution scanning electron microscope (HR-SEM), X-ray diffraction (XRD), and Fourier transform infrared spectroscopy (FTIR). The Ca-BTC/MCC MOF hybrid, examined under the HR-SEM, showed morphological features different from the MCC and the Ca-BTC MOF. The diffraction patterns of Ca-BTC/MCC composites clearly displayed the characteristic Ca-BTC MOF diffraction bands, indicating that MCC was successfully incorporated in the formation of crystalline MOF hybrids. The FTIR spectra show the bands of MCC, as well as the bands of Ca-BTC MOFs. The prepared nanoprobe was successfully applied as a sensitive sensor for the determination of MSG in food sample. The method was validated following the International ICH (Q2)R2 guidelines in terms of precision, trueness and other main analytical figures of merit, comprised the green profile and practicability metrics. A wide linearity range was achieved (5-50 µg/mL) with good correlation coefficient (R2≥0.9993). The recoveries (%) were found in the range of 100.0 to 101.5 and the RSDs (%) were in the range of 0.1 to 0.9%. These results show that the developed nanoprobe was selective, and highly accurate to determine this important food additive in the seasonings of instant noodles, also showing a reduced environmental impact based on the metrics currently accepted for the evaluation of the green profile and practicability.

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Dear Editor,

Please find enclosed the revised manuscript "*A luminescent metal-organic framework composite as a turn-on sensor for the selective determination of monosodium glutamate in instant noodles*" submitted to the **Microchemical Journal** as a full research article

We want to thank the Reviewers for their comments and suggestions, which allowed us to improve the quality of the article.

All their suggestions and comments were accepted and reported in the revised version.

All changes are reported using "track changes" in the word document attached in this submission.

Sincerely,

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Dear Prof. Dr Wilkinson (Editor, Microchemical Journal)

Thank you for the review of our manuscript (MICROC-D-24-03363) entitled **"*A luminescent metal-organic framework composite as a turn-on sensor for the selective determination of monosodium glutamate in instant noodles*"**. We have considered the referees' comments and made the suggested changes to the best of our ability. These revisions are highlighted in the manuscript (using track changes mode) and are summarized below:

Reviewer # 1

1.   In the introduction section, MCC-MOF used as fluorescent sensor has to be mentioned for highlight the merits of prepared MCC/Ca-BTC MOF in this study. The novelty and advantage of prepared sensor should be stated more clearly.
The novelty and advantage of prepared sensor have been emphasized in the introduction section (Lines 91-95).

2.   What is the effect of MCC in this study? The author said "By integrating MCC into MOFs, the resulting materials exhibit elevated surface areas", there are no characterization of BET to show the elevated surface areas.
The effect of MCC on the Ca-BTC/MCC MOF has been discussed, and the surface area of Ca-BTC/MCC MOF has been mentioned (Lines 77-85 & 187-189).

3.   In the preparation of Ca-BTC/MCC MOF composites, the preparation condition such as the temperature and the reaction time was not the same as MOF synthesis. The reason has to be provided. Whether is essential to optimize the preparation condition of the composite?
We thank the reviewer for this comment. The temperature and reaction time for the synthesis of Ca-BTC and Ca-BTC/MCC MOF composites were the same. This has been clarified in the text. (Line 123-129)

4.   In Fig. 1 and Fig. 2, the peak should be marked in the corresponding location to make the figures more clearly to understand.
The peaks in Fig.1 and Fig.2 have been marked in the corresponding location to make the figures easier to understand

5.   In Fig. 3, there may be some mistake in the sentence of "the crystal size of the hybrid was determined to be 12.10 Ã— 2.20 mm."
The sentence has been rephrased to avoid any confusion (Line 184-186)

6.   In line 249-251 and 253-254, these sentences are duplication.
We thank the reviewer for this comment. The duplication has been removed.

7.   The fluorescence lifetime of prepared MCC-MOF has to be evaluated
We thank you the reviewer for his valuable feedback and suggestion. However, we would like to clarify that our primary objective was to utilize the MCC-MOF for the measurement of MSG concentration rather than monitoring the fluorescence change of the MCC-MOF. The fluorescence lifetime, while an important parameter in certain contexts, does not directly impact the results or conclusions of our study.

Our focus has been on the concentration measurement capabilities of the MCC-MOF, which we have thoroughly validated through our experiments. Unfortunately, we currently do not have access to the instrumentation required for fluorescence lifetime measurements. Nevertheless, we believe that the absence of this data does not compromise the validity or integrity of our findings, as our methods and results have been robustly demonstrated through alternative means.

8.   The standard curve for quantification of MSG has to be added in supporting information.
The standard curve for quantification of MSG has been added in the supporting information (**Figure S2**)

9.   The method comparison has to be added and shown in Table.
Table 3 has been added to compare the proposed method with recent reported methods for MSG determination.

10.   Some figures are not clear, especially in supporting information.
The resolution of the figures in the supplementary materials has been improved. Specifically, the figures relating to the AGREEprep and BAGI scores, being obtained directly from the pdf report (screenshot), have been enlarged and made clearer as suggested by the Reviewer.

11.   The pretreat method of food sample is missing.
The pretreat method of food sample has been indicated (Line 273-276).

Reviewer # 2

This paper describes a sensor composed of hybridized Ca 1,3,5-benzenetricarboxylic acid metal organic framework with Ca-BTC/MCC MOF as a fluorescent probe for the determination of the monosodium glutamate. This is an interesting study, and the authors tried to adopt several techniques to prove the conclusion, but they missed some key information. Therefore, I may doubt the reliability of the conclusions. After a review of the manuscript, I recommend a major modification. I have some questions and specific comments about the paper:
We thank the reviewer for this comment.

1.   I suggest that in the Introduction, the authors should focus more on the challenges of fluorescent MOF and the more excellent fluorescence performance demonstrated by functional nanomaterials (MCC) in modifying MOF.
We thank the reviewer for this comment. The challenges of fluorescent MOF and the merits demonstrated by functional nanomaterials (MCC) in modifying MOF have been elaborated on (Lines 77-85)

2.   In the Introduction, it is recommended to change "MCC/Ca-BTC MOF" to "Ca-BTC/MCC MOF" to maintain consistency in the text.
We agree with the reviewer. The abbreviation "Ca-BTC/MCC MOF: has been used consistently throughout the manuscript (Line 87,89,123,132,150,210 and 211)

3.   Is the synthesis of the Ca-BTC-MCC method new? If so, what are the advantages of the method? If not, please cite refs. What is "1N NaOH solution".
The protocol followed during the synthesis of Ca-BTC/MCC MOF has been cited (Line 129). 1N NaOH has been replaced with 1 M NaOH to avoid confusion (Line 125)

4.   For the XRD, it is suggested to mark the characteristic peaks to help readers identify the structural features of the material.
We thank the reviewer for this comment. The characteristic peaks have been marked in the XRD figure.

5.   I suggest the author add data on the stability and reproducibility of the method?

The stability and reproducibility of the method have been studied (Line 191-195 & 261-268)

6.   Please provide the key parameters of the fluorescent materials, such as the fluorescence yield, etc.
The key parameters of the fluorescent materials including excitation wavelength, emission wavelength, and quantum yield have been provided (Lines 234-235)

7.   The author claimed "MSG is commonly used as a flavor enhancer in a variety of foods and medications". Why did no actual sample detect the target? Is there a problem with the sample selection? Or is the method not sensitive enough?
The method has been applied to a real sample of instant noodles seasoning (Line 274). The method was sufficiently sensitive to measure MSG in the seasoning sachet as shown in Table 2.

We hope the changes that have been made were appropriate and the manuscript can now be accepted for publication. Please address all correspondence to the author indicated below.
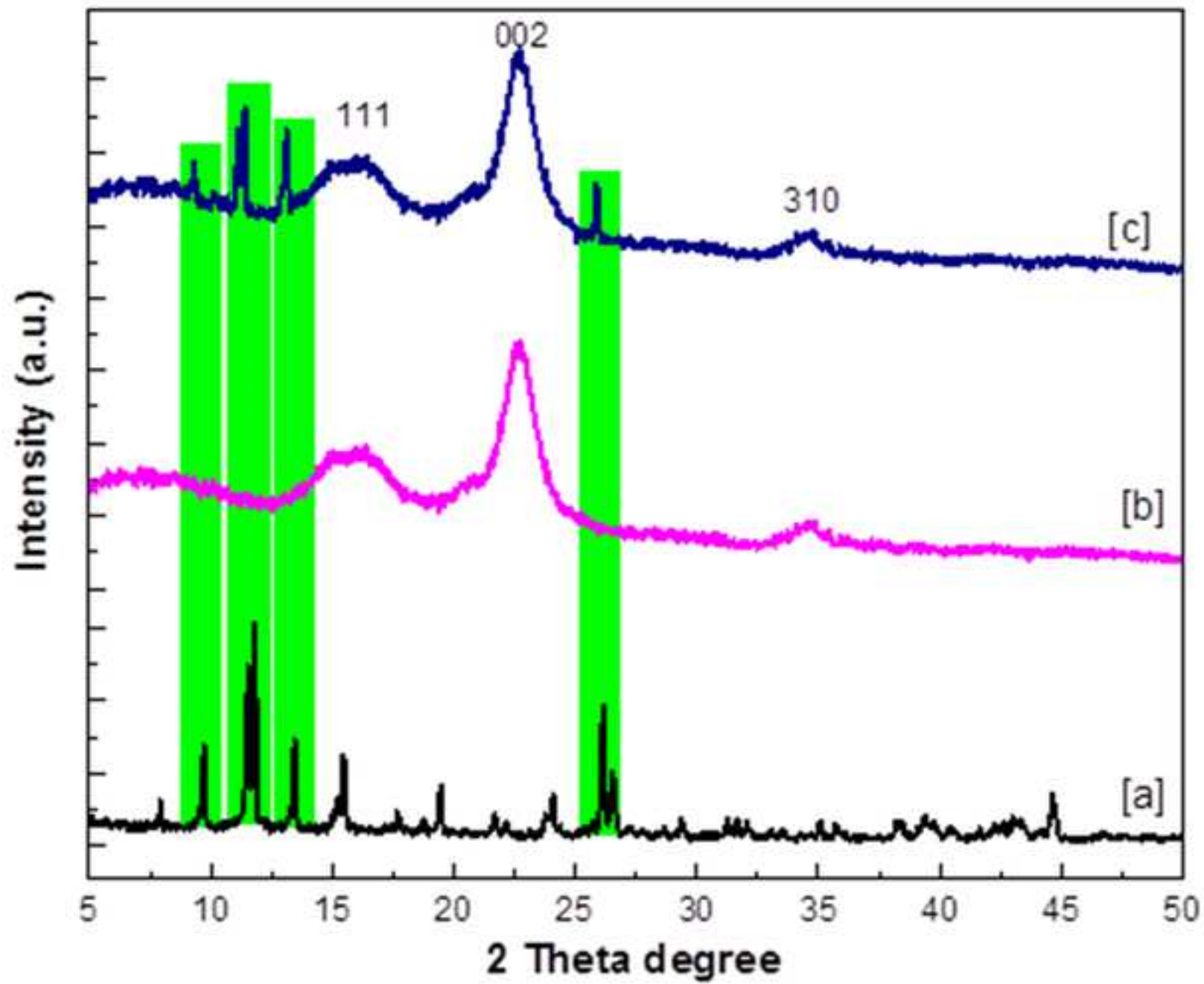Best regards,

Sincerely,
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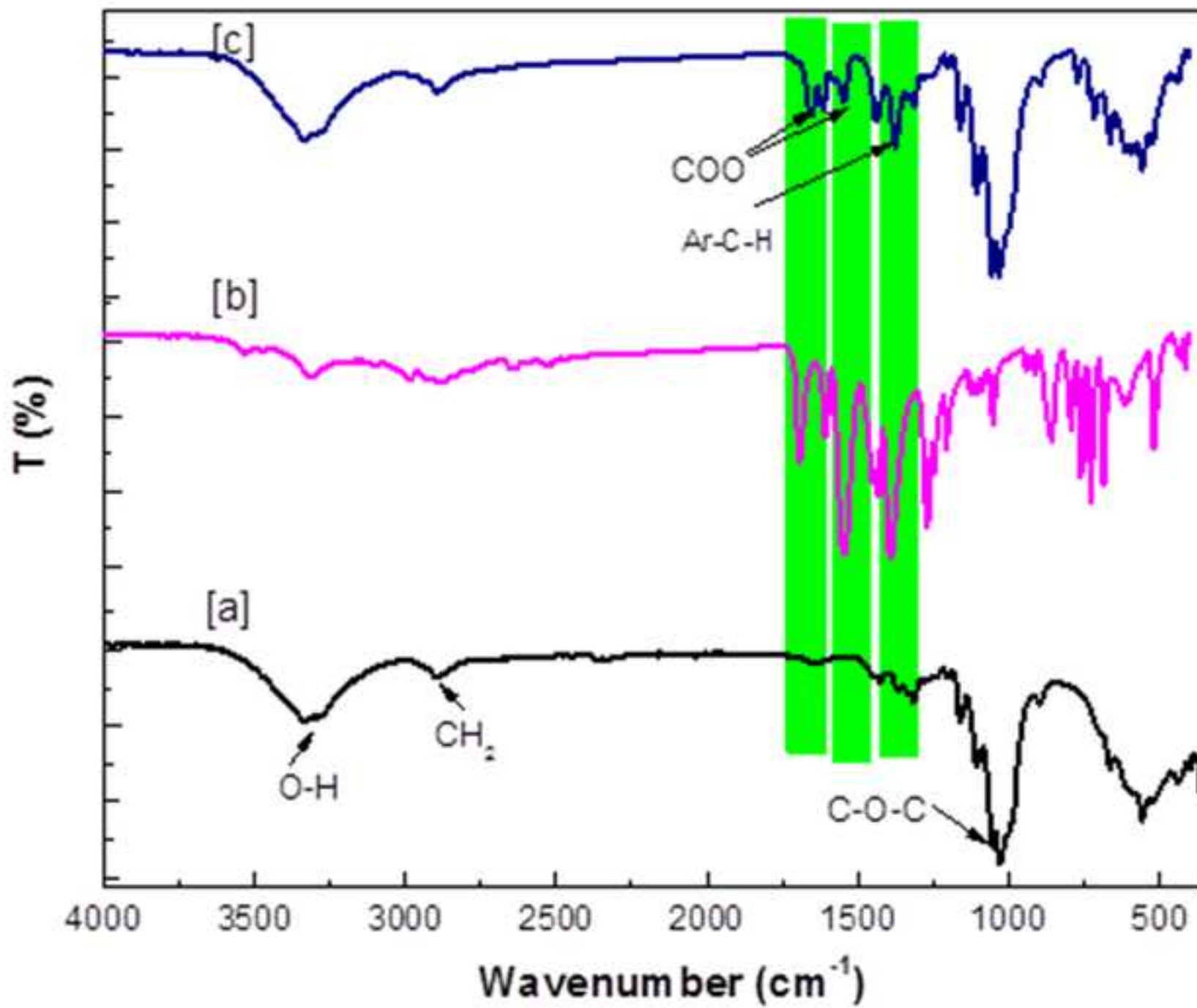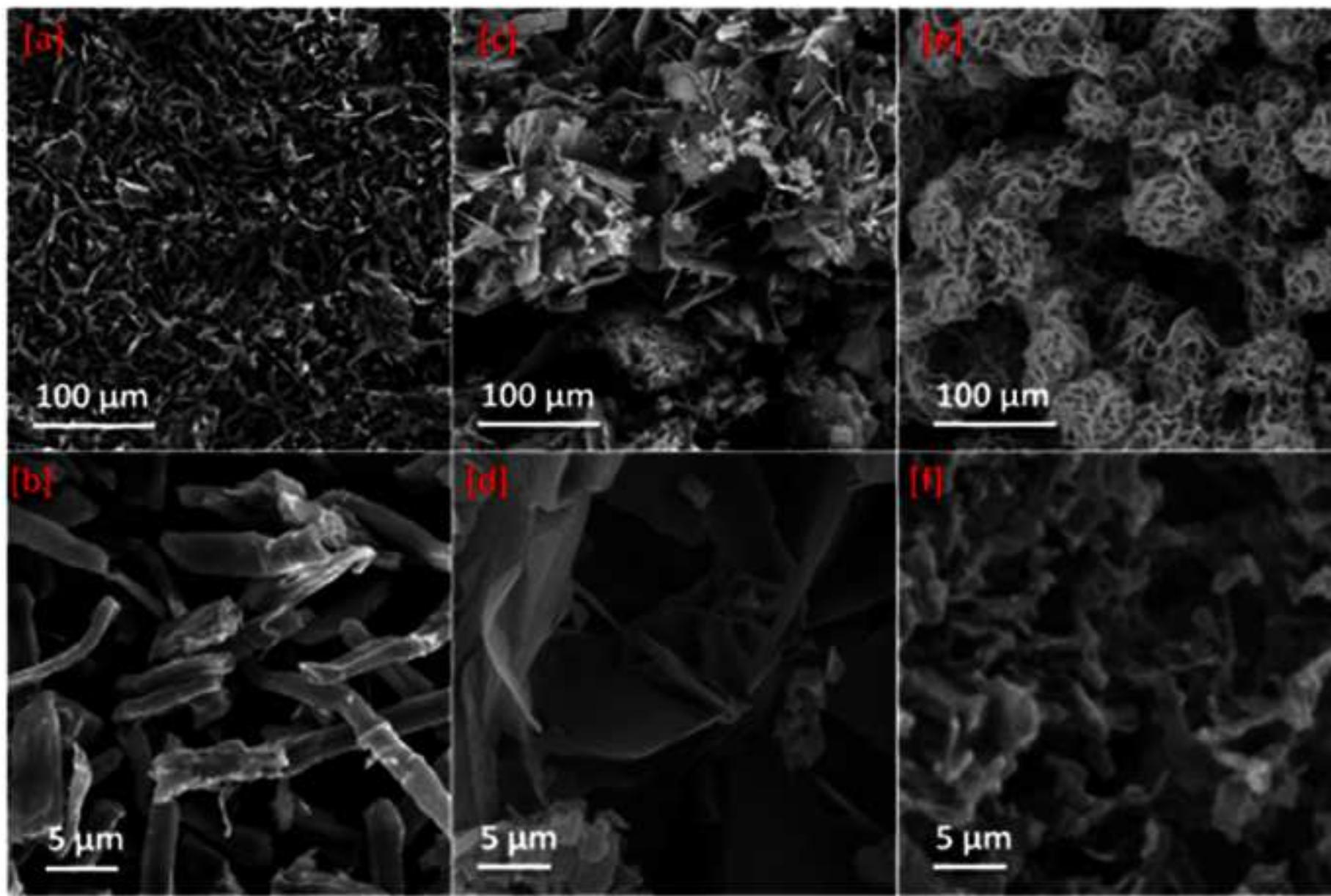

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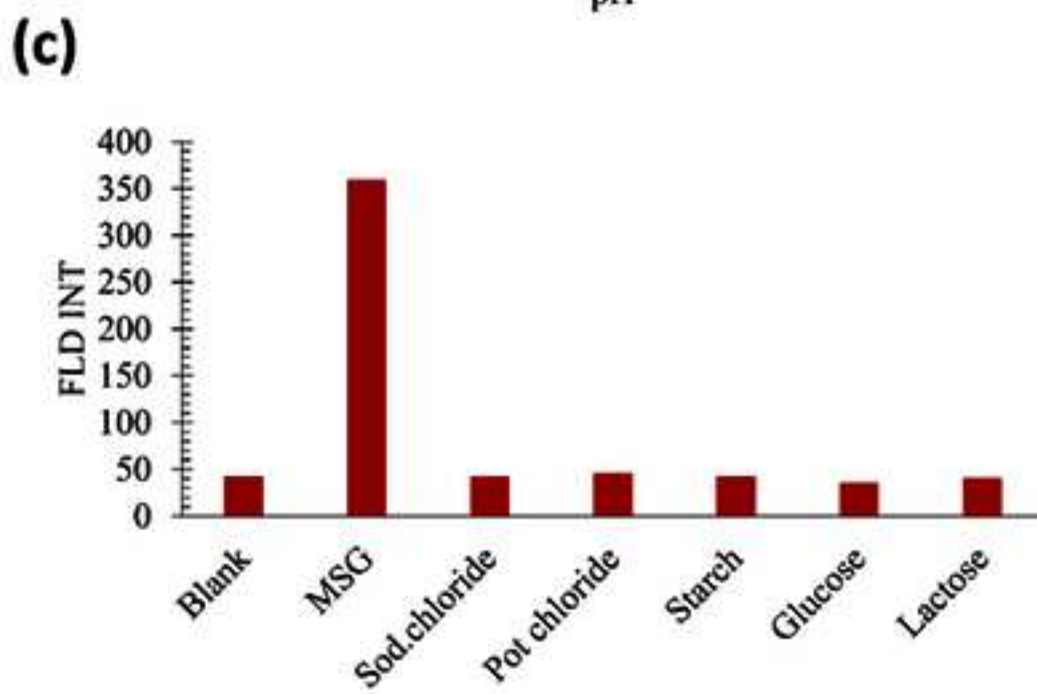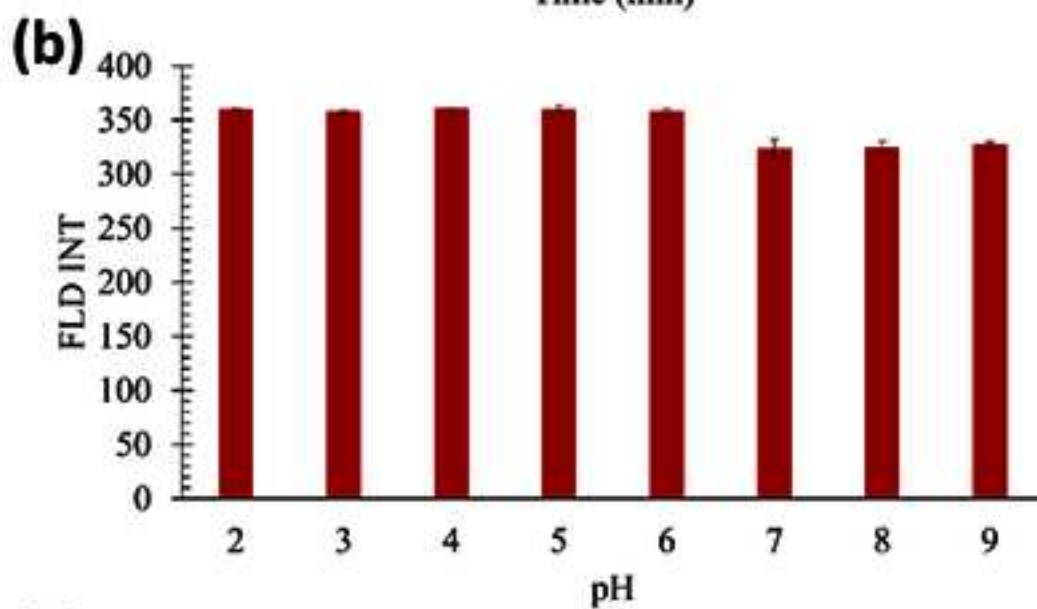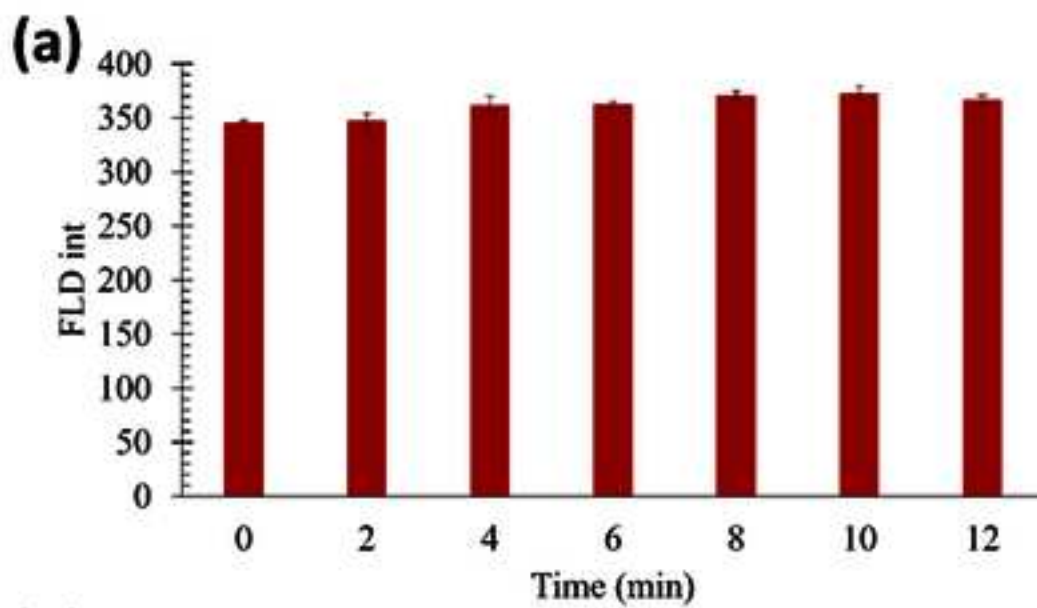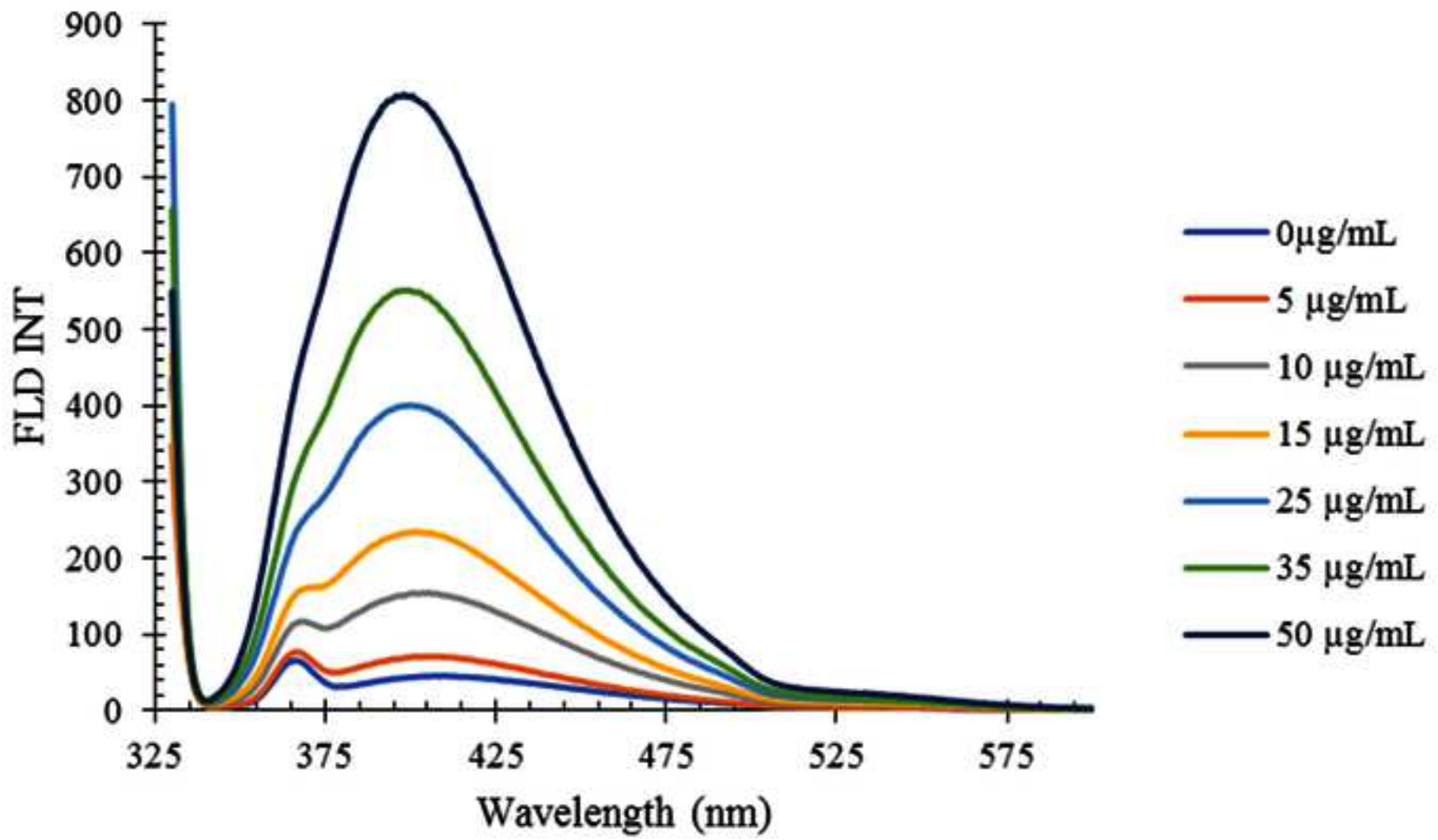
Highlights

- Fluorescent nanoprobe sensor depending on using luminescent metal organic framework (LMOF).
- Fluorescent probe for a non-chromophoric food additive monosodium glutamate(MSG)
- The nanoprobe was applied to determine this food additive in the instant noodles
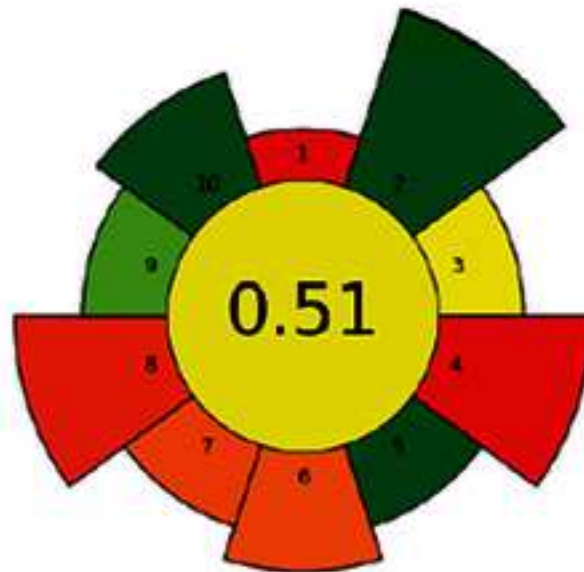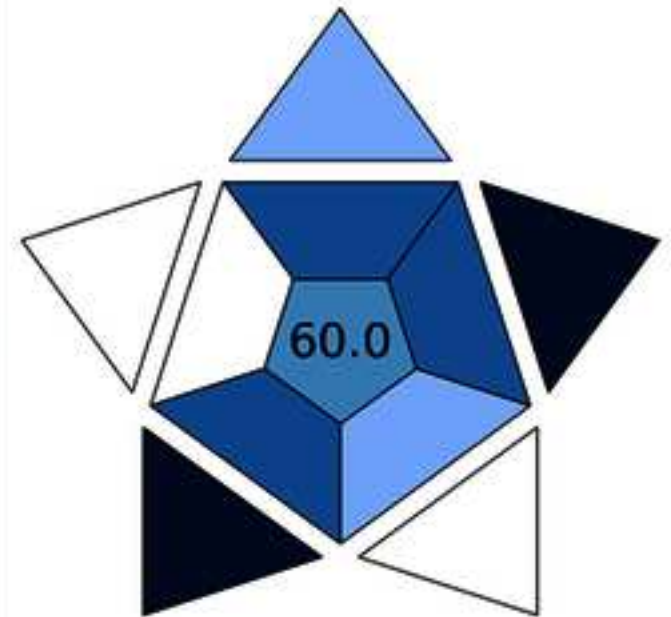- AGREE, AGREEprep, and BAGI metrics were evaluated for the method

Figure 1

Figure 2

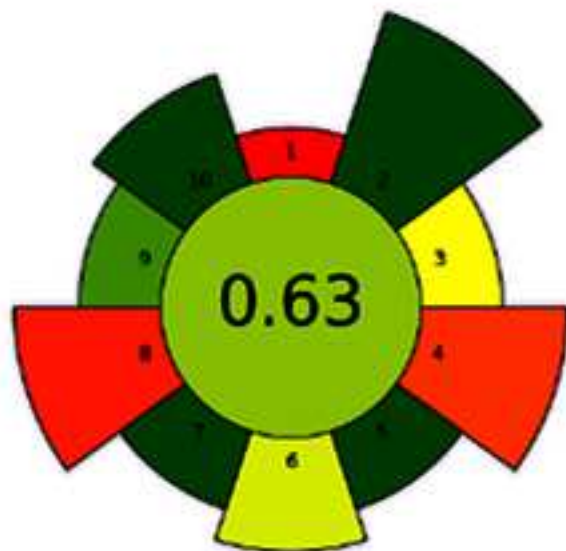Figure 3

Click here to access/download;Figure;Figure 3 MSG MOF.tif ⬇

Figure 4

Figure 5

Figure 6

Click here to access/download;Figure;Figure 6 MSG MOF.tif

AGREE

AGREEprep

BAGI

Figure 7

AGREE — 0.73

AGREEprep — 0.63

BAGI — 70.0

Declaration of interests

The authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

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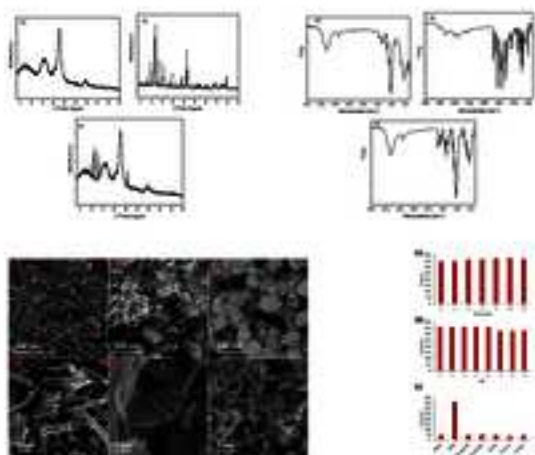
Investigation: Reda M. Abdelhameed, Alaa Bedair,;

Methodology: Reda M. Abdelhameed, Sherin F. Hammad, Inas A. Abdallah, Marcello Locatelli, Fotouh R. Mansour;

Project administration: Sherin F. Hammad, Inas A. Abdallah, Fotouh R. Mansour;
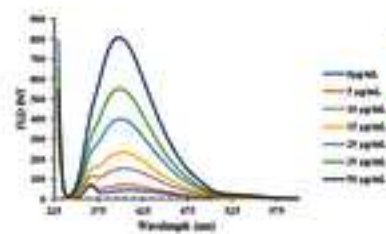
Supervision: Sherin F. Hammad, Inas A. Abdallah, Fotouh R. Mansour;

Roles/Writing – original draft: Reda M. Abdelhameed, Alaa Bedair, Marcello Locatelli, Fotouh R. Mansour.

A luminescent metal-organic framework composite as a turn-on sensor for the selective determination of monosodium glutamate in instant noodles

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Abstract

This work reports the development and application of a new fluorescent nanoprobe sensor depending on using luminescent metal organic framework (LMOF). The developed sensor composed of hybridized Ca 1,3,5-benzenetricarboxylic acid metal organic framework with microcrystalline cellulose (Ca-BTC/MCC MOF) as a fluorescent probe for the determination of the monosodium glutamate (MSG), a non-chromophoric food additive. The developed sensor was characterized using a high-resolution scanning electron microscope (HR-SEM), X-ray diffraction (XRD), and Fourier transform infrared spectroscopy (FTIR). The Ca-BTC/MCC MOF hybrid, examined under the HR-SEM, showed morphological features different from the MCC and the Ca-BTC MOF. The diffraction patterns of Ca-BTC/MCC composites clearly displayed the characteristic Ca-BTC MOF diffraction bands, indicating that MCC was successfully incorporated in the formation of crystalline MOF hybrids. The FTIR spectra show the bands of MCC, as well as the bands of Ca-BTC MOFs. The prepared nanoprobe was successfully applied as a sensitive sensor for the determination of MSG in food sample. The method was validated following the International ICH (Q2)R2 guidelines in terms of precision, trueness and other main analytical figures of merit, comprised the green profile and practicability metrics. A wide linearity range was achieved (5-50 µg/mL) with good correlation coefficient ($R^2 \geq 0.9993$). The recoveries (%) were found in the range of 100.0 to 101.5 and the RSDs (%) were in the range of 0.1 to 0.9%.

These results show that the developed nanoprobe was selective, and highly accurate to determine this important food additive in the seasonings of instant noodles, also showing a reduced environmental impact based on the metrics currently accepted for the evaluation of the green profile and practicability.

1. Introduction

Monosodium glutamate (MSG, E621) is a common food additive with a distinct Umami flavor [1,2]. This widely used additive is the sodium salt of glutamate, a non-essential amino acid with the chemical name 2-aminopentanedioic acid [3,4]. MSG is commonly used as a flavor enhancer in a variety of foods and medications [5]. The reasonable consumption of MSG was assessed by the Food and Drug Administration (FDA) to be roughly 0.55 g/day, with a maximum limit of 1.0 g/day [6]. This threshold is related to the fact that glutamate is an effective excitatory neurotransmitter in the human brain. Excessive MSG consumption could causes neurological illnesses such as Parkinson's and Alzheimer's diseases [7]. Glutamate may accumulate and become harmful if the glutamate receptor inactivation is not balanced by glutamate absorption in the synaptic cleft [8]. Accordingly, memory, learning, and regulatory processes are all affected by excessive MSG intake. According to the Federation of American Societies for Experimental Biology (FASEB), high-dose MSG exposure can cause a transient MSG disorder known as Chinese restaurant syndrome [9], manifested as flushing, headache, numbness in the mouth, and other symptoms such as burning sensations, facial pressure, and chest pains [6]. Furthermore, high MSG consumption is linked to diabetes and obesity. For these reasons, routine determination of MSG in food stuff is critical [10].

Several methods for the determination of MSG have been developed, including UV/Visible spectrophotometry [7,11–15], spectrofluorimetry [16–18], paper and thin layer chromatography [19], High Performance Liquid Chromatography (HPLC) combined with different detectors [20–22], electrochemistry [9,23,24] and capillary electrophoresis [25]. The spectroscopic determination of MSG is challenging because it is a non-aromatic amino acid with no extended conjugation or strong chromophoric groups, which hinders its direct detection by spectrophotometric or spectrofluorometric methods. Alternatively, MSG is commonly determined by employing selective enzymatic processes, chemical derivatization of the aliphatic amino group, or inserting the amino acid into a complex formation reaction that results in the synthesis of colored or luminous compounds. However, these procedures need the use of costly chemicals, extensive reaction times, heating, or catalysis, making MSG determination hard, time-consuming and expensive [26].

Metal-organic frameworks (MOFs) are a novel class of sensing materials that have emerged in the porous materials regime [27–29]. Built from sensitive organic ligands and a wide range of

58 metal ion/clusters, these materials outperform their contemporaries due to their large surface area,

59 structural tunability of the pore metrics, functional nano-spaces [30]. MOFs have received a lot of

60 attention in the scientific community as fluorometric sensors for detecting a lot of analytes [31].

61   Luminescent MOF (LMOFs) have so gained interest due to their improved guest identification

62 capabilities and subsequent analyte specific optical response. The sensing mechanism may be

63 divided into two categories based on the electrical nature of the analyte and/or MOFs: *a)* "turn-

64 off" and *b)* "turn-on" sensing. In general, a turn-on response may be elicited by constraining non-

65 radiative relaxations in MOFs via *a)* integration of stiff functional groups, *b)* or exciplex/excimer

66 production with incoming guest molecules, and so on. Thus, contemporary research efforts are

67 directed towards the creation of appropriate sensors capable of eliciting a turn-on response based

68 on LMOFs. Aromatic conjugated organic linkers have been discovered to be particularly important

69 for the emission property of LMOFs in the majority of situations. Light is absorbed by π-rich

70 conjugated linkers, and the subsequent radiative transition of this energy results in the

71 luminescence characteristic of LMOFs. Apart from ligand-based luminescence, charge transfer

72 mechanisms involving aromatic organic linkers (inter-ligand charge transfer (ILCT), metal-ligand

73 charge transfer (MLCT), ligand-metal charge transfer (LMCT), etc.) have also been reported. Such

74 ligand-based luminescence in LMOFs has demonstrated enormous potential for the fabrication of

75 sensory materials [32].

76   Microcrystalline cellulose (MCC) modified MOFs offer several advantages over their

77 traditional inorganic counterparts. The incorporation of MCC into MOFs results in a material with

78 high surface area, providing an increased number of active sites available for interaction. As a

79 result, MCC-MOFs have demonstrated enhanced efficiency in various extraction applications [33].

80 Furthermore, the use of MCC as a raw material is advantageous due to its renewable and

81 sustainable nature, being derived from plant-based sources. Additionally, the cost-effectiveness of

82 MCC as compared to other materials commonly used in MOFs adds to its appeal for large-scale

83 production. Finally, MCC's biodegradability makes it more environmentally friendly than

84 traditional MOFs which often contain non-biodegradable components.

85   In this work, Ca-BTC/MCC MOF hybrid was prepared and applied for the selective detection

86 of MSG in instant noodles seasonings. To the best of our knowledge, this work is the report of

87 using Ca-BTC/MCC MOF as a fluorescent sensor. Compared with the other reported methods of

88 MSG determination, this spectrofluorometric method is rapid, reliable, selective and

environmentally friendly which make it suitable for the routine analysis of MSG in food and food derived products. To the best of our knowledge, this work reports for the first time the application of Ca-BTC/MCC MOF composite as a sensitive sensor for spectrofluorometric detection. Compared with Ca-BTC MOF, the composite has higher surface area which offers higher sensitivity for the determination of MSG. Moreover, the prepared composite is biodegradable, stable, eco-friendly, and efficient nanoprobe.

2. Experimental

2.1. Instrumentation

All fluorescence spectra measurements were recorded using a Jasco model FP-8300 spectrofluorometer (Tokyo, Japan) equipped with a 1-cm quartz cuvette, both excitation and emission bandwidths were set at 10 nm. The excitation wavelength was set at 325 nm while the emission wavelength was set at 422 nm**.** The software of Spectra Manager (Jasco Co., Tokyo, Japan) was used for spectral data processing and acquisition. Jenway® 3510 pH-meter (Staffordshire,UK) was also employed for phase pH adjustment. BET measurements were carried out using Autosorb-01 (Quantachrome TouchWin™). To analyze the morphological characteristics of MOFs, SEM images were collected using an HRSEM Quanta FEG 250 with field emission gun. To characterize the crystallinity and phase purity of the produced MOFs, a Malvern Panalytical X'PertPRO PANalytical diffractometer (K X-ray at 45 kV, 40 mA, = 1.5406) was utilised. A JASCO FT/IR 6100 spectrometer was used to analyze the Fourier transforms infrared spectra of MOFs.

2.2. Materials

Monosodium glutamate (99%) was kindly supplied from by Sigma Pharmaceutical Industries (Quesna, El-Menoufia, Egypt). Methanol, ethanol and acetonitrile, $CaCl_2$, 1,3,5-benzenetricarboxylic acid (BTC), sodium hydroxide, and microcrystalline cellulose were purchased from Merck (Darmstadt, Germany).

2.3. Synthesis of Ca-BTC/MCC MOF

Ca-BTC was prepared, as reported [28] by using the following conditions: 1,3,5-benzenetricarboxylic acid (0.42 g) was dissolved in 100 mL of 1 M NaOH solution. In parallel,

CaCl$_2$ (0.316 g) was dissolved in 10 mL of purified water. At 25°C, the two solutions were combined and agitated for 20 min. The reaction mixture was maintained at 90 °C for 24 hrs in the oven. Following this time, Ca-BTC was collected, washed with 99.9% ethanol, and then passed through a Whatmann filter paper.

Ca-BTC/MCC MOF composites was prepared under the same conditions in the synthesis of Ca-BTC MOF as follows [28]: MCC (0.5 g) and of 1,3,5-benzenetricarboxylic acid (0.42 g) were dissolved in 100 mL of 1 M NaOH solution and water soluble CaCl$_2$ (0.316 g) was added dropwise to the mixture of MCC/BTC at 25°C while shaken the solution for 20 minutes. Then, the mixture was added in dry oven at 90 °C for 24 hrs. The white solids were formed in the bottom of the vessel. Following a centrifugation of the mixture, two ethanol washes, and a 12-hour vacuum drying process at 60°C, the composites were obtained and stored until used.

2.4. Procedures for determination of MSG.

An amount of 5 mg/mL of Ca-BTC-MCC stock were prepared by addition of 500 mg of Ca-BTC/MCC composite in 100 volumetric flask, the volume was completed to 100 mL by deionized water. The system was sonicated for 30 min to enhance dispersion of the composite. Finally, the dispersion system was filtrated by 0.22 µm syringe filter. For MSG detection, 125 µL of Ca-BTC-MCC system was added to 25 mL of MSG aqueous solution and the mixture was measured immediately at 422 nm after excitation at the wavelength of 325 nm.

2.5. Measurement of quantum yield

The QY of the Ca-BTC/MCC MOF was detected using the single-point method (Eq.1):

$$QY = QY_{QS} \times (F_{Ca\text{-}BTC/MCC} / F_{QS}) \times (A_{QS}/ A_{Ca\text{-}BTC/MCC}) \times (\eta_{Ca\text{-}BTC/MCC} /\eta_{QS})^2$$

Where F is the integrated fluorescence intensity, A is the absorbance and η is the refractive index of the solvent. Quinine sulfate (QS) was used as the standard. QS was dissolved in 0.1 M sulfuric acid .The absorbance value was set at 0.05 to standardize the absorbance impact. In an aqueous solution, the $\eta CQD/ \eta QS = 1$.

2.6. Method validation

The proposed method was validated according to International Guidelines ICH Q2(R2) [36] in terms of selectivity, linearity, limit of quantitation, and accuracy (trueness and precision).

3. Results and discussion

3.1. Characterization of Ca-BTC/MCC MOF

The structures of Ca-BTC and MCC experienced alterations during the synthesis of the Ca-BTC/MCC MOF composite sorbent, and these changes in chemical bonds and interactions were studied by FTIR. **Figure 1a** displays MCC's FTIR spectrum. The band at 1024 cm^{-1} was assigned to C-O, whereas the CH$_2$-CH group emerged at 2900 cm^{-1}, and the O-H group appeared at 3347 cm^{-1}. The O-H expansion over hydrogen bonding with water and CaO was illustrated by the peaks at 3306 cm^{-1}, 1149 cm^{-1}, and 1021 cm^{-1}, respectively, as shown in the Ca-BTC FT-IR spectrum (**Figure 1b**). At 1632.01 cm^{-1}, one may observe the isotope of the bending mode of unbound water. The region of 1700 to 1300 cm^{-1} is where asymmetric and symmetric O-C-O stretching of the carboxyl groups occur. Asymmetric O-C-O stretching is linked to the peaks at 1574.50 cm^{-1}, 1556 cm^{-1}, and 1510 cm^{-1}, whereas symmetric O-C-O stretching is responsible for the peaks at 1435.50 cm^{-1} and 1392 cm^{-1}. The FTIR spectrum interaction between Ca-BTC and MCC is presented in **Figure 1c**. These results indicated that the composite showed distinct Ca-BTC uptake bands in addition to the MCC uptake bands.

Figure 1. Infrared spectra of [a] the MCC polymer, [b] the Ca-BTC MOF, and [c] the Ca-BTC/MCC hybrid

The crystallinity of the prepared hybrid was studied and compared with MCC and Ca-BTC MOF using PXRD. **Figure 2a** reports the diffraction pattern of MCC. The MCC crystal structures showed the large peaks at 12.10°, 20.10°, 22.30°, and 34.60°, which were characteristic for cellulose II crystals. The Ca-BTC diffraction pattern is seen in **Figure 2b**. The PXRD peaks have the following unit cell parameters: a = 10.94, b = 6.73, c = 18.58, and α = β = γ = 90.00° (orthorhombic). Space group Pnm a 63 has been used to index the PXRD peaks. The Ca-BTC/MCC diffraction patterns are shown in **Figure 2c**. The compounds exhibited distinct Ca-BTC diffraction bands, suggesting that MCC has been effectively integrated into the crystalline Ca-BTC production process.

Figure 2. X-ray diffraction pattern of the MCC polymer, [b] the Ca-BTC MOF, and [c] the Ca-BTC/MCC MOF hybrid

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For the sake of comparison, the morphology of MCC was examined. As seen in the SEM pictures in **Figures 3a** and **3b**, the 3D lattice structure with uniformly dispersed particles and massive particle agglomerations was clearly visible. The FE-SEM images displayed in **Figures 3c** and **3d** depicted the typical crystal structure of Ca-BTC. Using an electron microscope, the morphological properties of the Ca-BTC/MCC MOF were investigated and the findings displayed in **Figures 3e** and **3f**. Measured under a microscope, the crystal size of the hybrid material was two-dimensional, with one side measuring 2.20 μm and the other side measuring 12.10 μm. The fact that the composite shape's characteristics were entirely distinct from those of MCC and Ca-BTC indicates that both compounds were successfully encapsulated. The measured BET surface areas from N_2 adsorption-desorption for MCC, Ca-BTC, and Ca-BTC/MCC were 10.60, 560.00, and 820.00 $m^2\,g^{-1}$, respectively. Figure S1 shows an overlay of the excitation and emission spectra of Ca-BTC/MCC MOF. The stability the MOF composite was assessed on short- and long-term basis. The Ca-BTC/MCC MOF was found stable in benchtop study over 24 hours, and the in the fridge at -4°C for seven days. The prepared Ca-BTC/MCC MOF was stored in solid form at room temperature, and its fluorescence intensity remained stable with no significant changes observed over a period of 6 months.

Figure 3. SEM images of [a,b] the MCC polymer, [c,d] the Ca-BTC MOF, and [e,f] the Ca-BTC/MCC MOF hybrid

3.2. Method optimization

Studying the different experimental variables that may affect the method performance is crucial. The one-variable-at-a-time (OVAT) approach was used in the optimization process. Different factors were investigated, including excitation wavelength, disperser solvent of MOF, incubation time, and pH of the aqueous sample. Fluorescence intensity was monitored at each condition to reach the maximum sensitivity.

3.2.1. Excitation wavelength optimization

Changing the excitation wavelength can greatly influence the emission intensity in fluorescence spectroscopy. The impact of excitation wavelength on the intensity of Ca-BTC/MCC MOF was

213   examined across the range 225-350. As reported in *Supplementary materials section S.1*, the
214   highest emission was observed at 422 nm with an excitation wavelength of 325 nm. This specific
215   excitation wavelength was utilized in subsequent steps to determine the concentration of MSG in
216   both aqueous solutions and instant noodles seasonings.

217

218   **3.2.2. Effect of disperser solvent of MOF**
219   Different solvents were used for dispersion of Ca-BTC/MCC MOF composite including
220   methanol, ethanol, acetonitrile and deionized water. A concentration of 5 mg/mL of Ca-BTC/MCC
221   MOF composite was prepared in different solvents, and then the dispersion system was sonicated
222   for 30 min followed by filtration using a syringe filter (0.22 µm). Only water achieved fluorescence
223   intensity while the other organic solvents achieved negligible fluorescence intensity. It could be
224   attributed to the low tendency of organic solvents to achieve a good dispersion MOF hybrid.

225

226   **3.2.3. Effect of incubation time**
227   Different incubation times were investigated in the range from 0 to 12 min as indicated in
228   **Figure 4a**. There was no significant change in FLD intensity over time. This is because the
229   interaction between MSG and the Ca-BTC/MCC MOF hybrid is instantaneous, which allows for
230   the rapid measurement of MSG and makes the developed method time-saving besides being less-
231   laborious than other derivatization-based methods.

232

233   **3.2.4. Effect of pH on MOF emission**
234   Different pH values were investigated over the range 2 to 9. As indicated in **Figure 4b**, there
235   was no significant change with pH variations over the studied range. This could be explained by
236   the high stability of Ca-BTC/MCC MOF and the negligible effect of pH on the predominately
237   charged amine group in MSG at pH values ≤9. Accordingly, deionized water was used as diluent
238   throughout the following procedure. The calculated quantum yield of Ca-BTC/MCC MOF was
239   found to be 3.8% at an excitation wavelength of 325 nm, and an emission wavelength of 422 nm.

240

241   **Figure 4.** The effect of incubation time (a), pH (b) and interferences (c) on the fluorescence
242   intensity using water as a disperser solvent, 125 µL of Ca-BTC/MCC , 25 mL of MSG aqueous
243   solution.

244

3.3. Method validation

3.3.1. Selectivity

Selectivity of analytical methods is a key parameter during method development. The method is deemed selective if there is no interference from interfering substances, according to ICH guidelines. The reaction was examined in the presence of chemicals that may be present as a contemporaneous component with MSG in food preparations to determine the method's selectivity such as glucose, lactose, sodium chloride, potassium chloride, and starch. No significant changes were observed in the fluorescence intensity, using saturated solutions of theses food ingredients, which indicated the adequate method selectivity for MSG, as shown in **Figure 4c**.

3.3.2. Linearity, range and limit of quantitation.

To investigate the linearity of the method, a calibration curve was constructed by plotting the FLD intensity on the y-axis and the concentration of MSG (in µg/mL) on the x-axis. The calibration curve indicated that the technique exhibited linearity within the 5-50 µg/mL MSG concentration range (**Figure 5**). The calculated coefficient of determination (r^2) was 0.9993. The limit of quantitation was found to be 5 µg/mL, demonstrating the high applicability of the proposed method in food analysis. The constructed calibration curve is shown in Figure S2.

Figure 5. Overlaid spectra of different concentrations of MSG over the studied linearity range.

3.3.3. Accuracy (precision and trueness)

The accuracy of the method was evaluated by analyzing three quality control samples spiked with MSG at three different concentrations (8, 30, and 45 µg/mL). MSG concentrations were analyzed in triplicate. **Table 1** shows that the procedure trueness (given in terms of recovery %) was adequate for the application of the proposed method on food sample. The recoveries (%) were found in the range of 100.0 to 101.5 and the %RSDs were in the range of 0.1 to 0.9%. Accordingly, the developed nanoprobe spectrofluorimetric analytical method is accurate according to ICH (Q2)R2 guidelines.

Table 1. Intra-day and inter-day precision and trueness

4. Application on food sample

The developed nanoprobe spectrofluorometric method was utilized for the determination of MSG from a single packet of instant noodles containing a sachet of seasoning powder. Since the application was performed on seasoning powder, no extensive sample preparation was required. 100 mg of the powder was diluted to 100 mL, and then the mixture was sonicated for 20 min. Subsequently, the solution was filtered through a 0.22 μm syringe filter. A 1000 μL aliquot from the previous system was further diluted to 25 mL, and 125 μL of Ca-BTC/MCC MOF was added to this solution. These procedures resulted in a concentration of 20.15 μg/mL.

Standard addition was employed to assess the matrix effect; specifically, 5 μg/mL of MSG was added to the previous system, and six replicates were performed. As shown in **Table 2**, the percent recovery fell within the range of 98.1% to 101.5%, with a percent relative standard deviation (RSD%) of 1.4%. These results indicated that the developed method can been successfully applied for the determination of MSG in food samples. **Table 3** compares between the developed method and other recent methods for MSG determination in different food matrices.

Table 2. Application of the developed method for determination of MSG in food sample using standard addition method.

Tablet 3. Comparison between the developed method and other reported methods for MSG determination in different food matrices

5. Green Profile evaluation

The developed nanoprobe spectrofluorometric method was further evaluated in terms of green profile by means of the recent accepted tools [42] like AGREE (Analytical GREEnness Metric Approach) [43], AGREEprep (Analytical greenness metric for sample preparation) [44], and BAGI (Blue applicability grade index) [45].

Figure 6. Pictograms related to AGREE, AGREEprep, and BAGI evaluation of the proposed procedure.

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As highlighted in **Figure 6**, based on the metrics currently accepted for the evaluation of the green profile, the method reported here certainly shows a reduced environmental impact both on the basis of the AGREE (criteria 2, 4, 6, 9, 11 and 12), and based on AGREEprep (criteria 2, 5, 9 and 10). Based on the score obtained from BAGI, can be stated that the method can be considered "practical" (score of 60). The specific inputs used are reported in *Supplementary materials section S3*.

Certainly, the procedure could be improved compared to the procedure reported here with a view to obtaining an even greener profile and a higher BAGI score. In particular, if the procedure is improved by using a sample preparator (automated) which also increases the number of samples that can be processed (approx. 10 samples/h) and by reducing the quantity of sample (10 mg) and proportionally the quantity of waste (12.5 mL) can see in **Figure 7** how the green and BAGI profiles improves significantly. The specific inputs used are reported in *Supplementary materials section S.4*.

Figure 7. Pictograms related to AGREE, AGREEprep, and BAGI re-evaluation of the proposed procedure following some improvements.

6. Conclusions

A novel turn-on spectrofluorometric method has been developed for the determination of MSG in food samples with acceptable accuracy and precision. MOFs, composed of metal ions/clusters and organic ligands, offer versatile applications due to their inherent crystallinity, distinct structure, adjustable porosity, and diverse functionalization. The structural and chemical adaptability of MOFs allows for high selectivity through pore-sieving mechanisms, making LMOFs a notable choice as sensing materials in recent times. By leveraging their high internal surface areas, MOFs can concentrate analytes effectively, leading to lower detection limits and enhanced sensitivity.

This study presents the synthesis and characterization of a reusable, biodegradable, stable, eco-friendly, and efficient nanoprobe sensor for MSG detection using the Ca-BTC/MCC MOF hybrid. The ligand-based luminescent sensor was thoroughly characterized using FTIR, HR-SEM, and PXRD techniques. The developed nanoprobe spectrofluorimetric approach enables the selective

337 determination of MSG in food samples with good sensitivity. The method offers a quick, cost-
338 effective procedure with high recovery rates, rendering it a valuable asset for MSG detection in
339 food samples.

340   Notably, the proposed method demonstrates excellent selectivity in identifying MSG in instant
341 noodles' seasonings, achieving good linearity, and accuracy (precision and trueness), in line with
342 the ICH Q2(R2) guidelines, but also showing an interesting reduced environmental impact
343 following the metrics currently accepted for the evaluation of the green profile and practicability.
344

345 **CRediT authorship contribution statement**
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358

359 **Declaration of Competing Interest**
360   The authors declare that they have no known competing financial interests or personal
361 relationships that could have appeared to influence the work reported in this paper**.**
362

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A luminescent ~~MOF~~metal-organic framework composite as a turn-on sensor for the selective determination of monosodium glutamate in ~~food products~~instant noodles

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Abstract

This work reports the development and application of a new fluorescent nanoprobe sensor depending on using luminescent metal organic framework (LMOF). The developed sensor composed of hybridized Ca 1,3,5-benzenetricarboxylic acid metal organic framework with microcrystalline cellulose (Ca-BTC/MCC MOF) as a fluorescent probe for the determination of the monosodium glutamate (MSG), a non-chromophoric food additive. ~~The constructed sensor~~The developed sensor was characterized using a high-~~resolution~~resolution scanning ~~electron microscopy for morphology,~~electron microscope (HR-SEM), X-ray diffraction ~~for crystallinity,~~(XRD), and ~~Fourier~~Fourier transform infrared ~~spectroscopy for surface functional groups. Examination of the~~ spectroscopy (FTIR). The Ca-BTC/MCC~~/~~ MOF hybrid~~with the scanning electron microscope revealed distinct~~, examined under the HR-SEM, showed morphological ~~features compared to those of~~features different from the MCC and ~~the~~ Ca-BTC MOF~~alone. The~~. The diffraction ~~patterns~~patterns of ~~the~~Ca-BTC/MCC composites ~~prominently exhibited the typical~~clearly displayed the characteristic Ca-BTC MOF diffraction bands ~~of Ca-BTC MOF, confirming the successful incorporation of~~, indicating that MCC ~~into the~~ was successfully incorporated in the formation of crystalline MOF hybrids. ~~Additionally, the infrared spectra displayed~~The FTIR spectra show the bands ~~corresponding to both~~of MCC ~~and~~, as well as the bands of Ca-BTC MOFs~~, further supporting the formation of the hybrid material.~~

~~.~~ The prepared nanoprobe was successfully applied as a sensitive sensor for the ~~assay~~determination of MSG in food sample. The method was validated following the International ~~ICH~~ (Q2)R2 guidelines in terms of precision, trueness and other main analytical figures of merit, comprised the green profile and practicability metrics. A wide linearity range was achieved (5-50 µg/mL) with good correlation coefficient ($R^2 \geq 0.9993$). The recoveries (%) were found in the range of 100.0 to 101.5 and the RSDs (%) were in the range of 0.1 to 0.9%.

These results show that the developed nanoprobe was selective, and highly accurate to determine this important food additive in the seasonings of instant noodles, also showing a reduced environmental impact based on the metrics currently accepted for the evaluation of the green profile and practicability.

Keywords: Metal organic framework; Fluorescence; Sensor; Monosodium glutamate; microcrystalline cellulose; Instant noodles
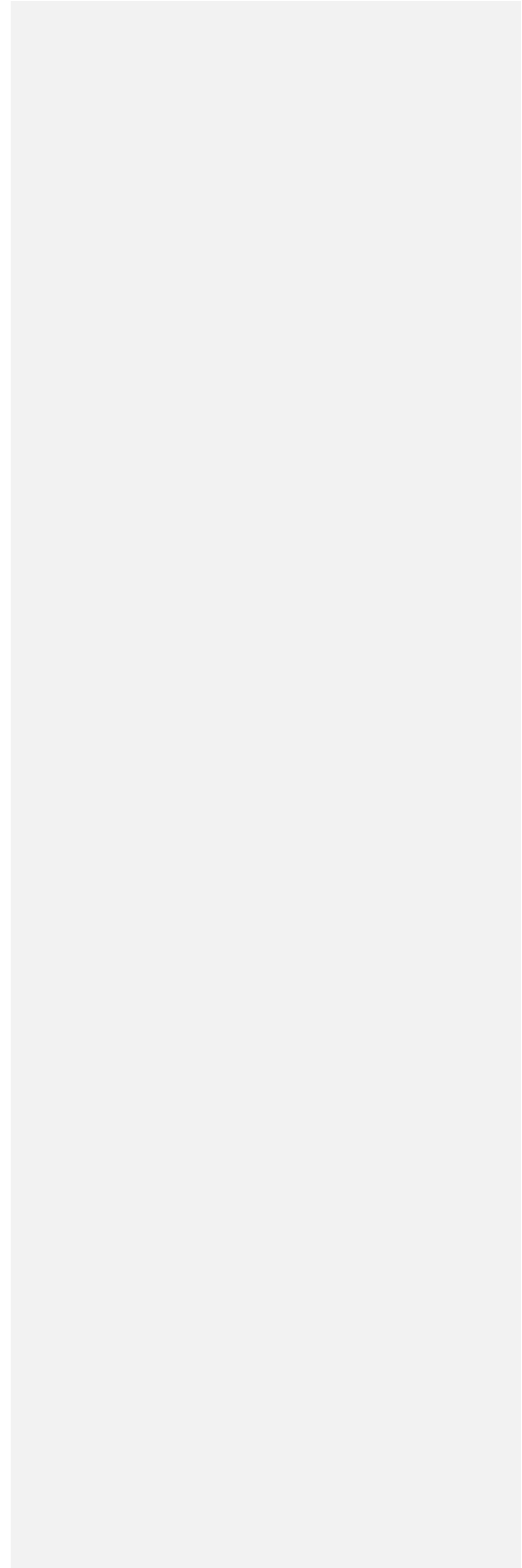
1. Introduction

Monosodium glutamate (MSG, E621) is a common food additive with a distinct Umami flavor [1,2]. This widely used additive is the sodium salt of glutamate, ~~which is an~~a non-essential amino acid with the chemical name 2-aminopentanedioic acid [3,4]. MSG is commonly used as a flavor enhancer in a variety of foods and medications [5]. The reasonable consumption of MSG was assessed by the Food and Drug Administration (FDA) to be roughly 0.55 g/day, with a maximum limit of 1.0 g/day [6]. This threshold is related to the fact that glutamate is an effective excitatory neurotransmitter in the human ~~body~~brain. Excessive MSG consumption could causes neurological ~~disorders~~illnesses such as Parkinson's and Alzheimer's ~~and Parkinson's~~ diseases [7]. Glutamate ~~accumulation can~~may accumulate and become ~~detrimental~~harmful if the glutamate receptor inactivation ~~of glutamate receptors~~ is not ~~adequately~~ balanced by ~~its~~glutamate absorption in the synaptic cleft [8]. ~~Excessive intake of monosodium glutamate (MSG) consequently impacts~~Accordingly, memory, learning, and ~~various~~ regulatory processes. ~~The~~ are all affected by excessive MSG intake. According to the Federation of American Societies for Experimental Biology (FASEB~~) reports that~~), high ~~doses of~~dose MSG exposure can ~~induce~~cause a transient ~~condition~~MSG disorder known as Chinese restaurant syndrome [9]~~. This syndrome is characterized by symptoms such as~~, manifested as flushing, headache, numbness in the mouth, and other ~~effects including~~ symptoms such as burning sensations, facial pressure, and chest ~~pain~~pains [6]. ~~Additionally, excessive~~ Furthermore, high MSG consumption ~~of MSG has been associated with increased risks of~~is linked to diabetes and obesity. ~~Therefore, the~~For these reasons, routine determination of MSG in food ~~products~~stuff is ~~essential~~critical [10].

Several methods for the ~~assay~~determination of MSG have been developed, ~~such as~~including UV/Visible spectrophotometry [7,11–15], spectrofluorimetry [16–18], paper and ~~TLC~~thin layer chromatography [19], High Performance Liquid Chromatography (HPLC~~ coupled)~~ combined with ~~various~~different detectors [20–22], electrochemistry [9,23,24] and capillary electrophoresis [25]. The spectroscopic determination of MSG is challenging because it is a non-aromatic amino acid with no extended conjugation or strong chromophoric groups, which hinders its direct detection by spectrophotometric or spectrofluorometric methods. Alternatively, MSG is commonly determined by employing selective enzymatic processes, chemical derivatization of the aliphatic amino group, or ~~involving both~~ inserting the amino ~~and carboxyl groups~~acid into a complex formation reaction that ~~leads to~~results in the synthesis of colored or luminous compounds.

64   YetHowever, these procedures need the use of costly chemicals, extensive reaction times,
65   temperatureheating, or catalyst additioncatalysis, making MSG assaydetermination hard,
66   slowtime-consuming and expensive [26].
67   Metal-organic frameworks (MOFs) are a novel categoryclass of sensing chemicalsmaterials
68   that have emerged in the porous materials regime [27–3129]. Built from sensitive organic ligands
69   and a wide range of metal ion/clusters, these chemicalsmaterials outperform their contemporaries
70   due to the hightheir large surface area, possibilitystructural tunability of the pore control, and
71   variousmetrics, functional cavitiesnano-spaces [3230]. MOFs have received a lot of attention in
72   the scientific community as fluorometric sensors for detecting a lot of analytes [331].
73   Luminescent metal-organic frameworksMOF (LMOFs) have garnered significantso gained
74   interest due to their enhancedimproved guest identification capabilities and subsequent analyte-
75   specific optical responsesresponse. The sensing mechanisms of LMOFs canmechanism may be
76   categorizeddivided into two categories based on the electronicelectrical nature of the analyte
77   and/or MOFs into: a) "turn-off" and b) "turn-on" sensing. AIn general, a turn-on response is
78   generally achievedmay be elicited by inhibitingconstraining non-radiative relaxations in MOFs
79   through thevia a) integration of rigidstiff functional groups, b) or the formation of
80   exciplexes/excimersexciplex/excimer production with incoming guest molecules, among other
81   methods. Consequently, currentand so on. Thus, contemporary research efforts focus on
82   developingare directed towards the creation of appropriate sensors that elicitcapable of eliciting a
83   turn-on response viabased on LMOFs. Aromatic conjugated organic linkers are have been
84   discovered to be particularly crucialimportant for the emission propertiesproperty of LMOFs in
85   most cases. Thesethe majority of situations. Light is absorbed by π-rich conjugated linkers absorb
86   light, and the subsequent radiative transition of this energy results in the luminescence
87   characteristic luminescence of LMOFs. In addition toApart from ligand-based luminescence,
88   charge transfer mechanisms involving aromatic organic linkers, such as (inter-ligand charge
89   transfer (ILCT), metal-ligand charge transfer (MLCT), and ligand-metal charge transfer (LMCT),
90   etc.) have also been documented. Thesereported. Such ligand-based luminescence properties ofin
91   LMOFs have shown greathas demonstrated enormous potential for the developmentfabrication of
92   sensory materials [3432].
93   Microcrystalline cellulose (MCC)-) modified MOFs have multiple advantages compared to
94   conventionaloffer several advantages over their traditional inorganic equivalents. By integrating

counterparts. The incorporation of MCC into MOFs~~, the resulting materials exhibit elevated surface areas, which~~ results in ~~turn offer a greater quantity of active sites~~material with high surface area, providing an increased number of active sites available for ~~interactions~~interaction. As a ~~result~~result, MCC-MOFs ~~have shown improved effectiveness~~have demonstrated enhanced efficiency in ~~several extraction~~various extraction applications [~~35~~33]. ~~Moreover, the utilization~~Furthermore, the use of MCC as a ~~primary substance~~raw material is ~~beneficial because of~~ advantageous due to its ~~renewable~~renewable and sustainable ~~characteristics, as it is produced~~nature, being derived from plant-~~based~~based sources. ~~The~~Additionally, the cost-~~effectiveness~~effectiveness of MCC~~, in comparison to other regularly utilized materials~~ as compared to other materials commonly used in MOFs~~, significantly increases~~ adds to its ~~attractiveness~~appeal for ~~large-scale manufacturing. Ultimately, the biodegradability of MCC renders it more ecologically sustainable compared to conventional~~large-scale production. Finally, MCC's biodegradability makes it more environmentally friendly than traditional MOFs~~,~~ which ~~frequently have~~often contain non-~~biodegradable constituents.~~biodegradable components.

In this work, ~~an MCC/~~Ca-BTC/MCC MOF hybrid was prepared and applied for the selective detection of MSG in instant ~~noodle~~noodles seasonings. To the best of our knowledge, this ~~study~~work is the~~first to~~ report ~~the use~~ of ~~MCC/~~using Ca-BTC/MCC MOF as a fluorescent sensor. Compared ~~to~~with the other reported methods ~~for~~of MSG determination, this spectrofluorometric ~~approach~~method is rapid, reliable, selective~~,~~ and environmentally friendly~~, making~~ which make it suitable for the routine analysis of MSG in food and food-~~ ~~derived products. To the best of our knowledge, this work reports for the first time the application of Ca-BTC/MCC MOF composite as a sensitive sensor for spectrofluorometric detection. Compared with Ca-BTC MOF, the composite has higher surface area which offers higher sensitivity for the determination of MSG. Moreover, the prepared composite is biodegradable, stable, eco-friendly, and efficient nanoprobe.

2. Experimental

2.1. Instrumentation

All fluorescence spectra measurements were recorded using a Jasco model FP-8300 spectrofluorometer (Tokyo, Japan) equipped with a 1-cm quartz cuvette, both excitation and emission bandwidths were set at 10 nm. The excitation wavelength was set at 325 nm while the emission wavelength was set at 422 nm. The software of Spectra Manager (Jasco Co., Tokyo,

Japan) was used for spectral data processing and acquisition. Jenway® 3510 pH-meter (Staffordshire,UK) was also employed for phase pH adjustment. BET measurements were carried out using Autosorb-01 (Quantachrome TouchWin™). To ~~investigate~~analyze the morphological characteristics of ~~the~~ MOFs, ~~scanning electron microscopy (~~SEM~~)~~ images were ~~obtained~~collected using an HRSEM Quanta FEG 250 ~~equipped~~ with ~~a~~ field emission gun. ~~The~~ To characterize the crystallinity and phase purity of the ~~synthesized~~produced MOFs ~~were characterized using~~, a Malvern Panalytical X'PertPRO PANalytical diffractometer (~~Cu Kα radiation~~K X-ray at 45 kV, 40 mA, ~~λ = 1.5406 Å).~~) was utilised. A JASCO FT/IR 6100 spectrometer was used to analyze the Fourier ~~transform~~transforms infrared ~~(FTIR)~~ spectra of ~~the~~ MOFs ~~were analyzed with a JASCO FT/IR 6100 spectrometer~~.

2.2. Materials

Monosodium glutamate (99%) was ~~generously provided~~kindly supplied from by Sigma Pharmaceutical Industries (Quesna, El-Menoufia, Egypt). Methanol, ethanol~~,~~ and acetonitrile, ~~calcium chloride~~CaCl$_2$, 1,3,5-benzenetricarboxylic acid (BTC), ~~NaOH~~sodium hydroxide, and microcrystalline cellulose were ~~obtained~~purchased from Merck (Darmstadt, Germany).

2.3. Synthesis of Ca-BTC~~-~~/MCC MOF

~~To prepare a transparent solution of~~ Ca-BTC~~, 0.42 g of~~ was prepared, as reported [28] by using the following conditions: 1,3,5-benzenetricarboxylic acid (0.42 g) was dissolved in 100 mL of ~~1N~~1 M NaOH solution. ~~Concurrently,~~ In parallel, CaCl$_2$ (0.316 g ~~of CaCl$_2$~~) was dissolved in 10 mL of purified water. ~~The~~At 25°C, the two solutions were combined ~~at 25°C~~ and ~~stirred~~agitated for 20 ~~minutes~~min. The reaction mixture was ~~then~~ maintained at 90 °C for 24 ~~hours~~hrs in ~~an~~the oven. ~~After~~Following this ~~period, the~~time, Ca-BTC ~~product~~ was collected, washed with 99.9% ethanol, and ~~filtered~~then passed through ~~Whatman~~a Whatmann filter paper.

~~For the preparation of~~ Ca-BTC/MCC MOF composites~~, 0.5 g of microcrystalline cellulose (MCC) was immersed in a 50 mL aqueous solution containing 0.316 g of CaCl$_2$. The mixture~~ was ~~agitated for 1 hour at room temperature. Subsequently, 50 mL of an aqueous solution of 0.42 g~~prepared under the same conditions in the synthesis of Ca-BTC MOF as follows [28]: MCC (0.5 g) and of 1,3,5-benzenetricarboxylic acid (0.42 g) were dissolved in 100 mL of 1 M NaOH solution and water soluble CaCl$_2$ (0.316 g) was added dropwise to the mixture ~~with constant stirring. After~~

8 hours, the MCC turned white. The of MCC/BTC at 25°C while shaken the solution for 20 minutes. Then, the mixture was added in dry oven at 90 °C for 24 hrs. The white solids were formed in the bottom of the vessel. Following a centrifugation of the mixture was then centrifuged, washed twice with, two ethanol washes, and subjected to a 12-hour vacuum drying process at 60°C for 12 hours. The resulting, the composites were obtained and stored for further use. until used.

2.4. Procedures for determination of MSG.

An amount of 5 mg/mL of Ca-BTC-MCC stock were prepared by addition of 500 mg of MCC/Ca-BTC/MCC composite in 100 volumetric flask, the volume was completed to 100 mL by deionized water. The system was sonicated for 30 min to enhance dispersion of the composite. Finally, the dispersion system was filtrated by 0.22 μm syringe filter. For MSG detection, 125 μL of Ca-BTC-MCC system was added to 25 mL of MSG aqueous solution and the mixture was measured immediately at 422 nm after irradiation excitation at the wavelength of 325 nm.

2.5.2.5. Measurement of quantum yield

The QY of the Ca-BTC/MCC MOF was detected using the single-point method (Eq.1):

$$QY = QY_{QS} \times (F_{Ca\text{-}BTC/MCC} / F_{QS}) \times (A_{QS} / A_{Ca\text{-}BTC/MCC}) \times (\eta_{Ca\text{-}BTC/MCC} / \eta_{QS})^2$$

Where F is the integrated fluorescence intensity, A is the absorbance and η is the refractive index of the solvent. Quinine sulfate (QS) was used as the standard. QS was dissolved in 0.1 M sulfuric acid .The absorbance value was set at 0.05 to standardize the absorbance impact. In an aqueous solution, the $\eta_{CQD} / \eta_{QS} = 1$.

2.6. Method validation

The proposed method was validated according to International Guidelines ICH Q2(R2) [36] in terms of selectivity, linearity, limit of quantitation, and accuracy (trueness and precision).

3. Results and discussion

3.1. Characterization of Ca-BTC-/MCC MOF

The structures structures of both Ca-BTC and MCC were subjected to experienced alterations during the synthesis of the composite sorbent, as illustrated by the infrared spectra. **Figure 1a**

187 ~~shows the FTIR spectrum of MCC. The~~Ca-BTC/MCC MOF composite sorbent, and these changes

188 in chemical bonds and interactions were studied by FTIR. **Figure 1a** displays MCC's FTIR

189 spectrum. The band at 1024 cm^{-1} ~~is assigned~~was assigned to ~~the~~ C-O ~~stretching vibration, while~~

190 ~~the band~~, whereas the CH$_2$-CH group emerged at 2900 cm^{-1} ~~corresponds to the aliphatic CH~~

191 ~~group, and the~~, and the O-H ~~stretching vibration appears~~group appeared at 3347 cm^{-1}. ~~In the Ca-~~

192 ~~BTC FTIR spectrum (**Figure 1b**), the peaks at 3306 cm^{-1}, 1149 cm^{-1}, and 1021 cm^{-1} illustrate the~~

193 The O-H ~~stretching due to hydrogen~~expansion over hydrogen bonding with ~~water~~water and CaO~~.~~

194 ~~Additionally, a peak at~~ was illustrated by the peaks at 3306 cm^{-1}, 1149 cm^{-1}, and 1021 cm^{-1},

195 respectively, as shown in the Ca-BTC FT-IR spectrum (**Figure 1b**). At 1632.01 cm^{-1} ~~is observed,~~

196 ~~corresponding to~~, one may observe the isotope of the bending mode of unbound water. The region

197 ~~from~~of 1700 to 1300 cm^{-1} ~~shows both symmetric and~~$^{-1}$ is where asymmetric and symmetric O-C-

198 O stretching of the ~~COOH~~carboxyl groups occur. Asymmetric O-C-O stretching is ~~associated~~

199 ~~with~~linked to the peaks at 1574.50 cm^{-1}, 1556 cm^{-1}, and 1510 cm^{-1}, ~~while~~whereas symmetric O-

200 C-O stretching is responsible for the peaks at 1435.50 cm^{-1} and 1392 cm^{-1}. **Figure 1c** ~~presents~~

201 ~~the~~ The FTIR spectrum ~~of the~~ interaction between Ca-BTC and MCC~~. The~~ is presented in **Figure**

202 **1c**. These results indicated that the composite ~~exhibited~~showed distinct Ca-BTC uptake bands

203 ~~corresponding to both Ca-BTC MOF and MCC polymer, confirming the successful integration of~~

204 ~~these components~~in addition to the MCC uptake bands.

205

206 **Figure 1.** Infrared spectra of [a] the ~~starting materials;~~MCC polymer~~[a] and Ca-BTC MOF.~~ [b~~,~~]

207 the Ca-BTC MOF, and [c] the ~~formed~~ Ca-BTC/MCC hybrid~~[c]~~.

208

209   The crystallinity of the prepared hybrid was studied and compared with MCC and Ca-BTC

210 MOF using PXRD. **Figure 2a** reports the diffraction pattern of MCC. The ~~polymer~~MCC crystal

211 structures showed the large peaks at 12.10°, 20.10°, 22.30°, and 34.60°, which were characteristic

212 for cellulose II crystals. The Ca-BTC diffraction pattern is seen in **Figure 2b**. The PXRD peaks

213 have the following unit cell parameters: ~~α=β=γ=90.00° and~~ a~~=~~ = 10.94, b~~=~~ = 6.73, c~~=~~ = 18.58, and

214 $\alpha = \beta = \gamma = 90.00°$ (orthorhombic). Space group Pnm a 63 has been used to index the PXRD peaks.

215 The Ca-BTC/MCC diffraction patterns are shown in **Figure 2c**. The compounds exhibited distinct

216 ~~MOF~~Ca-BTC diffraction bands, suggesting that ~~the polymer was~~MCC has been effectively

217 integrated into the crystalline ~~MOF during hybrid synthesis~~Ca-BTC production process.

218

219 **Figure 2.** X-ray diffraction pattern of the ~~starting materials;~~ MCC polymer~~[a] and,~~ [b] the Ca-BTC

220 MOF~~[b],~~, and [c] the ~~formed~~ Ca-BTC/MCC MOF hybrid~~[c]~~.

221

222   For the sake of comparison, the morphology of MCC was examined. As seen in the SEM

223 pictures in **Figures 3a** and **3b**, the 3D lattice ~~configuration~~structure with uniformly dispersed

224 particles and massive particle agglomerations was clearly visible. The FE-SEM

225 ~~photographs~~images displayed in **Figures 3c** and **3d** depicted the typical crystal structure of Ca-

226 BTC. Using an electron microscope, the morphological properties of the Ca-BTC/MCC~~/~~ MOF

227 ~~hybrid~~ were investigated and the findings displayed in **Figures 3e** and **3f**. Measured under a

228 microscope, the crystal size of the hybrid material was ~~determined to be~~two-dimensional, with one

229 side measuring 2.20 μm and the other side measuring 12.10 ~~× 2.20 mm~~μm. The fact that the

230 composite shape's characteristics were entirely distinct from those of ~~the starting materials~~MCC

231 and Ca-BTC indicates that both compounds were successfully encapsulated. The measured BET

232 surface areas from N_2 adsorption-desorption for MCC, Ca-BTC, and Ca-BTC/MCC were 10.60,

233 560.00, and 820.00 $m^2\,g^{-1}$, respectively. Figure S1 shows an overlay of the excitation and emission

234 spectra of Ca-BTC/MCC MOF. The stability the MOF composite was assessed on short- and long-

235 term basis. The Ca-BTC/MCC MOF was found stable in benchtop study over 24 hours, and the

236 in the fridge at -4°C for seven days. The prepared Ca-BTC/MCC MOF was stored in solid form at room

237 temperature, and its fluorescence intensity remained stable with no significant changes observed over a

238 period of 6 months.

239

240 **Figure 3.** SEM images of [a,b] the ~~starting materials;~~ MCC polymer~~[a,b] and,~~ [c,d] the Ca-BTC

241 MOF~~[c,d],~~, and [e,f] the ~~formed~~ Ca-BTC/MCC MOF hybrid~~[e,f]~~.

242

243 **3.2. Method optimization**

244   Studying the different experimental variables that may affect the method performance is crucial.

245 The one-variable-at-a-time (OVAT) approach was used in the optimization process. Different

246 factors were investigated, including excitation wavelength, disperser solvent of MOF, incubation

247 time, and pH of the aqueous sample. Fluorescence intensity was monitored at each condition to

248 reach the maximum sensitivity.

249

3.2.1. Excitation wavelength optimization

Changing the excitation wavelength can greatly influence the emission intensity in fluorescence spectroscopy. The impact of excitation wavelength on the intensity of ~~MOF~~Ca-BTC/MCC MOF was examined across the range 225-350. As reported in *Supplementary materials section S.1*, the highest emission was observed at 422 nm with an excitation wavelength of 325 nm. This specific excitation wavelength was utilized in subsequent steps to determine the concentration of MSG in both aqueous solutions and instant noodles seasonings.

3.2.2. Effect of disperser solvent of MOF

Different solvents were used for dispersion of ~~MCC/~~Ca-BTC/MCC MOF composite including methanol, ethanol, acetonitrile and deionized water. A concentration of 5 mg/mL of ~~MCC/~~Ca-BTC/MCC MOF composite was prepared in different solvents, and then the dispersion system was sonicated for 30 min followed by filtration using a syringe filter (0.22 µm). Only water achieved fluorescence intensity while the other organic solvents achieved negligible fluorescence intensity. It could be attributed to the low tendency of organic solvents to achieve a good dispersion MOF hybrid.

3.2.3. Effect of incubation time

Different incubation times were investigated in the range from 0 to 12 min as indicated in **Figure 4a**. There was no significant change in FLD intensity over time. This is because the interaction between MSG and the Ca-BTC/MCC~~/~~ MOF hybrid is instantaneous, which allows for the rapid measurement of MSG and makes the developed method time-saving besides being less-laborious than other derivatization-based methods.

3.2.4. Effect of pH on MOF emission

Different pH values were investigated over the range 2 to 9. As indicated in **Figure 4b**, there was no significant change with pH variations over the studied range. This could be ~~attributed to~~explained by the high stability of ~~composite~~Ca-BTC/MCC MOF and the negligible effect of pH on the predominately charged amine group in MSG at pH values ≤9. Accordingly, deionized water was used as diluent throughout the following procedure. The calculated quantum yield of Ca-

BTC/MCC MOF was found to be 3.8% at an excitation wavelength of 325 nm, and an emission wavelength of 422 nm.

Figure 4. The effect of incubation time (a), pH (b) and interferences (c) on the fluorescence intensity using water as a disperser solvent, 125 µL of Ca-BTC/MCC , 25 mL of MSG aqueous solution.

3.3. ~~Validation of the MOF composite-based method~~Method validation

3.3.1. ~~Method's~~Selectivity

Selectivity of analytical methods is a ~~crucial~~key parameter ~~in the~~ during method development ~~of analytical methods. According to ICH guidelines, a~~ . The method is ~~considered~~deemed selective if there is no interference from ~~other substances that might be present. To assess the selectivity of the method for MSG detection, the~~interfering substances, according to ICH guidelines. The reaction was ~~tested~~examined in the presence of ~~various~~ chemicals ~~commonly found alongside~~that may be present as a contemporaneous component with MSG in food preparations. ~~These potential interfering substances included~~ to determine the method's selectivity such as glucose, ~~NaCl, KCl,~~ lactose, sodium chloride, potassium chloride, and starch. ~~The absence of interference from these substances confirms the selectivity of the method.~~ No significant changes were observed in the fluorescence intensity, using saturated solutions of theses food ingredients, which indicated the adequate method selectivity for MSG, as shown in **Figure 4c**.

3.3.2. Linearity, range and limit of quantitation.

To investigate the linearity of the method, a calibration curve was constructed by plotting the FLD intensity on the y-axis and the concentration of MSG (in µg/mL) on the x-axis. The ~~plotted~~calibration curve indicated that the technique exhibited linearity within the 5-50 µg/mL MSG concentration range (**Figure 5**). The calculated coefficient of determination (r^2) was 0.9993. The limit of quantitation was found to be 5 µg/mL, demonstrating the high applicability of the proposed method in food analysis. The constructed calibration curve is shown in Figure S2.

Figure 5. Overlaid spectra of ~~MSG in~~different concentrations ~~varying around~~of MSG over the studied ~~dynamic~~linearity range.

311

3.3.3. Accuracy (precision and trueness)

The accuracy of the method was evaluated by analyzing three quality control samples spiked with MSG at three different concentrations (8, 30, and 45 µg/mL). MSG concentrations were analyzed in triplicate. **Table 1** shows that the procedure trueness (given in terms of recovery %) was adequate for the application of the proposed method on food sample. ~~The analytical method's precision was evaluated analyzing three quality control samples spiked with MSG at three different concentrations (8, 30, and 45 µg/mL). MSG concentrations were analyzed in triplicate.~~ The recoveries (%) were found in the range of 100.0 to 101.5 and the %RSDs were in the range of 0.1 to 0.9%. Accordingly, the developed nanoprobe ~~spectrofluorometric~~spectrofluorimetric analytical method is accurate according to ICH (Q2)R2 guidelines.

Table 1. Intra-day and inter-day precision and trueness

4. Application on food sample

The developed nanoprobe spectrofluorometric method was utilized for the determination of MSG from a single packet of instant noodles containing a sachet of seasoning powder. Since the application was performed on seasoning powder, no extensive sample preparation was required. 100 mg of the powder was diluted to 100 mL, and then the mixture was sonicated for 20 min. Subsequently, the solution was filtered through a 0.22 µm syringe filter. A 1000 µL aliquot from the previous system was further diluted to 25 mL, and 125 µL of Ca-BTC-/MCC- MOF was added to this solution. These procedures resulted in a concentration of 20.15 µg/mL.

Standard addition was employed to assess the matrix effect; specifically, 5 µg/mL of MSG was added to the previous system, and six replicates were performed. As shown in **Table 2**, the percent recovery fell within the range of 98.1% to 101.5%, with a percent relative standard deviation (RSD%) of 1.4%. These results indicated that the developed method can been successfully applied for the determination of MSG in food samples. **Table 3** compares between the developed method and other recent methods for MSG determination in different food matrices.

Table 2. Application of the ~~MOF composite based~~developed method for ~~the assay~~determination of MSG in food sample using standard addition method.

Tablet 3. Comparison between the developed method and other reported methods for MSG determination in different food matrices

5. Green Profile evaluation

The developed nanoprobe spectrofluorometric method was further evaluated in terms of green profile by means of the recent accepted tools [~~37~~42] like AGREE (Analytical GREEnness Metric Approach) [~~38~~43], AGREEprep (Analytical greenness metric for sample preparation) [~~39~~44], and BAGI (Blue applicability grade index) [~~40~~45].

Figure 6. Pictograms related to AGREE, AGREEprep, and BAGI evaluation of the proposed procedure.

As highlighted in **Figure 6**, based on the metrics currently accepted for the evaluation of the green profile, the method reported here certainly shows a reduced environmental impact both on the basis of the AGREE (criteria 2, 4, 6, 9, 11 and 12), and based on AGREEprep (criteria 2, 5, 9 and 10). Based on the score obtained from BAGI, can be stated that the method can be considered "practical" (score of 60). The specific inputs used are reported in *Supplementary materials section* ~~*S.2*~~*S3*.

Certainly, the procedure could be improved compared to the procedure reported here with a view to obtaining an even greener profile and a higher BAGI score. In particular, if the procedure is improved by using a sample preparator (automated) which also increases the number of samples that can be processed (approx. 10 samples/h) and by reducing the quantity of sample (10 mg) and proportionally the quantity of waste (12.5 mL) can see in **Figure 7** how the green and BAGI profiles improves significantly. The specific inputs used are reported in *Supplementary materials section S.~~3~~4*.

Figure 7. Pictograms related to AGREE, AGREEprep, and BAGI re-evaluation of the proposed procedure following some improvements.

6. Conclusions

A novel turn-on spectrofluorometric ~~strategy~~method has been ~~presented~~developed for the ~~assay~~determination of MSG in food samples with acceptable ~~validation criteria~~accuracy and precision. MOFs, composed of metal ions/clusters and organic ligands, offer versatile applications due to their inherent crystallinity, distinct structure, adjustable porosity, and diverse functionalization. The structural and chemical adaptability of MOFs allows for high selectivity through pore-sieving mechanisms, making LMOFs a notable choice as sensing materials in recent times. By leveraging their high internal surface areas, MOFs can concentrate analytes effectively, leading to lower detection limits and enhanced sensitivity.

This study presents the ~~preparation~~synthesis and characterization of ~~an~~a reusable, biodegradable, stable, eco-friendly, and efficient nanoprobe sensor for MSG detection using the Ca-BTC/MCC MOF hybrid. ~~This~~The ligand-based luminescent sensor was thoroughly characterized using FTIR, HR-SEM, and PXRD techniques. The developed nanoprobe spectrofluorimetric approach enables the selective ~~assay~~determination of ~~Chinese salt~~MSG in food samples with good sensitivity. The method offers a quick, cost-effective procedure with high recovery rates, rendering it a valuable asset for MSG detection in food samples.

Notably, the proposed method demonstrates excellent selectivity in identifying MSG in instant noodles' seasonings, achieving good linearity, and accuracy (precision and trueness), in line with the ICH Q2(R2) guidelines, but also showing an interesting reduced environmental impact following the metrics currently accepted for the evaluation of the green profile and practicability.

CRediT authorship contribution statement

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper**.**

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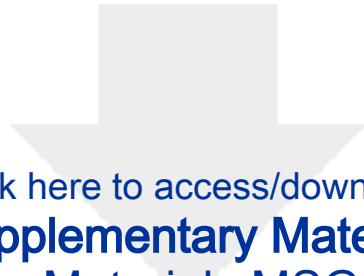
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Table 1

Table 1. Intra-day and inter-day precision and trueness

	Intraday			Interday		
	Added (µg/mL)	**Found (µg/mL)**	**Found (%) ±RSD**	**Added (µg/mL)**	**Found (µg/mL)**	**Found (%) ±RSD**
MSG	8	8.1	100.8±0.1	8	8.0	100.4±0.5
	30	30.2	100.6±0.1	30	30.0	100.0±0.8
	45	45.7	101.5±0.4	45	45.2	100.4±0.9
Mean			100.96			100.3
RSD (%)			0.2			0.7

Table 2

Table 2. Application of the developed method for determination of MSG in food sample using standard addition method.

	Added (µg/mL)	Found (µg/mL)	Found (%)
MSG	5	5.0	100.5
	5	4.9	98.1
	5	5.1	100.9
	5	5.1	101.5
	5	4.9	99.5
	5	4.9	98.6
Mean			99.9
%RSD			1.4

Table 3

Table 3: Comparison between the developed method and other reported methods for MSG determination in different food matrices

Sample	Analytical technique	Nanoparticles	Analysis time	LOQ	Solvent	Ref
Vegetable soup	Electrochemical	Gold nanoparticles decorated on molybdenum disulfide chitosan	1 hr	0.1 µM	Ethanol	[37]
Tomato soup	Electrochemical	Montmorillonite decorated poly caprolactone and chitosan based nanofibers	1 hr	5.42 µM	Formic acid, acetone	[38]
Mandarin fish	Electrochemical	Gold nanoparticles	24 hr	Not reported	Acetic acid	[39]
Vegetable soup	Electrochemical	Platinum nanoparticles	24 hr	1.59 µM	Acetic acid and methanol	[40]
Instant noodles, chicken cubes	Spectroflourimetry	Carbon quantum dots	1.5 min	66 µM	water	[41]
Instant noodles	Spectroflourimetry	Ca-BTC/MCC MOF	1 min	5 µg/mL	water	This work

Declaration of interests

The authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.