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All Organic Label-like Copper (II) Ions Fluorescent Film Sensors with High Sensitivity and Stretchability

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Keywords: high sensitivity, fluorescent, copper ions sensor, chlorophyll-a, biosensor

ABSTRACT: Deep learning and analysis of heavy metal concentration are very crucial to our life, for it plays an essential role in both environmental and human health. In this paper, we developed a new Cu (II) ions sensor made by all organic material with bending and stretching properties. The new sensor consists of chlorophyll-a extracted from fresh leaves of Common Garcinia, plant fiber and with the use of PDMS as a substrate. Fluorescence spectra study shows that chlorophyll-a is significantly much more sensitive to Cu (II) ions than any other heavy metal ions and the device sensitivity outperforms all the Cu (II) ions sensors ever reported. The result fully shows the selectivity of chlorophyll-a toward Cu (II) ions. Bending and stretching tests show that the sensor has an outstanding durability, which can be used to develop accompanying applications, such as real-time sampling and the analysis of Cu (II) concentration specified in athlete's sweat or patients with brain dead and Parkinson's disease.

Nowadays, people show much more concern on their surroundings with the expectation to improve the quality of life. Therefore, human beings have made progress on technology focusing on environmental health, such as the use of green energy with the aim to reduce environmental pollution. Speaking of heavy metals, copper is an essential trace element for the human to maintain necessary requirement, but copper overdoses would cause severe damage to liver and lung or even worse with the following symptom - Wilson's disease and Alzheimer's disease.[1-5] When it comes to biological issues, the green oyster is one of the most famous cases with regard to copper pollution. Also, copper ions suspended in the air with the combination of rain would contaminate crop as well as drinking water.[6-8] Although lots of methods have been developed and widely used to detect heavy metals such as atomic absorption spectroscopy, atomic emission spectroscopy and fluorescent sensor in aqueous solution or inductively coupled plasma mass spectroscopy,[9-12] there still exist some shortcomings following with high cost, time-consuming process, and inaccessible instruments.

According to IC Insights' new 2016 O-S-D Report - A Market Analysis and Forecast for Optoelectronics, Sensors/Actuators, and Discretes,[13] in 2015, sales of sensors and actuators have achieved a prominent growth. The report also predicted that the worldwide sales of sensors and actuators would expand by a compound annual growth rate of approximately 6 % through 2020 with the help of the Internet of Things (IoT). As the rise of Internet of Things (IoT) and the demand for wearable devices, the new requirements appear, such as in the design of device, how to produce a sensor that has flexibility and high impact resistance. This part of research has already become the focal point of the field. Flexible and stretchable optoelectronics not only enrich our lives by providing smart functions but also offer health information by sensing body conditions. Recently, flexible and stretchable biosensors have numerous clinical applications, including diagnostic and monitoring utilization, such as biochemicals, physiology, and motion sensing.[14-15] Flexible and stretchable biosensors, which can accommodate strain and maintain high performance, will become one of the most popular technologies for the next generation. It has a great potential to create products with new applications, which were considered impractical or impossible in the past.

In this work, we used the material of fresh chlorophyll-a extracted from Common Garcinia, natural cotton fiber, PDMS substrate and polymethylmethacrylate in the middle as an adhesive layer to design an organic Cu (II) ion fluorescence sensor with the characteristics of low cost, high stability, and fast response time. Besides, the developed device can be attached to any curved surface. The design of our device was inspired by the previous work, in which M. Hu *et al.*'s study shows that chlorophyll-a is notably more sensitive to Cu (II) ion than other investigated ions.[16] Indeed, fluorescence spectra show an excellent sensitivity of the sensor, and durability study shows that the device can sustain stretching and bending tests for more than several hundred cycles. Our newly developed film sensor possesses an ultrahigh precision, and it is much more user friendly compared with previously reported copper ion sensors based on chlorophyll-a. We therefore believed that the cost-effective, highly sensitive and stretchable sensor for detecting Cu (II) at room temperature could pave a crucial step for the development of next-generation biosensors.

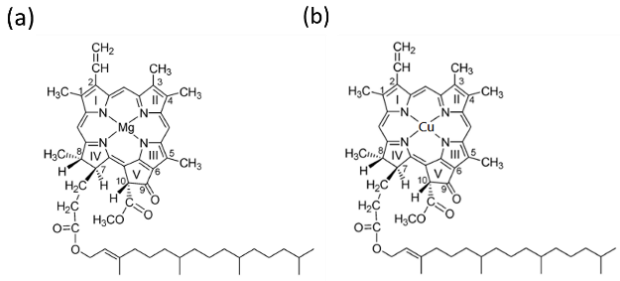
EXPERIMENTAL SECTION

Materials. In this paper, we have demonstrated a flexible and stretchable Copper (II) ions fluorescent film sensor extracted from biological materials using Common - Garcinia Chlorophyll-a. First, the leaves were washed with deionized water and dried with nitrogen gas gun to remove the surface dust as well as the drop. Furthermore, the leaves were chopped and put into the beaker. After mixing with the absolute alcohol, the solution was then stored and kept at 4 ℃ in the refrigerator for 24 hours

to extract sufficient Chlorophyll-a. Finally, the leaves and impurities were removed by centrifugation (4 °C, 3000 rpm, 10 minutes). The upper clarified liquid was taken while using the technology of UV visible spectrum to detect the concentration of the chlorophyll-a extract solution.

Given the fact that copper chlorophyll-a is much more stable than chlorophyll-a while interacting with copper (II) ions, magnesium ions in the center of chlorophyll-a molecules will be replaced by copper (II) ions to form a stable copper chlorophyll-a. Scheme 1 shows the chemical structure of chlorophyll-a and copper chlorophyll-a.[16-18] With the combination of copper (II) ions and chlorophyll-a, we observed the changes in fluorescence intensity, which provides a useful route for detecting the concentration of copper (II) ions.

Scheme 1. The chemical structures of chlorophyll-a (a) and copper chlorophyll-a (b).



Sensor structure and synthesis. The solution of polydimethylsiloxane (PDMS) and stiffener were mixed with the weight ratio of 10 to 1 and placed it into the vacuum chamber to remove extra air within polydimethylsiloxane. Then, it was dried at 80 ℃ to receive polydimethylsiloxane with the high-flexible and high-transmission attribute as a substrate.

Natural cotton fibers were used to form a fiber absorption layer with 0.2 mm thickness, length, and width of 1cm. The solution of chlorophyll-a was dropped on the fiber absorption layer 10 μL each time with a total of 30 μL and placed it in the vacuum chamber for 10 minutes to remove extra alcohol to form a copper (II) fluorescent detection layer. All processes were carried out in a dim light and at room temperature.

We use polymethylmethacrylate $(C_5O_2H_8)_n$ as an adhesive layer, which makes a good connection between PDMS substrate and copper (II) fluorescent detection layer due to high flexibility, stretchability, and transparency. The schematic of our newly developed flexible and stretchable Cu (II) ions film sensor is shown in Figure 1.

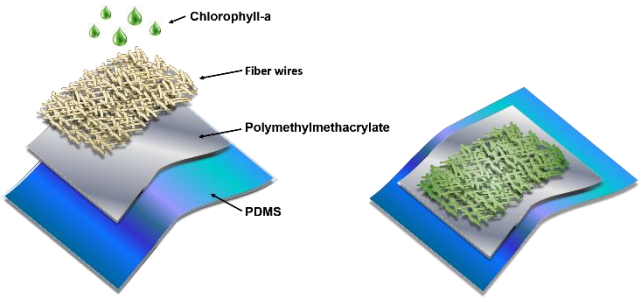


Figure 1. Schematic of all organic label-like flexible and stretchable Cu (II) ions film sensor.

The reaction of chlorophyll-a with Cu (II) ions. The alcohol solution containing 0.2 mole·ml^{-1} chlorophyll-a was completely absorbed into the natural fiber layer. After vacuum drying process, Cu (II) ion aqueous solution was dropped on the film sensor, and the fluorescence spectra were measured using a fluorescence spectrophotometer (SPEX 1403 0.85m Double Spectrophotometer) with an ultraviolet light-emitting diode as the excitation light source. The reaction time and the Cu (II) ion concentration of the test solution were analyzed by measuring the fluorescence intensity of the film sensor.

RESULTS AND DISCUSSION

Chlorophyll is extracted from the leaves of plants or marine algae and is divided into chlorophyll-a, chlorophyll-b, chlorophyll-c, chlorophyll-d, chlorophyll-f. In this study, chlorophyll-a was extracted from the leaves of Common Garcinia, and the main peak of the luminescence analysis was measured at 679 nm by the fluorescence spectrometry system as shown in Figure 2. Figure 3 shows the absorption spectra of 4×10^{-3} mole·ml^{-1} chlorophyll-a in an alcohol solution (blue line) and the mixture of the chlorophyll-a solution with Cu (II) ions (red line). We mix 4×10^{-3} mole·ml^{-1} chlorophyll-a alcohol solution with an equivalent 1.5×10^{-4} M Cu (II) aqueous solution for reaction 200 seconds. The main absorption peaks for the chlorophyll-a solution were found at 289, 343, and 662 nm. In contrast, for the spectrum of Cu (II) mixed chlorophyll-a solution, the absorption peaks were found at 289, 342, and 659 nm. In addition, we also observed some slight absorption modes amplification in 400 ~ 460 nm region as shown in the insert of Figure 3, which might be attributed to the shift of degeneration orbital energy levels caused by the auto-replacement process between Mg and Cu ions.[16,19-20] In other words, the phenomenon may reflect the reaction of chlorophyll-a molecular and Cu (II) ions to form new molecules. In the red region, the 659 nm absorption for the Cu-chlorophyll-a was found to have 3 nm blue-shift compared with that of chlorophyll-a, which has also been observed in previous studies.[19-22] A number of medical studies showed that other heavy metals with high concentration, such as potassium (I), silver (I), sodium (I), calcium (II), zinc (II), manganese (II), magnesium (II), cobalt (II), nickel (II), lead (II), cadmium (II) and iron (III), can cause hazard to human and environment. However, they do not possess an obvious reaction with chlorophyll-a and reflect in the change of absorption spectra as shown in Figure 3.[16,22-24] In addition, the selectivity of chlorophyll-a toward copper ion has also been confirmed based on other studies.[16] For example, it is found that the fluorescence quenching due to the reaction between chlorophyll-a and others biologically relevant cations is less than 10 % of the chlorophyll-a and copper case.[16] This unique feature provides an excellent platform to develop a highly sensitive Cu (II) ions sensor by monitoring the fluorescence signal.

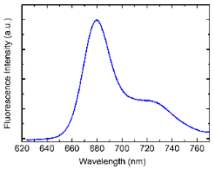


Figure 2. Fluorescence spectrum of chlorophyll-a extracted from the leaves of Common Garcinia and the peak of the luminescence intensity were found at 679 nm.

Table 1. Comparison of photoelectric performances of various sensors for copper (II) ions detection.

Reagent	Detection Limit (M)	Refs.
Fresh spinach leaves chlorophyll-a	**8.0×10^{-7}**	**12**
Macrocyclic dioxotetraamine and1,8-naphthalimide derivative	**3.0×10^{-7}**	**27**
Rhodamine B derivative	**3.42×10^{-6}**	**28**
Coumarin derivative	**-**	**29**
1-(RhodamineB)lactam-thiosemicarbazide	**4.10×10^{-8}**	**30**
Rhodamine B derivative	**1.50×10^{-8}**	**31**
Naphthalimide modified rhodamine B	**1.80×10^{-7}**	**32**
Schiff base of 5,50-methylene-bis-salicylaldehyde with amidol (2,4-diaminophenol)	**4.31×10^{-8}**	**33**
Xylylenebis(N,N-diisobutyldithiocarbamate	**4.90×10^{-7}**	**34**
Poly(n-butyl acrylate)	**1.89×10^{-7}**	**35**
Aminopyridine Schiff bases	**-**	**36**
Carbazole moiety and 2-(((pyridin-2- ylmethyl)amino)methyl)phenol group	**2.90×10^{-6}**	**37**
Hydrogen bond assisted azine-linkage covalent organic framework	**3.1×10^{-7}**	**38**
1,4,8,11- tetraazacyclotetradecane (Cyclam)-functionalized carbon dots (CCDs)	**100×10^{-9}**	**39**
Fresh Common Garcinia leaves chlorophyll-a (dry type)	**1.0×10^{-10}**	**This work**

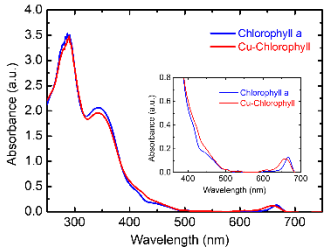


Figure 3. Absorption spectra of 4×10^{-3} mole·ml^{-1} chlorophyll-a in the alcohol solution (blue line) and the mixture of chlorophyll-a solution and Cu (II) ions (red line). Mixing 4×10^{-3} mole·mL^{-1} chlorophyll-a alcohol solution with an equivalent 1.5×10^{-4} M Cu (II) aqueous solution for the reaction of 200 seconds. The main absorption peaks for the chlorophyll-a solution were found at 289, 343, and 662 nm. In contrast, for the spectrum of Cu (II) mixed chlorophyll-a solution, the absorption peaks were found at 289, 342, and 659 nm.

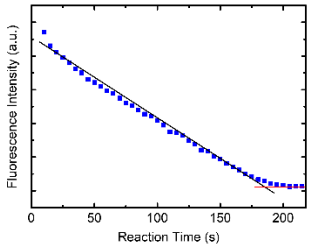


Figure 4. Time-dependent fluorescence intensity graph of 1×10^{-5} M Cu (II) ions aqueous solution at 25 ℃ and there was an interval of five seconds between each measurement point. The fluorescence intensity shows a distinctly linear fluorescence decrease phenomenon with the increase of reaction time.

Figure 4 shows effects of reaction time on the fluorescence spectra of 1×10^{-5} M Cu (II) ion aqueous solution at 25 ℃, in which the interval between each measurement point is five seconds. The fluorescence spectra show a clearly linear fluorescent intensity decreasing phenomenon with the increasing of reaction time. Initially, we dropped Cu (II) ion aqueous solution on the detection area of the film sensor, and after the reaction continues for about 200 seconds, the fluorescent quenching tends to be stable. The underlying mechanism of the fluorescence quenching can be understood as follows. The molecule structure of chlorophyll-a is a kind of organic chelate formed by magnesium ion as the center, surrounded by porphyrin rings. The magnesium ions in the chlorophyll-a can be replaced easily by copper ions, the chemical reaction (1) and (2) can be expressed as below,

$$\text{Chlorophyll-a} \longrightarrow \text{Mg (II)} + \text{Pheophytin} \qquad (1)$$

$$\text{Pheophytin} + \text{Cu (II)} \longrightarrow \text{Cu-chlorophyll-a} \qquad (2)$$

According to previous reports, the fluorescence quenching can be attributed to two main reasons.[16,25-26] The paramagnetism and heavy metal effect of Cu (II) ion may cause electron spin-orbit coupling and transform the excited single-line state into triplet state, and the internal molecular conversion can cause the fluorescence intensity quenching. Besides, paramagnetic Cu (II) ion can also induce the effect of reversible electron transfer to quench fluorescence intensity.

Figure 5a is the natural cotton fiber optical micrograph, showing that the width of every fiber wire is approximately 10 microns. As the schematic indicates, fiber wires play the role of containers to speed up the reaction rate by shortening the distance between chlorophyll-a molecules and Cu (II) ions (Figure 5b). Compared with other studies using fluorescence

detection in aqueous solution,[19-20] our film sensor has a shorter response time.

Figure 6a shows the Cu (II) concentration dependence of fluorescence spectra under the reaction time of 200 seconds at 25 °C. With increasing Cu (II) ion concentrations (0 - 10^{-3} M), fluorescence intensity is significantly decreased. Figure 6b shows the graph obtained with Cu (II) concentration vs. fluorescence intensity, which shows a linear relationship in the Cu (II) concentration ranging from 1×10^{-5} to 1×10^{-10} M. Notably, the detection limit can reach as small as 1×10^{-10} M. This highly sensitive characteristic can be well understood based on the fact that fiber wires provide a similar structure as optical cavity to trap emitted light and enhance the fluorescence intensity change due to the reaction of chlorophyll-a and copper ions. The comparison of detection limits with other reported copper ion sensors is given in Table 1.[13,27-39] Remarkably, our film sensor outperforms all published reports by more than two orders of magnitude in terms of the detection limit. We have analyzed the copper ions concentration from 1 to 10 μM, which is the copper pollution region associated with human life, such as raining water, running water, drinking water, and even our sweat as shown in the insert of Figure 6b. The result suggests that our film sensor can be used to detect Cu (II) ion concentration with high sensitivity in a wide range.

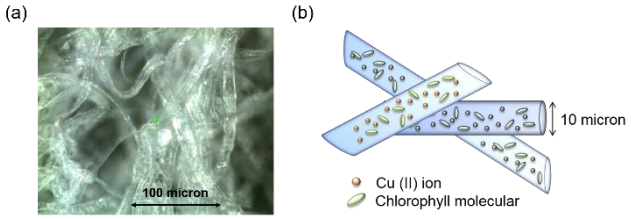


Figure 5. Natural cotton fiber optical micrograph (a) and schematic diagram (b), the width of every fiber wire is approximately 10 microns, as what schematic diagram indicates that fiber wires play the role of containers to speed up the reaction rate by shortening the distance between chlorophyll-a molecules and Cu (II) ions.

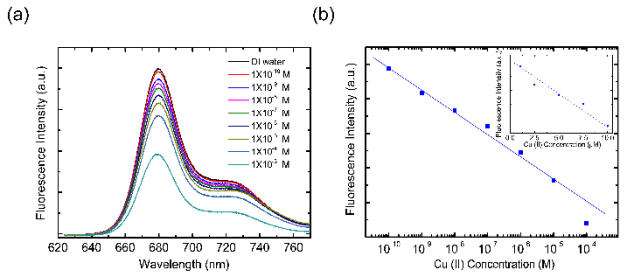


Figure 6. (a) Cu (II) concentration dependence of fluorescence spectra under fixing conditions of 200 seconds reaction time at 25 °C. With increasing Cu (II) ion concentrations (0 - 10^{-3} M), fluorescence intensity is significantly decreased. (b) Cu (II) concentration vs. fluorescence intensity graph was linear in the Cu (II) concentration range of 1×10^{-5} - 1×10^{-10} M and the detection limit arrives 1×10^{-10} M. Particularly we analyze the region from 1 to 10 μM, which is the copper pollution region associated with human life.

Mechanical flexibility is an essential parameter for a portable and wearable device. In this work, label - like copper ion film sensor was designed to be attachable to the body surface to achieve the real-time sampling and detection. Figure 7 shows the changing rates of fluorescence intensity after 50 bending cycles, carried out at the different radius of curvatures (0.75, 1.25, 2, and 4.5 cm) for fixing Cu (II) concentration of 1.6×10^{-5} M. Under bending test, fluorescence signals remain almost unchanged even after 700 times of bending cycles. It is clearly observed that the bending of film sensor has no significant effect on its sensing performance. The outstanding mechanical flexibility is likely due to the long chain molecule structure of PDMS and polymethylmethacrylate. In addition to these two layers made from polymer materials, natural cotton fiber wires also provide an excellent flexibility.

To experimentally demonstrate the stretchability, the film sensor was mechanically stretched under 1 %, 3 %, 5 %, and 10 % strain. Figure 8 shows the changing rates of fluorescence intensity ($\Delta I / I_o$) for fixing Cu (II) concentration of 1.6×10^{-5} M. The result indicates that a negligible effect caused by 1 %, 3 %, 5 % and 10 % stretching tests. The film sensor has been stretched up to more than 600 cycles, and the fluorescence signals remain stable. Based on the stretching analysis, we can infer that our film sensor has no significant structural damage or apparent cracks to affect the sensing performance in the stretching process.

After demonstrating the flexibility, stretchability, and durability, we then tried to label our device onto different curved surfaces and detect different analyte solutions. First, we detect the Cu (II) concentration of the sweat on human skin. Initially, the film sensors were labeled onto the skin of arm and palm.

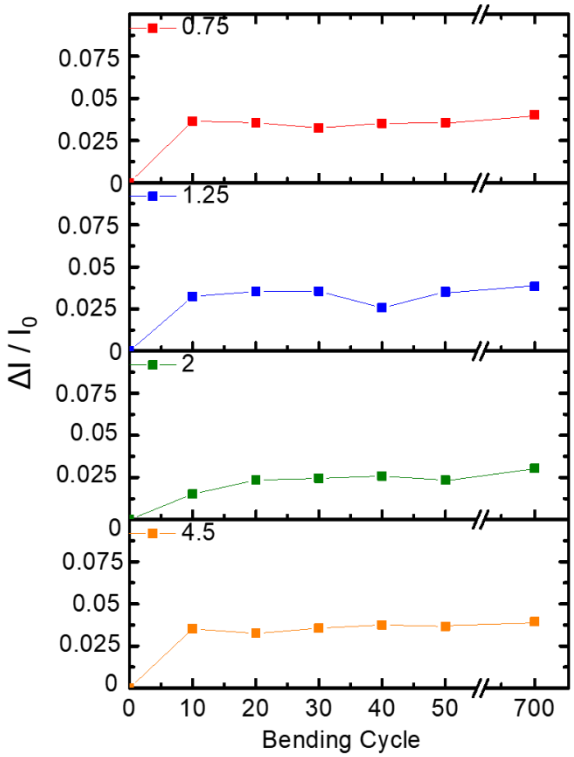


Figure 7. The changing rates of fluorescence intensity under 50 bending cycles, carried out at the different radius of curvature (0.75, 1.25, 2, and 4.5 cm) for fixing Cu (II) concentration of 1.6×10^{-5} M. Unger bending test, fluorescence signals remain almost unchanged.

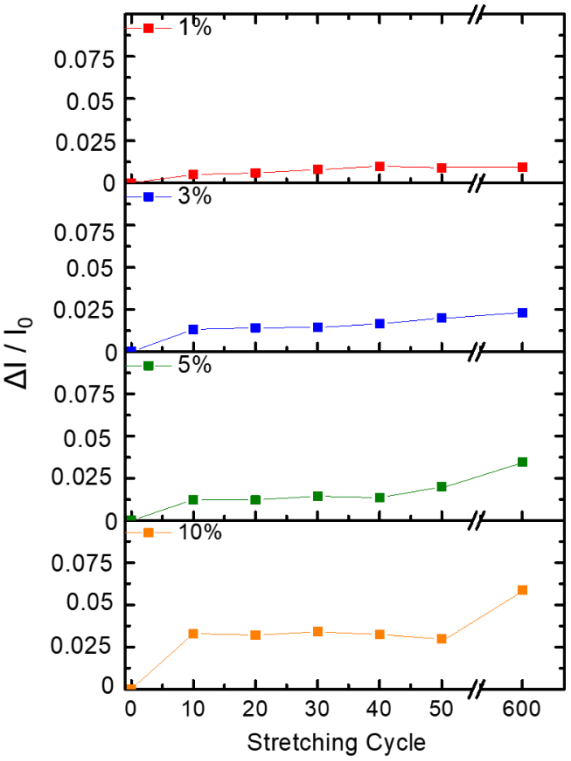


Figure 8. The changing rates of fluorescence intensity under different stretching cycles by 1 %, 3 %, 5 %, and 10% for fixing Cu (II) concentration of 1.6 $\times 10^{-5}$ M. The result shows a negligible effect caused by stretching. The changing rate of fluorescence intensity for 10 % strain is also less than 0.04.

After that, participants continue jogging for 10 minutes to let the film sensors absorb the sweat. In the jogging process, film sensors remain firmly attachable to the participant's skin, the results in Figure 9a show that the Cu (II) concentration of the sweat is around 1.4×10^{-5} M, and the obtained value is comparable to the result of J. R. Cohn *et al.*'s study.[40] Figures 9b and 9c show that the film sensor can be firmly labeled onto the surface of glass and water pipe to accurately detect the copper ion concentration of drinking water and running water, and the obtained results are 8.5×10^{-6} M and 8.75×10^{-6} M, respectively. Although the water purification of water plant and the filtration system of water dispenser can provide us with clean water, the old water pipe or metal oxidation often cause the contamination of drinking water and running water. The two obtained values are both lower than copper ion pollution standards of running water and drinking water in most countries. From the above demonstrations, our film sensor can be freely attached to diverse surfaces including soft, flexible, rough, and nonplanar surfaces. These results prove that our film sensor is feasible to serve as a functional label on various surfaces of objects in our daily life, while keeping its high performance.

On the whole, all optical studies and demonstration experiments unanimously indicated the outstanding characteristics of the film sensor compared with previously reported copper ion sensors. Regarding precision, micron scale of fiber wires structure enabled to lower the detection limit efficiently, and dry type sensor can avoid optical interfering caused by absorption and scattering of liquid. Note that most of the reported copper ion sensors based on chlorophyll-a were used in liquid state. Moreover, in this work, label - like copper ion film sensor was designed to be attachable to the body surface to achieve the real-time sampling. Our film sensors therefore present outstanding operation convenience compared with previously reported study, such as analysis of Cu (II) concentration specified in athlete's sweat, paralytic patients or the analyte solution on the curved surface.

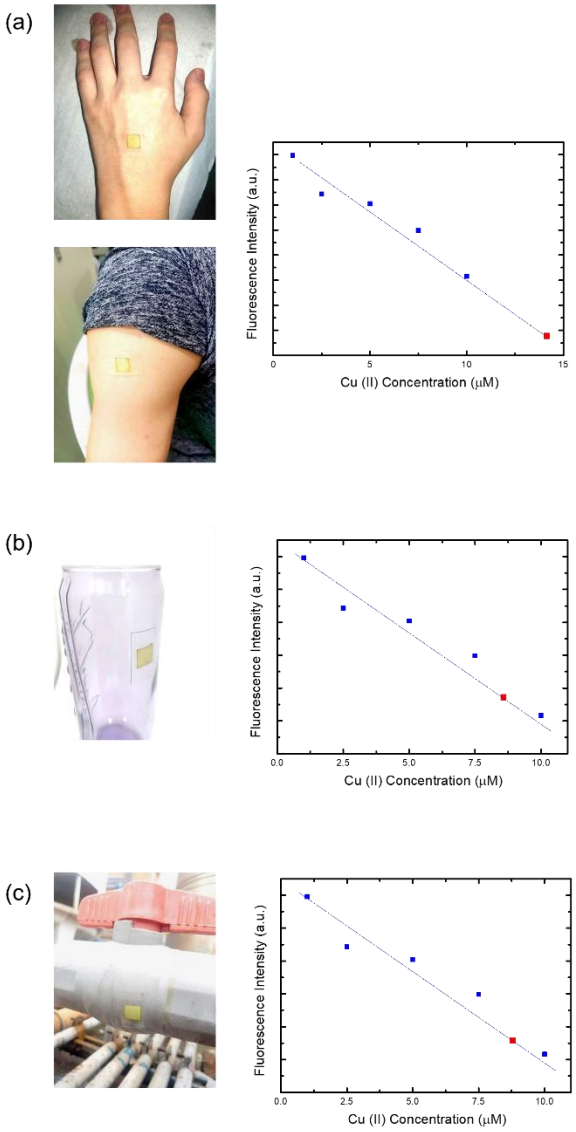


Figure 9. Demonstrations of the film sensor labeled onto different curved surface and Cu (II) concentration of analyte solution vs. fluorescence intensity graph, including sensing the (a) human sweat on the skin, (b) drinking water on the surface of glass, (c) running water on the surface of water pipe. (Red data points represent Cu (II) concentration of human sweat, drinking water, and running water. Blue data points represent Cu (II) concentration of standard solution).

CONCLUSIONS

In conclusion, a label - like copper (II) ion sensor has been successfully designed, fabricated, and demonstrated based on PDMS substrate, polymethylmethacrylate adhesive layer, natural cotton fiber wires and chlorophyll-a extracted from the

leaves of Common Garcinia. The simple and effective processes enable to improve production efficiency and achieve the goal of low cost. Characteristics of elastic materials provide outstanding mechanical flexibility and stretchability, and the excellent diaphaneity is what optical sensor required. It shows an extremely high sensitivity, a wide sensing range covering from 0.1 nM to 0.1 mM and a shorter reaction time ~ 200 seconds. The detection limit exceeds all of the majority of copper ion sensors ever reported. The advantage of dry type sensor also includes eliminating optical interfering signals of liquid. The film sensor with a highly mechanical flexibility and durability can be attached on an arbitrary surface, even pasting on the human skin to achieve human sweat detection. Furthermore, the all organic label-like copper (II) ions fluorescent film sensor described here demonstrates the potential for the application of the organic integrated optoelectronic devices in the medical device field. The high sensitivity of our film sensor may be able to lead to the development of convenient and accurate environmental monitors, and the inexpensive processing and flexibility of organic optoelectronics will allow the sensors to be designed for any shape and size.

ASSOCIATED CONTENT

Supporting Information

Supporting Information Available: The following files are available free of charge.

Supporting Information for All Organic Label-like Copper (II) Ions Fluorescent Film Sensors with High Sensitivity and Stretchability (PDF). The effect of salt on the sensing performance; Visualization test of the all organic label-like copper (II) ions fluorescent film sensors; Fluorescent assays with different Cu (II) ions concentrations in liquid state; Stability test under mechanical stress (movie file).

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Author Contributions

M. J. W. conceived the original idea for the project and wrote the manuscript. M. J. W. performed all the measurements with the help of Hsiu-Hao Hu. Yu-Ming Liao and M. Y. L. assisted to deal with technical problems. The chlorophyll-a was extracted by C. Z. S.. J. H. C. performed the optical micrograph of fiber. T. Y. L. and Y. F. C. provided many professional suggestions for the project. Y. F. C. supervised the project. All authors accepted the final version of the manuscript.

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In this study, an innovative label-like copper ions fluorescent film sensor with high sensitivity and stretching properties has been successfully designed, fabricated, and demonstrated. The film sensor exhibits an extremely high sensitivity with a wide sensing range covering from 0.1 nM to 0.1 mM, which outperforms all the Cu (II) ions sensors ever reported. The bending and stretching tests show that the film sensor has an excellent mechanical stability. In addition, the film sensor can be attached onto freeform surfaces.

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