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COLORIMETRIC DETECTION OF FORMALDEHYDE USING GOLD NANOPARTICLES

MODIFIED WITH 4-AMINOPHENYL SULFONE

Mr. Arnupab Kritanusorn

A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science Program in Chemistry

Department of Chemistry

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งานวิจัยนี้มีจุดมุ่งหมายเพื่อพัฒนาวิธีการตรวจวิเคราะห์ปริมาณฟอร์มาลดีไฮด์ด้วยเทคนิค การตรวจวัดเชิงสีบนกระดาษ โดยใช้ 4-อะมิโนฟีนิลซัลโฟนสำหรับดัดแปรพื้นผิวอนุภาคระดับนาโน เมตรของทองคำ อาศัยหมู่ฟังก์ชันเอมีนในการเกิดปฏิกิริยากับฟอร์มาลดีไฮด์ในสภาวะที่มีไฮดรอกซีลา มีนไฮโดรคลอไรด์ ส่งผลทำให้เกิดกระบวนการรวมตัวกันของอนุภาคระดับนาโนเมตรของทองคำที่ถูก เหนี่ยวนำโดยฟอร์มาลดีไฮด์ในสภาวะที่มีไฮดรอกซีลามีนไฮโดรคลอไรด์ เพื่อยืนยันการเกิด กระบวนการรวมตัวกันของอนุภาคระดับนาโนเมตรของทองคำที่ผ่านการดัดแปรนั้น ได้ตรวจสอบ คุณลักษณะโดยใช้เทคนิคยูวี-วิซิเบิลสเปกโทรสโกปีและกล้องจุลทรรศน์อิเล็กตรอนชนิดส่องผ่าน วิธีที่ ได้พัฒนาขึ้นนี้มีสภาพไวและมีความจำเพาะเจาะจงสำหรับการตรวจวิเคราะห์ฟอร์มาลดีไฮด์มากกว่า สารเคมีและไอออนชนิดอื่น ๆ การเปลี่ยนสีของสารละลายอนุภาคระดับนาโนเมตรของทองคำจากสี แดงเป็นสีน้ำเงินสามารถสังเกตเห็นได้ด้วยตาเปล่า กราฟเทียบมาตรฐานเป็นเส้นตรงในช่วง 40 – 110 ไมโครกรัมต่อมิลลิลิตร (ค่าสัมประสิทธิ์สหสัมพันธ์เท่ากับ 0.9979) ขีดจำกัดการตรวจวัดเท่ากับ 35 ไมโครกรัมต่อมิลลิลิตร ด้วยการวิเคราะห์โดยการใช้โปรแกรมประยุกต์อิมเมจเจ วิธีที่ได้พัฒนาขึ้นนี้ถูก นำไปประยุกต์ใช้สำหรับการตรวจวัดฟอร์มาลดีไฮด์ที่ปนเปื้อนอยู่ในตัวอย่างจริงด้านอาหาร และ สิ่งแวดล้อม ซึ่งให้ผลการตรวจวัดสอดคล้องกับวิธีมาตรฐาน

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ARNUPAB KRITANUSORN: COLORIMETRIC DETECTION OF FORMALDEHYDE USING GOLD NANOPARTICLES MODIFIED WITH 4-AMINOPHENYL SULFONE. ADVISOR: ASSOC. PROF. NARONG PRAPHAIRAKSIT, Ph.D., CO-ADVISOR: PROF. ORAWON CHAILAPAKUL, Ph.D., 70 pp.

This research aimed to develop a colorimetric method for the determination of formaldehyde on a paper-based device, using 4-aminophenyl sulfone for surface modification of gold nanoparticles (AuNPs) with an amine group that can react with formaldehyde in the presence of hydroxylamine hydrochloride. The process resulted in the aggregation of modified gold nanoparticles (modified-AuNPs) induced by formaldehyde in the presence of hydroxylamine hydrochloride. To verify this aggregation, the modified-AuNPs were characterized using ultraviolet-visible spectroscopy (UV-vis) and Transmission electron microscopy (TEM). This method offers a high sensitivity and selectivity for the determination of formaldehyde over other chemical and ions. The color change of modified-AuNPs from red to blue can be monitored by naked eyes. The relevant calibration curves was linear in the range of 40 - 110 µg mL^{-1} (R^2 = 0.9979) and the limit of detection was found to be 35 µg mL^{-1} by using ImageJ software for image processing. This developed method was applied to detect formaldehyde in real samples (e.g. food and environmental), which the results were in good agreement with those obtained from the standard methods.

Department:	Chemistry	Student's Signature	....
Field of Study:	Chemistry	Advisor's Signature	....
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ABBREVIATIONS

μL	microliter
μm	micrometer
°C	celsius
Ag	silver
AgNPs	silver nanoparticles
AO	alcohol oxidase
AOAC	Association of Official Analytical Chemists
Au	gold
Au@Ag	silver nanoparticle coated on the surface of gold nanoparticle
AuNPs	gold nanoparticles
AuNRs	gold nanorods
CCD	charge-coupled device
cm	centimeter
EFSA	European Food Safety Authority
eV	electron volt
Fe	iron
FTIR	fourier transform infrared spectroscopy
g	gram
GC	gas chromatography
H	hydrogen
HCHO	formaldehyde

Hg	mercury
HPLC	high-performance liquid chromatography
IARC	International Agency for Research on Cancer
kg	kilogram
kV	kilovolt
L	liter
LOD	limit of detection
LOQ	limit of quantitation
LSPR	localizes surface plasmon resonance
m	meter
MBTH	3-methyl-2-benzothiazolinone hydrazone
mg	milligram
mL	milliliter
mM	millimolar
mm	millimeter
Modified-AuNPs	modified gold nanoparticles
MS	Mass spectrometry
N	Nitrogen
ng	nanogram
nm	nanometers
nM	nanomolar
NPs	nanoparticles
O	oxygen

PADs	paper-based analytical devices
PAN	polyacrylonitrile
Pd	palladium
PDMS	polydimethysiloxane
PEG	poly(ethylene glycol)
pH	potential of hydrogen
ppb	parts per billion
ppm	parts per million
Pt	platinum
Purpald	4-Amino-3-hydrazino-5-mercapto-1,2,4-triazole
rpm	revolutions per minute
RSD	relative standard deviation
SPE	Solid-phase extraction
SPR	surface plasmon resonance
TEM	Transmission electron microscopy
UV-Vis	ultraviolet-visible spectroscopy
w/w	weight per weight
WHO	World Health Organization
XPS	X-ray photoelectron spectroscopy
ε	molar absorptivity

CHAPTER I

INTRODUCTION

1.1 Introduction

Currently, toxic residues in food and environment have been concerned as one of major problems affected to human health for both short and long periods. The rapid and simple detection methods of toxic residues are thus necessary for food safety and environmental monitoring. Among these, formaldehyde is one of the most toxic substance which is naturally occurring in fruits, foods and environment. Formaldehyde is colorless, strong-smelling gas and is often found in aqueous solutions (known as formalin). It is used in several industries, for example, polymer industry, textile industry and medicinal industry because of its ability to restrain the growth of fungi and bacteria. However, the vast amount of formaldehyde present in food and environment threatens human health upon contact. Exposure of formaldehyde causes serious health problems including headache, tachycardia, skin irritation, and failure of circulatory system. Moreover, the accumulation of formaldehyde in human body can cause a certain type of cancer [1]. Although many countries strictly regulate the use of formaldehyde in food, its usage still appeared illegally in dietary such as meat, vegetables, and seafood. World Health Organization (WHO) has defined formaldehyde as a carcinogenic substance and limited its utilization. Therefore, a simple yet accurate detection of formaldehyde is necessary to control its levels in foodstuffs in order to protect human health.

To date, several analytical approaches for formaldehyde determination have been developed such as gas chromatography–mass spectrometry (GC-MS) [2, 3], fluorescence spectrometry [4, 5], and high-performance liquid chromatography (HPLC) [6-9]. Even though these methods provide high sensitivity, selectivity, and accuracy, they suffer from being high cost, labor-intensive, time consuming, and non-portable.

Paper-based analytical devices (PADs) are one of the alternative methods yet very attractive for point-of-care formaldehyde detection because of their low sample and reagents consumption, disposability, and portability [10-12]. These low-cost platforms have been integrated with both colorimetric, and electrochemical detection systems. Colorimetric detection is a particularly attractive partner for PADs because such analysis is relatively simple, and the technology is compatible with smartphone based reporting systems. Previously, the colorimetric methods for formaldehyde detection have been proposed. For example, Suslick et al. [13] demonstrated a sensitive formaldehyde colorimetric sensor array using the reaction between primary amine and formaldehyde. The detection principle is based on nucleophilic addition of an amine to the aldehyde, forming an imine via a carbinolamine intermediate, and the imine formation generates a color change. The sensor array was fully reversible, but it relied on a series of pH indicators and statistical data-processing. To overcome the pervious drawbacks, colorimetric sensors based on metal nanoparticles (NPs) have attracted a great deal of attention due to the distinctive optical property related to the size and shape of the nanoparticles.

Gold nanoparticles (AuNPs) are particularly interesting and widely used as probes for colorimetric analysis because they display typical properties of surface plasmon resonance (SPR) absorption, high extinction coefficient in the visible region and color-tunable behavior, which are highly dependent on the size and shape of the AuNPs as well as the interparticle distance. Zeng et al. [14] proposed a colorimetric assay for formaldehyde detection using AuNPs and Tollens reagent in agarose gel media. Au@Ag core-shell NPs were produced when formaldehyde was exposed along with distinct color change from pink to deep yellow. This method provides high sensitivity, however long reaction time and the use of high amount of reagent are still required. Thus, the development of a fast, simple, sensitive, and low-cost formaldehyde detection method is still highly desired and challenged.

Therefore, the objective of this research is to develop a fast and simple paper-based colorimetric sensor for the determination of formaldehyde using gold nanoparticles, 4-aminophenyl sulfone, and hydroxylamine hydrochloride. This paper-based colorimetric sensor is based on the aggregation of 4-aminophenyl sulfone-AuNPs induced by formaldehyde and hydroxylamine hydrochloride and is developed for the highly selective and sensitive detection of formaldehyde.

1.2 Objectives of the research

This research consists of two goals as following:

1. To develop a paper-based colorimetric assay for the determination of formaldehyde using gold nanoparticles, 4-aminophenyl sulfone, and hydroxylamine hydrochloride.

2. To apply the developed method for the determination of formaldehyde in real food samples.

1.3 Scope of the research

The paper-based device was fabricated by wax printing to obtain hydrophobic area for the determination of formaldehyde. The influences of experimental variables on the sensitivity of the proposed method were investigated. Under optimal conditions, the analytical performance of the proposed method was studied, including range of linearity, limits of detection and quantification, repeatability, and reproducibility. The selectivity for the determination of formaldehyde was studied using various interferences including 2-propanol, acetaldehyde, acetone, acetylacetone, ammonium acetate, benzaldehyde, calcium chloride, ethanol, ethyl acetate, methanol, potassium chloride, sodium bicarbonate and sodium chloride. Finally, the proposed method was applied to detect formaldehyde in real food samples such as fresh shrimp, frozen shrimp and shiitake mushroom with high sensitivity, accuracy and precision.

CHAPTER II

THEORY AND LITERATURE SURVEY

2.1 Formaldehyde

2.1.1 Chemistry and application of formaldehyde

Formaldehyde is an organic compound containing carbon, oxygen, and hydrogen with the formula of CH_2O, as shown in figure 2.1. Formaldehyde is known by its systematic name as methanal. Furthermore, it is also known by other names include methyl aldehyde, formalin (aqueous solution) and carbonyl hydride. Formaldehyde possesses flammable, colorless, pungent odor, volatile, photo-oxidized and disinfecting properties. Generally, formaldehyde can be found naturally with low levels in various foods such as fruits, vegetables, mushrooms and seafood. In addition, it was found in many housewares such as furniture, wallpaper and particle board. In our daily life, formaldehyde is widely used with different purposes and properties such as a reagent in concretes, plaster additives, cosmetics, and disinfectants, and also employed as a chemical in fumigants, photography, and wood preservation. However, it is mainly utilized as a preservative reagent due to its disinfection properties [1].

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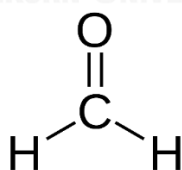
Figure 2.1 Structure of formaldehyde

2.1.2 Sources of formaldehyde

Formaldehyde can be generated naturally by different processes such as decomposition and photo-oxidation of living organisms: bacteria, algae, plankton, and vegetation. It is simply found in environment due to the combustion of forest, brush fires and irradiation of humic substances in water by sunlight. All reason mentioned above is the main source of formaldehyde production. Furthermore, formaldehyde can also be found from direct sources including fuel combustion, industrial onsite uses, and off-gassing from building materials and consumer products [15].

2.1.3 Health effect

Formaldehyde in blood can be metabolized to formic acid within 90 seconds and it is excreted within 12 hours through exhalation as carbon dioxide and via the urine and faces in rats. The remaining of it can be found in several tissues since metabolic incorporation into the single carbon pool and subsequent incorporation into biological macromolecules. In humans and the other mammalian species, formaldehyde concentrations in blood after exposure are comparable to physiological blood-levels (~ 0.1 mM) because its high chemical reactivity and rapid cellular metabolism in lining cells, local effects of formaldehyde seem to play a more tremendous role compared to systemic effects.

However, the vast amount of formaldehyde presence in the food and environment threatens human health upon contact. Exposure of formaldehyde causes serious health problems including headache, tachycardia, skin irritation, and failure of circulatory system. Moreover, accumulation of formaldehyde is reported in causing a certain type of cancer. Many countries strictly regulate the use of formaldehyde in food, still they are illegally incorporated in dietary such as meats, vegetables, and seafood. Many international organizations namely World Health Organization (WHO), European Food Safety Authority (EFSA), and International Agency for Research on Cancer (IARC) have defined formaldehyde as a carcinogenic substance and limited their usage. In Thailand, Ministry of Public Health entirely prohibits the application of

formaldehyde. Therefore, detection of formaldehyde in food or products is necessary [1, 15-18].

2.1.4 Conventional method for formaldehyde determination

According to the serious health risk obtained from the human consumption of formaldehyde in foods, the development of an alternative analytical approach with real-time detection of formaldehyde in the food, water and environment are still very important

The most common techniques used to determine formaldehyde in food, water and environment are high performance liquid chromatography – ultraviolet - visible spectrophotometer (HPLC-UV/Vis) [9, 19, 20], gas chromatography - mass spectrometry (GC-MS) [3] and colorimetric methods [13]. Although those techniques offer a high selectivity and sensitivity, they typically require high operation cost, time-consuming and need of sophisticated instruments.

2.2 Colorimetric method

Colorimetric method is an analytical method for the quantitative and qualitative analysis of analyte interest. The principle of colorimetric detection involves the measurement of the absorbed or emitted light. The results can be simply observed by naked-eye or a spectrophotometer. Hence, this method is widely used for determination of the analyte of interest because of ease detection and observation. The changed or absorbed light is proportional to the amount of the analyte in the solution. However, the absorbed light can be altered at a high concentration of the analyte based on beer's law. This leads to the nonlinear relationship between absorbance and concentration [21-23]. The application of this method for determination of $FeSCN^{2+}$ is shown in figure 2.2.

Wavelength Region Absorbed, nm	Color of Light Absorbed		Complementary Transmitted	
400-435	Violet		Yellow-green	
435-480	Blue		Yellow	
480-490	Blue-green		Orange	
490-500	Green-blue		red	
500-560	Green		Purple	
560-580	Yellow-green		Violet	
580-595	Yellow		Blue	
595-650	Orange		Blue-green	
650-750	red		Green-blue	

Source of white light   Lens   Absorbs at 460 – 500 nm   Human eye detector
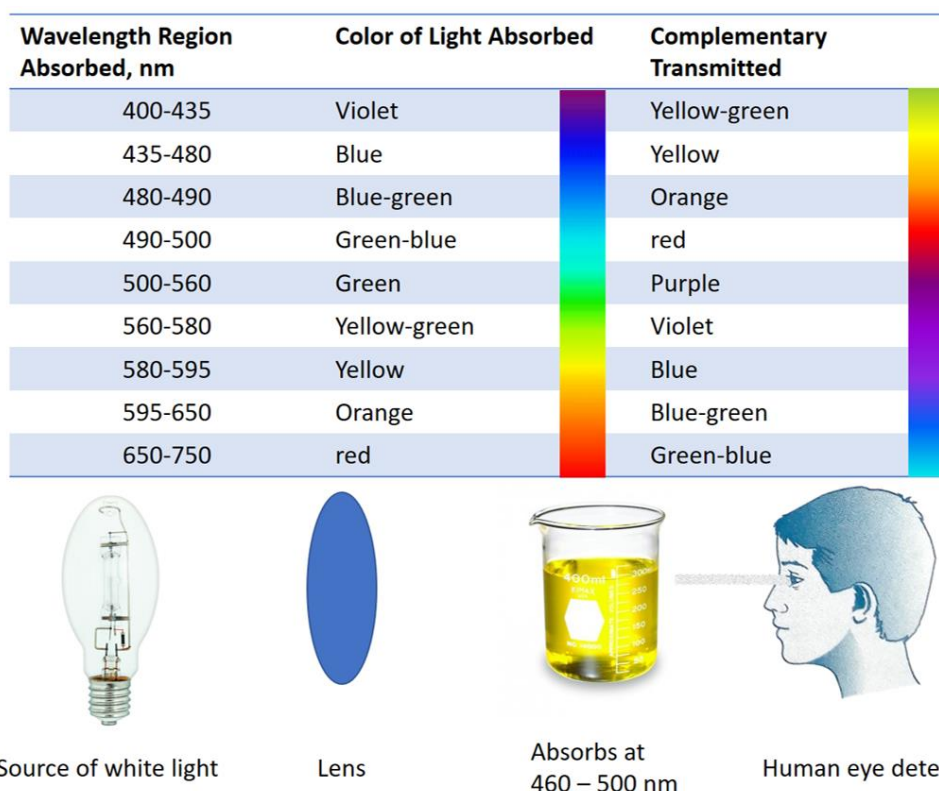
Figure 2.2 Color of the FeSCN^{2+} solution while the white light strikes the solution. The band broadening absorption shows a maxima absorbance around 460 to 500 nm. The complementary red color is transmitted.

Presently, the standard commercial pigments and dyes have been widely used as a colorimetric reagent to react with a target compound. However, the molar absorptivity (ε) of the pigment and dyes are still low which limit its applications. In the past decades, the nanoparticles (NPs) have been introduced to substitute pigment and dyes as it exhibits higher ε value. The scattered and absorbed light of NPs can be simultaneously measured, distinguishing to the pigments or dyes that can only be detected by absorption. However, the color change of NPs still required chemical reaction.

Colorimetric principle is used for designing sensors because chemical components and analysis methods are not expensive and easy to assess. Moreover, this method does not require highly trained personnel for use. However, typical colorimetric assays still suffer from the low sensitivity and inferior limit of detection (LOD), as shown in figure 2.3 [24].
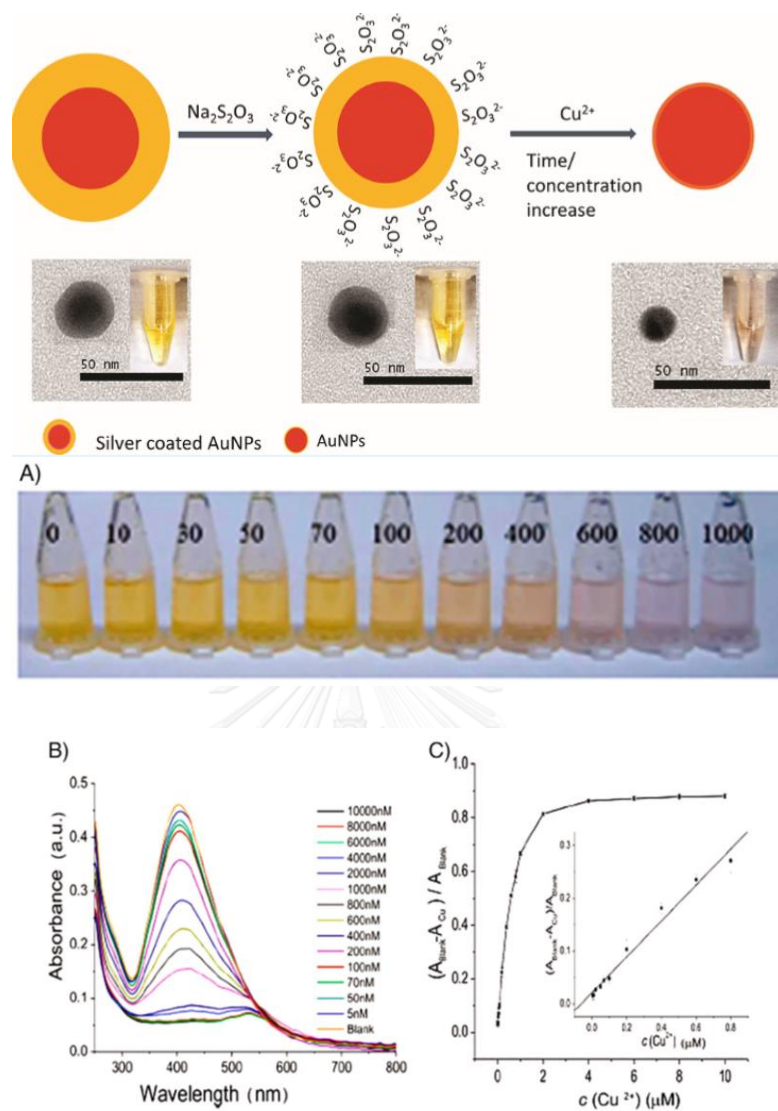
Figure 2.3 The colorimetric sensor for Cu^{2+} detection based on AgNPs coated AuNPs a) Photographs b) Absorption of S$_2$O$_3$$^{2-}$-Ag/AuNP solution on addition of Cu^{2+} and c) plot of colorimetric titration of Cu^{2+}

2.3 Nanoscience

Nanoscience is a branch of science studying materials in Nano-scale (1 nanometer (nm) is equal to one in billion meter and is about 100 nanometres or smaller) and relates to many fields of science such as physics, chemistry and biology [25]. It can be divided into many sub-branches; for example, nanoelectronics [26, 27], nanomedicine [28], bionanotechnology [29], nanosensor [30], nano-catalyst [31], nanoprocess [32] and etc.
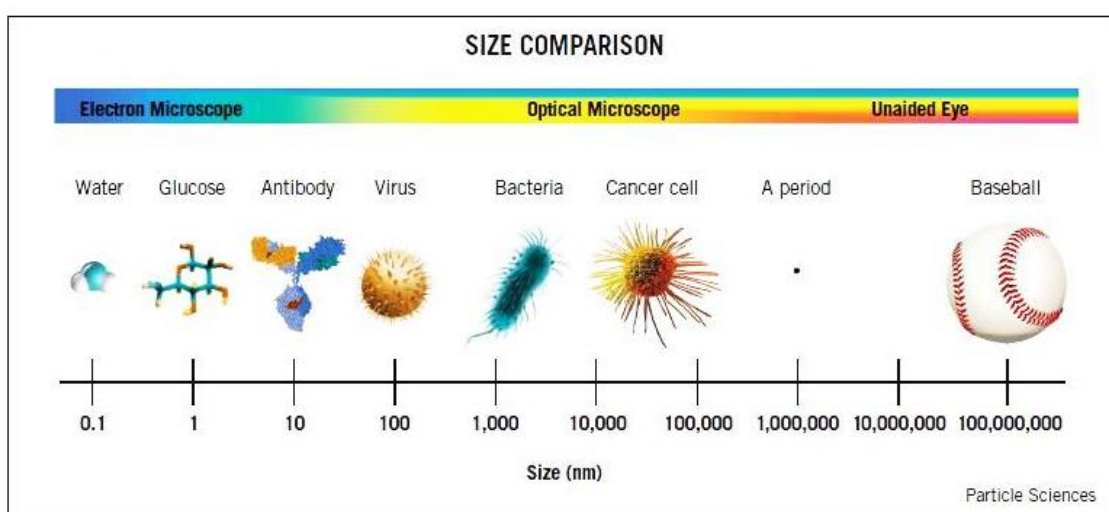
Figure 2.4 Size comparison in Nano-scale

Nanoparticles (NPs) are particles between 1 and 100 nanometers in size and are classified on its dimension, morphology, composition, and agglomeration and etc. as shown in Figure 2.5. For this work, gold nanoparticle is employed for the fabrication of sensor.
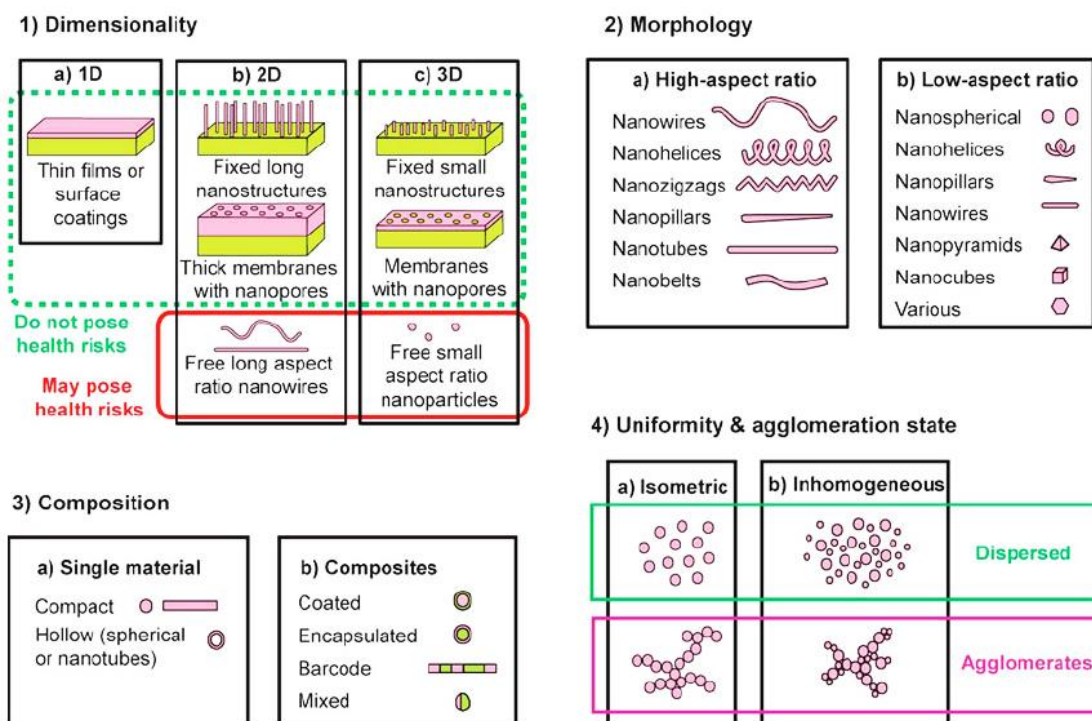
Figure 2.5 Classification of nanostructured materials

2.3.1 Localized Surface Plasmon Resonance (LSPR)

Surface plasmon resonance (SPR) is the basis for measuring adsorption of material onto surfaces of metal nanoparticles. It is a phenomenon that happens from resonant oscillation of electrons at interface by incident light. This oscillation can give a strong plasmon band that localizes surface plasmon resonance (LSPR). It can be changed by type of elements, particle shapes, ad sizes. This phenomenon can be applied to detect a compound both qualitatively and quantitatively [33]. The surface modification of nanoparticle is shown in figure 2.4.
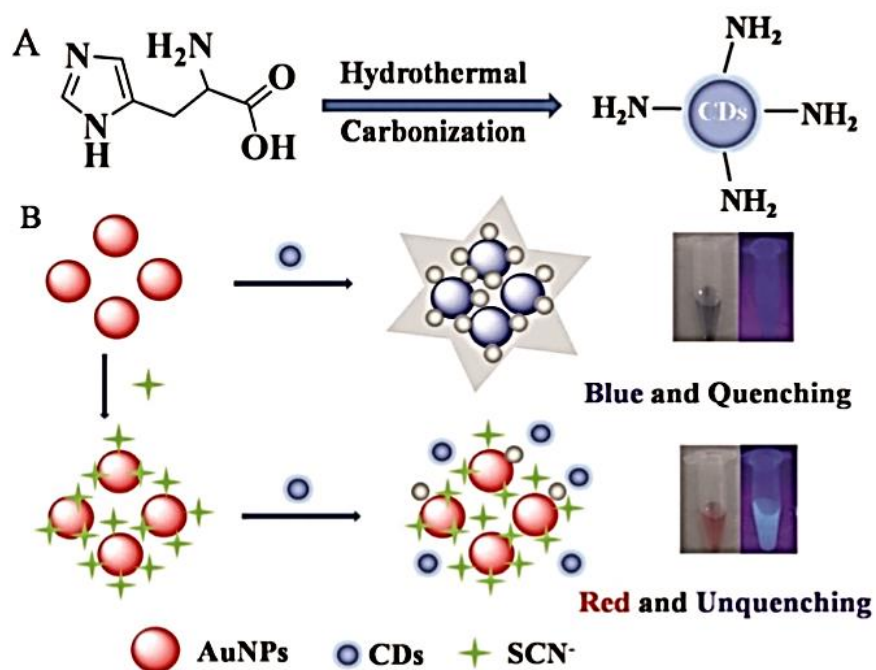
Figure 2.6 The surface modification of nanoparticle for SCN⁻ detection (A) the synthetic process of amino-functionalized carbon dots (CDs) and (B) the mechanism of the dual-readout nanosensor for SCN⁻ detection.

2.3.2 Gold nanoparticles (AuNPs)

The general form of Gold nanoparticles (AuNPs) is truncated cuboctahedron. However, other forms such as dodecahedron and icosahedron can be found. Normally, gold has yellow color because it can absorb the blue light. But AuNPs appear in different colors based on its size. This can be explained by surface plasmon resonance (SPR) phenomenon. This phenomenon is related to charge density wave from oscillation of free electron at the interface and can be controlled by shape, size and surrounding [34, 35]. AuNPs with different sizes are presented in Figure. 2.7.

Figure 2.7 Colors of various sized monodispersed gold nanoparticles

The surface chemistry of metal atoms has a role to their chemical and physical properties. Generally, metal surface is modified by interacting with donor-acceptor ligands related to metal complexes. The interaction of gold nanoparticles under the light is strongly dictated by environment, size and physical dimensions. Oscillating electric fields of a light ray interacts with the free electrons that are in resonance with the frequency of visible light. These oscillations are known as surface plasmons. For smaller gold nanoparticles of around 30 nm, the surface plasmon resonance phenomenon absorb the light in the blue to green range of the spectrum, so the red light can be reflected and its color is rich red. When the particle size increases, the wavelength of surface plasmon resonance absorption shifts to longer wavelengths and red light is absorbed, so the blue light is reflected and the color appear pale blue or purple. It means that optical properties of AuNPs depend on their size, shape and color because of individual spherical aggregation and electromagnetic properties are influenced by degree of dispersion and proximity.

The applications of gold nanoparticles (AuNPs) include electronics conductors from printable inks to electronic chips, photodynamic therapy for killing tumor cells in a treatment also known as hyperthermia therapy. Moreover, it is also employed in the fabrication of sensors for the detection of proteins, pollutants, and other molecules label-free, and as well as probes for transmission electron microscopy, and for detection biomarkers in the diagnosis of heart diseases. In addition, AuNPs is also used to fabricate sensor to detect cancers, infectious agents, and utilized as catalyst for selective oxidation as well as for fuel cell applications.

2.3.3 Modification of nanoparticles (NPs)

The modification of the surface of nanoparticles is important and challenging because metal nanoparticles possess unique features compared to equivalent larger-scale materials. The method for surface modification of AuNPs with small molecules was developed and used in many applications such as bio-sensing. The metal nanoparticles such as AuNPs were functionalized with small molecules to improve the stability, sensitivity, and selectivity for biochemical detection. It is important to summarize the strategies for surface modification of AuNPs with small molecules. Thus, this recent progress was focused on the surface chemistry for functionalization of AuNPs with small molecules including click chemistry, ligand exchange strategy, and coordination-based recognition [36].

The gold nanoparticles have numerous application in various fields, such as catalysis, chemical sensing, bio-labeling or photonics. Biological applications of gold nanoparticles are used because of a good oxidation resistance, easy synthesis and optical properties. The metal nanoparticles were modified by other compounds that will be provided in the following sections.

Thiols and disulfides, can be used to modify metal nanoparticles because organosulfur groups strongly coordinate to various metals, such as Ag, Cu, Pt, Hg, Fe, or Au. Sulfur possesses a huge affinity for metal surfaces. Moreover, the interaction between the metal-sulfur is also sufficiently strong to immobilize the thiol groups on the surface of metal nanoparticles. However, when the thiol functional is oxidized to sulfate or sulfonate, the interaction with gold will decrease. Thiol- or disulfide-capped nanoparticles can be prepared by two methods. First, sulfur compounds were grafted on the surface of resynthesized nanoparticles covered by solvent molecules which will be replaced by the sulfur containing ligands [37].

The second approach is the synthesis of an organosulfur-capped nanoparticle in a one-step process, where the metal precursor and the protective ligand are reacted simultaneously. In this case, two processes compete with each other. Chemisorption of thiols on the metal surface occurs with concomitant cleavage of the S–H bond. For carboxylic acids, the metal surfaces interact with negatively charged carboxylate groups by deprotonation of carboxylic acids [37].

For phosphines, the gold nanoparticles were protected by triphenylphosphine after the modification. The phosphine interaction with the metal nanoparticle is very weak and thus results in a very poor stability. The lack of stability results in an easy exchange with other ligands, which are more strongly bonded to the metal surface such as the thiol exchange and amine exchange [37].

And for amines and ammonium ions, it is generally applied to stabilize the particles. The Pd nanoparticles modified with hexadecylamine leads to a better dispersion and stability of the particles. The interaction between amino groups and metal nanoparticle surfaces is much weaker than those of thiol groups because the amine-modified nanoparticles are bigger and weaker than organosulfur-modified. Nevertheless, ammonium ions, having shorter chain lengths of 4–8 carbons, have also been used to stabilize transition metal nanoparticles. When the metal nanoparticles were synthesized electrochemically, the ammonium surfactant will serve as electrolytes stabilizer [37].

2.4 Literature survey

2.4.1 Conventional methods for formaldehyde detection

There are many analytical methods to determine formaldehyde such as high preperformance liquid chromatography (HPLC), gas chromatography–mass spectrometry (GC-MS), fluorescence spectrometry and colorimetric methods. These methods are illustrated below.

In 2007, Jianrong Li et al. [6] demonstrated the method of high performance liquid chromatography for formaldehyde's determination in aquatic products using 2,4-dinitrophenylhydrazine (DNPH) as a derivatizing agent. Formaldehyde in aquatic products was separated by steam distillation and the detection limit of this approach was found to be 8.92 μg L^{-1}. This method provided a rapid detection, high precision and high accuracy.

In 2009, Xiao-Qing Zhao et al. [38] developed a new analytical methodology for the identification and quantification of formaldehyde in beverage and dried food. The flow injection fluorometry based on microwave on-line accelerating Hantzsch reaction with cyclohexane-1,3-dione gave a high sensitivity and rapid detection. This developed method was successfully applied to food analysis without requiring any sample pretreatment. This method was applicable to detect formaldehyde content in the range from 0.05 ng mL^{-1} to 2.000 ng mL^{-1} and the detection limit obtained as low as 0.02 ng mL^{-1}.

In 2012, Ho-Sang Shin et al. [2] demonstrated a method of consecutive headspace solid-phase micro-extraction for the pre-concentration and separation of formaldehyde in fermented foods by gas chromatography-mass spectrometry. 2,2,2 trifluoroethyl-hydrazine (TFEH) in a headspace vial was used for the derivatization. The formaldehyde derivative was simultaneously vaporized and adsorbed onto carboxen–polydimethylsiloxane. A detection limit of this approach was found to be 0.1 μg kg^{-1} and linearity was in the range of 0.050 - 0.500 mg kg^{-1}. The methods provided simplicity to the elimination of matrix inferences in fermented foods and automatic method for formaldehyde detection.

In 2014, Lung-Ming Fu et al. [4] developed a novel fabrication of microfluidic chip by commercial CO_2 laser system with charge-coupled device (CCD) camera for formaldehyde determination. In their work, a microfluidic chip devices had a three-layer polymethyl methacrylate (PMMA) for mixing the analyze and fluorescence derivatization reagent (Fluoral-P) to produce 3,5-diacetyl-1,4-dihydrolutidine (DDL) and the fluorescence intensity was recorded by CCD camera. This provided a rapid and reliable tool for selective formaldehyde detection in the range of 1 – 50 ppm.

In 2016, Zhifen Deng et al. [9] developed a novel method using derivatization and solid-phase extraction (SPE). It was integrated into a novel calixarene SPE sorbent: tetraazacalix[2]arene[2]triazine bonded silica gel. Specifically, 2,4-dinitrophenylhydrazine was adsorbed onto the sorbent in advance, based on the charge-transfer interaction between the macrocyclic molecule and nitrobenzenes. This method used high performance liquid chromatography that can separate and react at the same time. Using UV-Vis spectrophotometry, formaldehyde can be determined as low as 3.0 ng mL^{-1} and linearity of formaldehyde determination within 0.080–3.2 μg mL^{-1} were reported.

Although, these conventional methods were able to achieve highly selective, sensitive and accurate quantification of formaldehyde, they are either expensive, complicated or time-consuming. Therefore, the colorimetric method has been widely used as an alternative for such determination recently.

2.4.2 Colorimetric method for formaldehyde detection

In 2008, Vladimir A. Sibirny et al. [39] used alcohol oxidase (AO), 3-methyl-2-benzothiazolinone hydrazone (MBTH) and ferric chloride for the analysis of methanol and formaldehyde in mixtures by flame-ionization detector. A detection limit of this approach was found to be 30 ng L^{-1} for formaldehyde. This method provides simplicity, selectivity and elimination of matrix interferences in waste water.

In 2009, April A. Hill et al. [40] presented a colorimetric method for the determination of formaldehyde in drinking water using solid phase extraction (C-SPE). The sample was passed through a cartridge containing sodium hydroxide to adjust pH and react with 4-amino-3-hydrazino-5-mercapto-1,2,4-triazole (purpald) to form colorimetric complex. The formaldehyde was detected by diffuse reflectance spectroscopy. This proposed method was used to measure formaldehyde in the range of $0.08 - 20$ mg L^{-1} with significantly reduced chemical consumption.

Xuan Weng et al. [41] designed and fabricated a microfluidic chip heated polydimethylsiloxane (PDMS). The proposed method was based on the reaction with acetylacetone in the presence of ammonium acetate to form yellow complex of 3,5-diacetyl-1,4-dihydrolutidine and it was detected by a digitized CCD camera. The limit of detection was found to be 2 µg mL^{-1}. This method are provided a rapid, low sample consumption, low-cost and multi-sample detection.

In the same year, Liang Feng et al. [13] successfully used a common pH indicator in the presence of primary amine on poly(ethylene glycol) (PEG) polymer for formaldehyde detection. This method provided a rapid, highly sensitive, and quantitative method for the portable monitoring of formaldehyde in the range of 250 ppb to 20 ppm.

In 2011, Julien A. Jendral et al. [42] reported a screen testing for formaldehyde using the purpald followed by chronotropic acid and detected by UV-Vis spectrophotometry. This method was used to detect the formaldehyde in alcoholic beverages as low as 0.09 mg L^{-1} and provided a simple, reliable and inexpensive measurement.

In 2013, Xueqin Wang et al. [43] described a new optical sensor using nano fibrous membranes to determine formaldehyde based on 4-amino-3-penten-2-one (fluoral-p) functionalized electrospun polyacrylonitrile (PAN) (PAN/fluoral-p). This naked-eye sensor provided a high sensitivity using UV-Vis spectrophotometry and can detect formaldehyde as low as 40 ppb with excellent selectivity towards formaldehyde.

From Previous researches, many colorimetric methods were developed for selective and sensitive for formaldehyde determination. However, the developed methods were complicated, operated with long analysis time and required the expensive instrument. Hence, the colorimetric assay based on metal nanoparticles has attracted increasing attention as a result of their simplicity, outstandingly prompt measurement and adequate miniaturization of the sensing devices with high sensitivity and selectivity.

2.4.3 Metal nanoparticles-based colorimetric methods for formaldehyde detection

In 2013, Md Alauddin et al. [44] successfully modified a sensor for the first time that used metal nanoparticle to detect formaldehyde. The colorimetric detection of AuNPs for detection of formaldehyde was investigated by using UV-Vis, TEM, and Raman spectroscopy. The AuNPs was prepared by laser ablation of a solid gold target in water. Aggregation of AuNPs was begun upon the addition of saturated formaldehyde to a solution of AuNPs because chemisorption of diol molecules in formalin on the AuNPs surfaces by formation of Au-O···H bonds. The surface plasmon resonance (SPR) band at 519 nm for AuNPs solution decrease and shifted to red while a new SPR band appeared at ~700 nm. The red-shift was increased with incubation time. The average size of the initial AuNPs was 12 nm but it increased to 23 nm after the addition of formaldehyde. This method was successfully used for the formaldehyde detection. However, the method was not sensitive and selective.

In 2014, Jing-bin Zeng et al. [14] developed a colorimetric assay based on nanotechnology involving Tollens reaction. The AuNPs were synthesized and immobilized into an agarose gel. After formaldehyde react with Tollens reagent to produce silver nanoparticles (AgNPs) to coat on the AuNPs surface, there have color change from colorless to light yellow along with the appearance of a surface plasmon resonance (SPR) band at 416 nm. A UV-Vis spectrometer was able to determine formaldehyde in the range of 0.1 – 40 mM and the limit of detection was found to be 50 nM.

In 2015, Jin-Mei Lin et al. [45] developed a colorimetric assay based on reduction of Ag^+ to Ag on the surface of gold nanorods (AuNRs). The AuNRs was used to formaldehyde detection in the presence of glycine and sodium hydroxide. Using a UV-Vis spectrometer can determination of formaldehyde in the range of $0.20 \times 10^{-9} - 14.0 \times 10^{-9}$ g mL^{-1}. and limit of detection were found to be 6.3×10^{-11} g mL^{-1}.

From previous studies, the nanoparticles-based colorimetric assay has been demonstrated as a potential analytical tool for the detection of formaldehyde. Therefore, the aim of this work is to develop a paper-based colorimetric assay for the determination of formaldehyde using 4-aminophenyl sulfone modified gold nanoparticles surface and to apply the developed method for the determination of formaldehyde in real food samples.

2.4.4 Fabrication of paper-based for colorimetric method

The fabrication methods of paper-based devices such as wax patterning, inkjet printing, photolithography, plotting and laser treatment can divide into two categories based on their physics and chemistry. The physical methods offer low cost, while the chemical methods offer high resolution as shown in table 2.1. However, in this work focused on the wax patterning because wax patterning offers low cost, simple, and fast fabrication as well as mass production. The wax patterning is classified as a physical method. Wax has been widely used in the fabrication of paper-based because it is a cheap hydrophobic material and it can be applied to paper by a variety of methods. In 2009, Lin et al. and Whitesides et al. reported a new method, wax printing. This method used a wax printer to print wax on filter paper in a designed pattern. After printing, the wax was melted in an oven. Due to the porous structure of the filter paper, the wax penetrates into the paper to form hydrophobic wall on the paper. This process is very simple and requires only a wax printer and an oven shown in figure 2.8. However, the resolution of the paper-based fabricated by this method is limited to millimeters. After that, Whitesides et al. reported a similar method and established a model for the melt rate of wax in the filter paper. In 2012, paper-based devices were fabricated by printing wax was used to print for the both

side of paper-based devices. The wax was printed as hydrophobic barriers to block the analyte solution, while the other side of the paper as a seal [46]. This method, the analyte solution can be protected from contamination or leakage.

Table. 2.1 The comparison of fabrication methods for the paper-based devices

Method	Material and reagents	Advantages	Disadvantages
Wax printing or dipping	Wax	Low cost, simple, fast and mass production	Low resolution and need to be heated
Plotting	PDMS, wax or marker	Low cost, flexible and easy to fabricate	Low resolution and complex feature
Inkjet etching	Polystyrene	Low cost and directly biochemicals printing	Complex steps
Flexographic	Polystyrene	Mass production	Expensive cost, complex reagents and templates
Laser-based direct-write	Light-sensitive polymer	High resolution and complex pattern	High cost, and complicated to operate
FFSL	PDMS	Low cost, simple and fast to fabricate	Low resolution

Table. 2.1 The comparison of fabrication methods for the paper-based devices (Continue)

Method	Material and reagents	Advantages	Disadvantages
Photolithography	SU8-2010 or TiO_2	High resolution and mass production	Expensive equipment and complex steps
Ink stamping	Paraffin	Low cost and easy to fabricate	Low resolution, need a special stamp
Lacquer spraying	Acrylic lacquer		Difficult mass production, poor resolution and biological compatibility
Screen-printing	Wax or polystyrene	Simple, low cost, mass production and high resolution	Complex steps, low resolution
Inkjet printing	AKD or UV curable acrylate		Need to use an improved inkjet printer
Plasma treatment	AKD or fluorocarbon	Low cost	High cost, need to make different metal masks
Vapor-phase deposition	Poly(chloro-p-xylene)	Simple steps and complex pattern	Expensive and need a metal mold

Table. 2.1 The comparison of fabrication methods for the paper-based devices **(Continue)**

Method	Material and reagents	Advantages	Disadvantages
Plasma treatment	AKD or fluorocarbon	Low cost	High cost, need to make different metal masks
Wet etching	Octadecyltrichlorosilane	Two-steps, simple and fast steps	Need a paper mask with special design and expensive
Hand-held corona treatment		Simple steps and low cost	Need to be heated
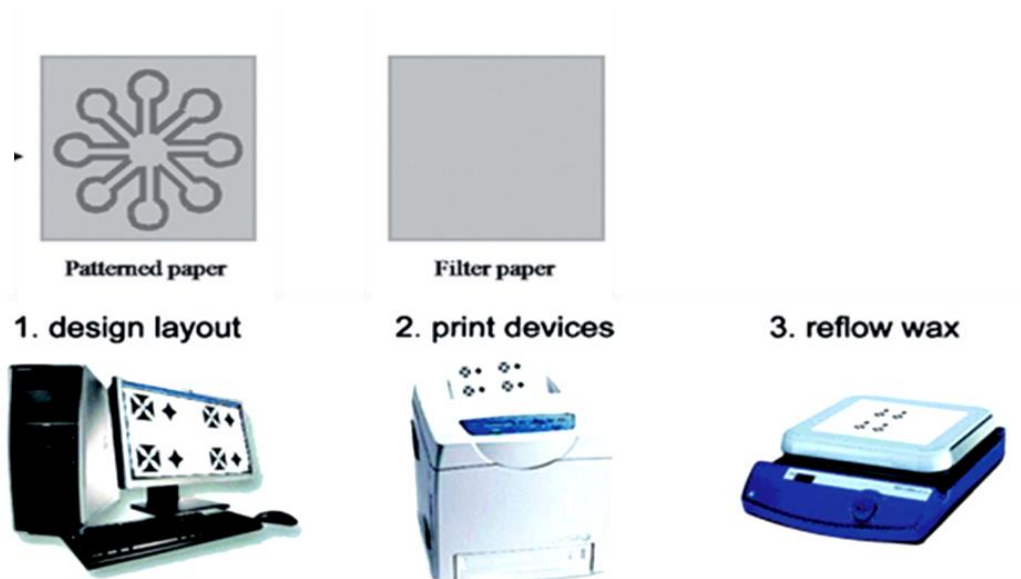
Figure 2.8 The process of Wax printing.

CHAPTER III

EXPERIMENTAL

This chapter describes the equipment and instruments, the chemicals, the chemical preparation, sample preparation and detection method used in this work

3.1 Equipment and instruments

The equipment and instruments for surface modification of AuNPs and formaldehyde detection are listed in table 3.1

Table 3.1 List of equipment and instruments for surface modification of AuNPs and formaldehyde detection

Equipment/instruments	Suppliers
Autopipette	Eppendorf, Germany
Cuvette quartz cell, 1 cm	
Digital camera	Canon EOS 1000D, Taiwan
Fourier transform infrared spectroscopy, Nicolet 6700	Nicolet, USA
Freeze dryer, Freezeone 77520	Labconco, USA
Hettich centrifuge, Universal 320 R	Hettich, Germany
Hot plate	IKA, Germany
Microcentrifuge tubes and tips	Axygen Scientific, USA
Milli-Q Water System, R ≥ 18.2 MΩcm^{-1}	Merck Millipore, Germany
Nylon (pore size 0.45 µm, diameter 13 mm)	
Timer	Samsung, China
Transmission electron microscope, JEM-2100F	JEOL, USA
UV-Visible spectrometer, HP, HEWLETT PACKARD 8453	Agilent Technologies, UK
Volumetric flask and other glassware	SCHOTT, Germany
Vortex mixer	Scientific Industries, United States
X-ray Photoelectron Spectrometer, AXIS ULTRA	KRATOS ANALYTICAL, UK

3.2 Chemicals

The Chemicals for surface modification of AuNPs and formaldehyde detection are listed in Table 3.2

Table 3.2 List of chemicals used for surface modification of AuNPs and formaldehyde detection

Chemicals	Suppliers
2-propanol	Merck, Germany
4-Aminophenyl sulfone,	Sigma-Aldrich, USA
Acetaldehyde	Sigma-Aldrich, Switzerland
Acetone	Merck, Germany
Acetylacetone	Fluka, Switzerland
Ammonium acetate	Sigma, Germany
Benzaldehyde	Sigma-Aldrich, Belgium
Calcium chloride	M&B, England
Colloidal Gold, 20 nanometers	Kestrel Bio Sciences, Thailand
Ethanol	Merck, Germany
Ethyl acetate	ACI Labscan, Thailand
Formaldehyde	BDH, England
Hydroxylamine hydrochloride	Sigma-Aldrich, Germany
Methanol	Merck, Germany
Potassium chloride	Merck, Germany
Sodium bicarbonate	M&B, England
Sodium chloride	Carlo ERBA, France
Acetic acid	Merck, Germany

3.3 Chemical preparation

3.3.1 Preconcentration of gold nanoparticles

The preconcentration of gold nanoparticles was obtained by pipetting stock solution of gold nanoparticles into 2 mL of microcentrifuge tubes. After that, the tubes were centrifuged at 12,000 rpm (4°C) for 30 minutes. The 1.667 mL of supernatant was removed and the mixture solution was stirred for 10 seconds.

3.3.2 A stock solution of 4-aminophenyl sulfone

A stock solution of 4 mM 4-aminophenyl sulfone was done by weighing 24.83 mg of 4-aminophenyl sulfone and adding into Milli-Q water. The mixture was boiled at 80°C for dissolution. After that, the solution was transferred a volumetric flask and adjusted to final volume of 25 mL.

3.3.3 A stock solution of hydroxylamine hydrochloride

A stock solution of 20 mM hydroxylamine hydrochloride solution was prepared by weighting 13.90 mg of hydroxylamine hydrochloride, dissolving in Milli-Q water and adjusting to the final volume of 10 mL.

3.3.4 A primary stock solutions of chemicals.

A primary stock solution of chemicals including methanol, ethanol, 2-propanol, acetone, acetaldehyde, benzaldehyde, formaldehyde, sodium chloride, calcium chloride, potassium chloride and sodium bicarbonate were prepared by pipetting or weighing the given amount listed in table 3.3 into Milli-Q water and adjusting to the final volume with volumetric flask.

Table 3.3 List of chemicals including methanol, ethanol, 2-propanol, acetone, acetaldehyde, benzaldehyde, formaldehyde, sodium chloride, calcium chloride, potassium chloride and sodium bicarbonate used to prepare the primary stock solutions.

Stock solutions	Concentration (g/L)	Pipetting (mL)	Weighing (g)	Final volume (mL)
Methanol	200	2.534	-	10
Ethanol	200	2.544	-	10
2-propanol	200	2.550	-	10
Acetone	40	0.507	-	10
Acetaldehyde	40	0.512	-	10
Benzaldehyde	2	0.019	-	10
Formaldehyde	6	0.199	-	10
Sodium chloride	2	-	0.02000	10
Calcium chloride	2	-	0.02000	10
Potassium chloride	2	-	0.02000	10
Sodium bicarbonate	2	-	0.02000	10

3.4 Surface modification

The modified-AuNPs was prepared by mixing 0.10 mL of 4-aminophenyl sulfone and 1.50 mL of the preconcentrated AuNPs solution. After that, the mixture solution was stirred for 15 minutes to ensure a complete self-assembly of 4-aminophenyl sulfone onto the surface of AuNPs.
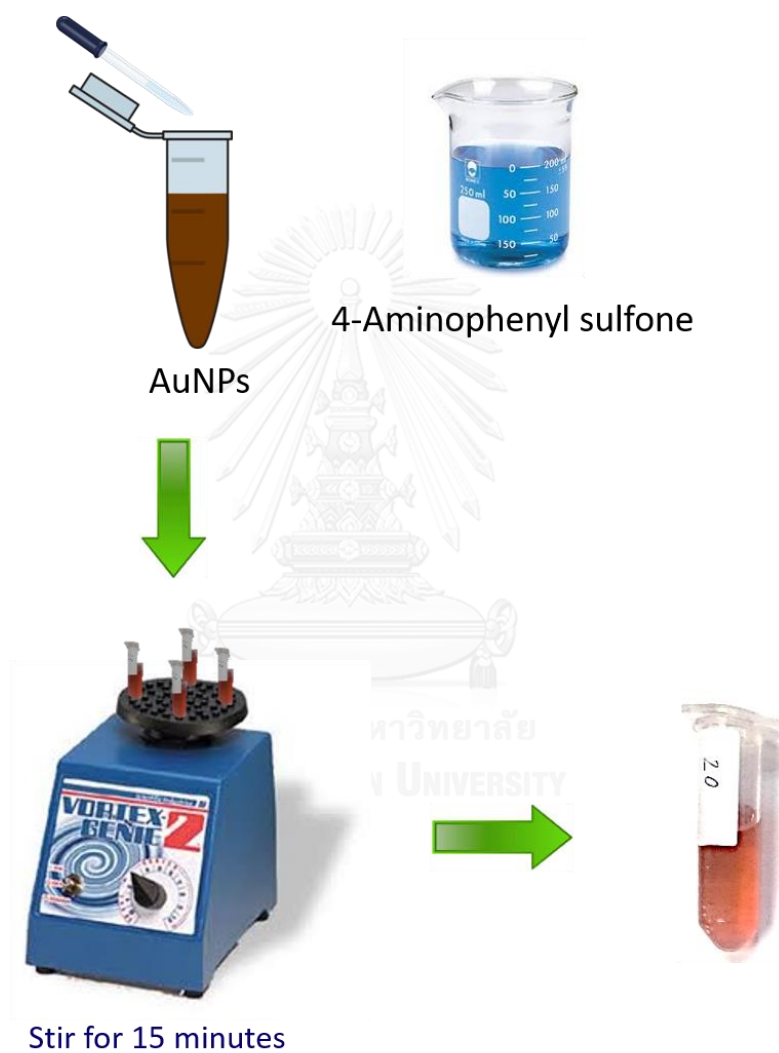
Figure 3.1 Schematic diagram for the surface modification of AuNPs with 4-aminophenyl sulfone

3.5 Fabrication of paper-based device

A portable formaldehyde detection device was fabricated on a filter paper using wax printing method, and the pattern was designed using Microsoft Power Point. The fabrication process includes three steps. First, the wax pattern was printed on the filter paper (Whatman no. 1) using the wax printer (Xerox Color Qube 8570, Japan). Second, the wax on printed paper was melted on a hot plate at 175 °C for 40 seconds. The wax covered area was hydrophobic, while the area without wax was hydrophilic as detection area. Finally, the tape was attached to the back side of the printed paper to prevent leakage. Using this process, the paper based devices can be fabricated within 2 minutes.

In this work, the paper-based device was designed in circle shape with 8 mm diameter detection zone and green color with RGB color is 000 255 000 for case of background cut off in imageJ software. After melting the wax, the detection zone was reduced to 7 mm. The maximum amount of liquid that can be contained in the detection zone is 100 µL as shown in figure. 3.2.
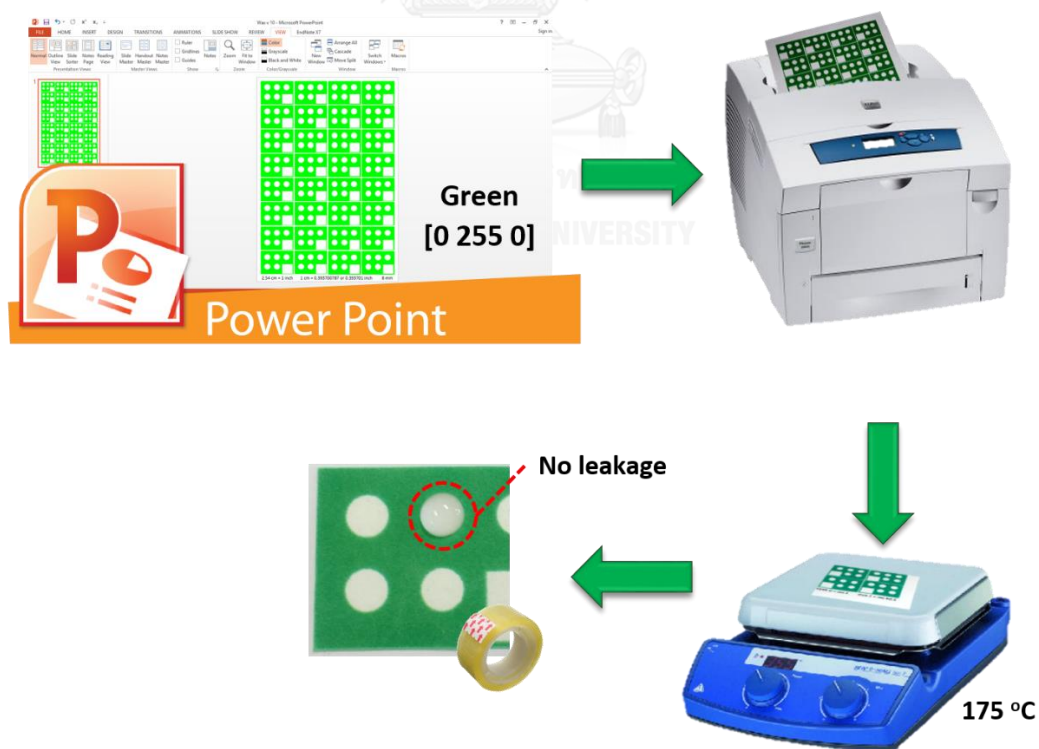
Figure 3.2 The fabrication of paper based devices.

3.6 Optimization parameter

      The colorimetric detection of formaldehyde was performed at room temperature by sequentially dripping of 4-aminophenyl sulfone-AuNPs, formaldehyde and hydroxylamine hydrochloride on the paper based-devices at the ratio 2 : 2 : 1, respectively. The Δ red intensity was measured by using digital camera (Canon EOS 1000D, Taiwan) to capture the picture and imageJ software for calculating the red color intensity with computer set shown in figure 3.3.
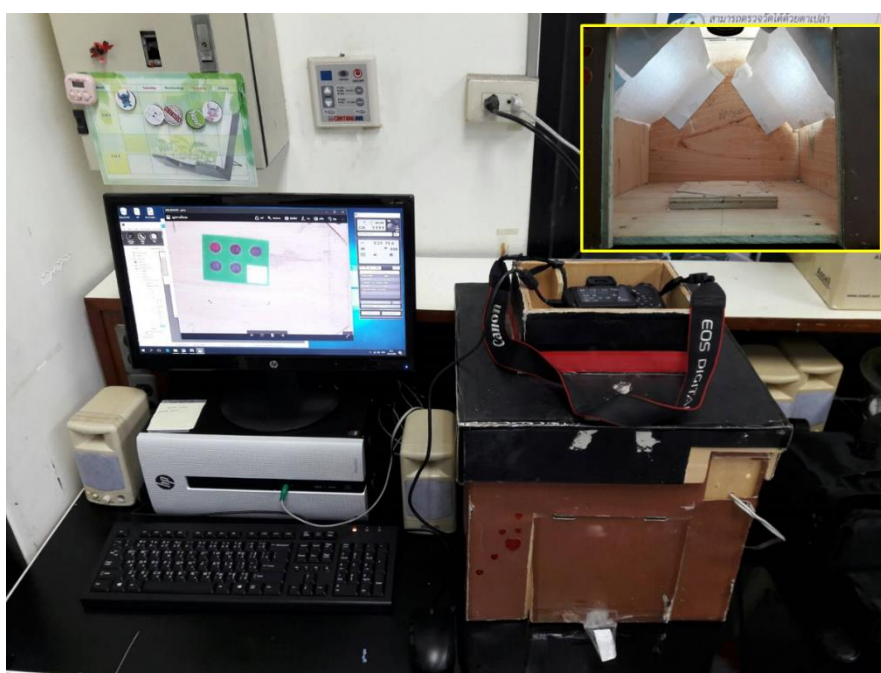
Figure 3.3 Computer set with digital camera (Canon EOS 1000D, Taiwan).

      For the optimization of formaldehyde detection, 4 significant parameters including the concentration of gold nanoparticles, incubation time, concentration of 4-aminophenyl sulfone and concentration of hydroxylamine hydrochloride were investigated. The concentration of gold nanoparticles was varied in the range of 0.01 – 0.10 %w/w. The aggregation of 4-aminophenyl sulfone-AuNPs induced by formaldehyde and hydroxylamine hydrochloride was investigated at various incubation times (1 – 20 minutes). After that, the effect of concentration both of 4-aminophenyl sulfone and hydroxylamine hydrochloride was studied in the range of 0 – 4 mM and 0 – 60 mM, respectively.

3.7 Characterization of 4-aminophenyl sulfone-AuNPs

The incorporation of 4-aminophenyl sulfone onto the AuNPs surface were investigated using fourier transform infrared spectroscopy (FTIR), X-ray photoelectron spectroscopy (XPS) and UV-visible spectroscopy (UV-Vis) for the identification of functional groups, binding energy and absorption measurement, respectively. For FTIR, AuNPs, 4-aminophenyl sulfone and 4-aminophenyl sulfone-AuNPs was initially suspended and then freeze dried. The FTIR spectra was recorded using KBr discs (Perkin Elmer, Spectrum One) with 64 scans at resolution of 4 cm^{-1}. A frequency of 400 - 4,000 cm^{-1} was scanned using lithium tantalate ($LiTaO_3$) detector. For XPS, 4-aminophenyl sulfone-AuNPs was initially suspended and then freeze dried. The XPS spectrum was recorded using X-ray Photoelectron Spectrometer (KRATOS ANALYTICAL, AXIS ULTRA). For UV-Vis, AuNPs, 4-aminophenyl sulfone-AuNPs, 4-aminophenyl sulfone-AuNPs in the presence of formaldehyde, 4-aminophenyl sulfone-AuNPs in presence of hydroxylamine hydrochloride and 4-aminophenyl sulfone-AuNPs in the presence of formaldehyde and hydroxylamine hydrochloride were dilute 10 times and the absorbance were recorded using a UV-Vis spectrophotometer (HEWLETT PACKARD 8453).

In addition, the morphology of AuNPs, 4-aminophenyl sulfone-AuNPs, 4-aminophenyl sulfone-AuNPs in the presence of formaldehyde, 4-aminophenyl sulfone-AuNPs in the presence of hydroxylamine hydrochloride and 4-aminophenyl sulfone-AuNPs induced by formaldehyde in the presence of hydroxylamine hydrochloride were studied using transmission electron microscope (TEM). For the TEM characterization, all solutions were incubated for 5 minutes. After that, a drop of suspension was dried on carbon grid at room temperature and inspected by TEM operated at 200 kV (JEOL Model JEM-2100F).

3.8 Analytical performance

3.8.1 Linearity

The Δ red intensity of 4-aminophenyl sulfone-AuNPs mixed with formaldehyde standard solution was captured and measured using digital camera (Nickon EOS 1000D) and imageJ software, respectively. Under the optimal conditions, the relationship between Δ red intensity of triplicate measurements and concentrations of formaldehyde between 40 – 110 ppm was plotted to observe linear range.

3.8.2 Limit of detection (LOD)

The limit of detection (LOD) was determined by statistical method from the calibration curve in the range of 40 to 110 ppm and calculated from $3SD_{blank}/S$. SD_{blank} is the standard deviation of blank measurement (n=14), and S is the sensitivity of the method obtained as the slope of the linearity.

3.8.3 Limit of quantitation (LOQ)

The limit of quantitation (LOQ) was determined by statistical method from the calibration curve in the range of 40 to 110 ppm and calculated from $10SD_{blank}/S$. SD_{blank} is the standard deviation of blank measurement (n=14), and S is the sensitivity of the method obtained as the slope of the linearity.

3.8.4 Repeatability

The repeatability was studied by eight replicated measurements of the analyte solution. The repeatability was assessed in terms of the relative standard deviation (%RSD), using the following formula:

$$\% \text{ RSD} = \frac{\text{Standard deviation}}{\text{Mean}} \times 100$$

3.9 Interference study

To investigate the selectivity of the colorimetric detection toward formaldehyde using 4-aminophenyl sulfone-AuNPs in the present of hydroxylamine hydrochloride, ten different interfering species including methanol, ethanol, 2-propanol, acetone, acetaldehyde, benzaldehyde, sodium chloride, calcium chloride, potassium chloride and sodium bicarbonate were used to study.

3.10 Sample analysis

The food samples including fresh shrimp, frozen shrimp and shiitake mushroom was weighed and soaked in water (sample 1 g : water 5 g) then filtered with nylon membrane (pore size 0.45 µm, diameter 13 mm) and extracted with mixture of water and ethyl acetate (ratio 1:1 by volume). After that, the aqueous phase was diluted by 10-fold. Under the optimal conditions, the proposed method was applied for the determination of formaldehyde in food samples. The results of this method were validated with UV-Visible spectrophotometry method following the AOAC 964.21 standard method.

CHAPTER IV
RESULTS AND DISCUSSION

4.1 Characterization of 4-aminophenyl sulfone-AuNPs

The characterization of the AuNPs modified with 4-aminophenyl sulfone were performed with FTIR, XPS and UV-Visible spectroscopy for the identification of functional groups, binding energy and absorption measurement, respectively. Figure 4.1 shows the comparison between the IR spectrum of 4-aminophenyl sulfone, AuNPs, and 4-aminophenyl sulfone-AuNPs. The IR spectrum of 4-aminophenyl sulfone (black line) show the characteristic peak of N-H stretches at 3,310 – 3,500 cm^{-1} and the IR spectrum of AuNPs (red line) had the band broadening at the same position. The IR spectrum of 4-aminophenyl sulfone-AuNPs (blue line) had the decreased band broadening especially in the range of 3,300 – 3,500 cm^{-1}, so the characteristic peak of N-H stretches of 4-aminophenyl sulfone at 3,310 – 3,500 cm^{-1} had significantly decreased or disappeared as compared to FT-IR spectra of 4-aminophenyl sulfone-AuNPs. This result indicated that 4-aminophenyl sulfone were successfully modified onto the surface of AuNPs corresponding to similar result in the previous literature report [47].
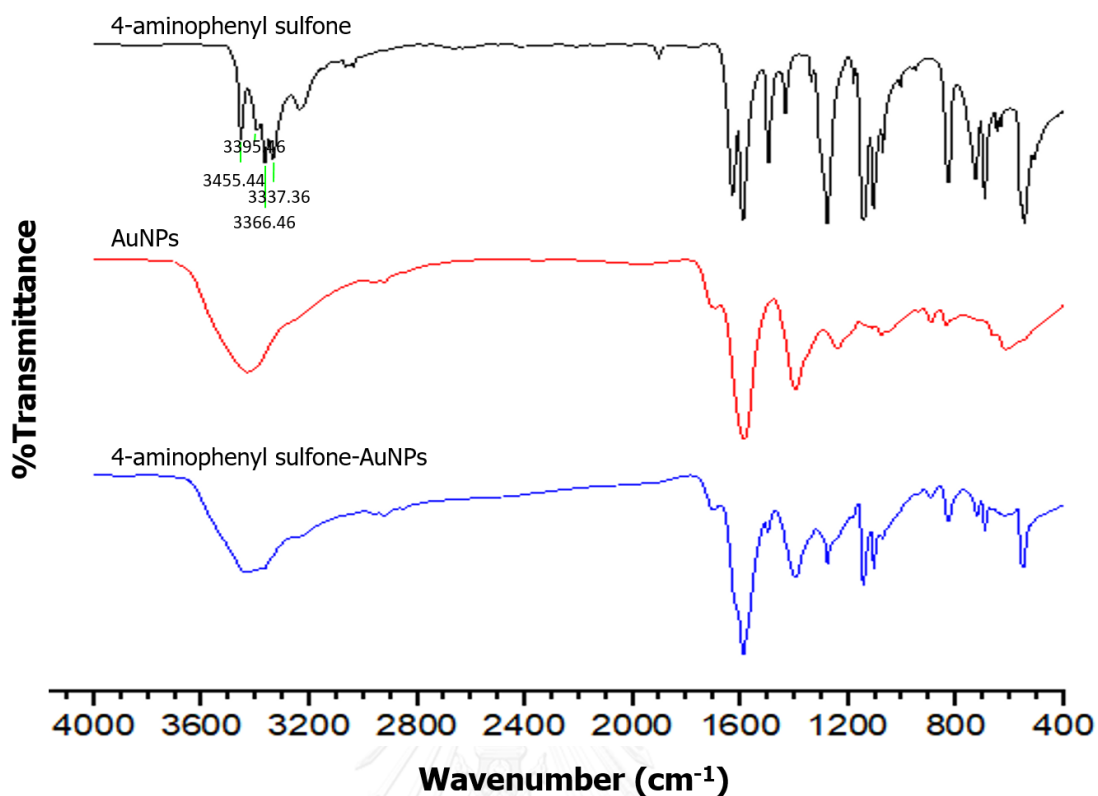
Figure 4.1 FTIR spectra of 4-aminophenyl sulfone (black line), AuNPs (red line) and 4-aminophenyl sulfone-AuNPs (blue line)

To identify the elemental contents in the sample, the XPS analysis was used. The Au 4f bands are recognized as metallic gold. As the obtained results, the Au $4f_{7/2}$ peaks appeared at 83.7 eV (red line) and 84.4 eV (blue line) for the Au and Au bind with positively charged nitrogen (N^+) in organic compound as shown in figure 4.2, respectively. For the N 1s bands (figure 4.3), the appeared peaks at 399.9 eV (red line) and 402.4 eV (blue line) represent -NH_2 and -NH_3^+ binding energy, respectively. That can be assigned to the positively charged nitrogen (N^+) from the viologen species in the nanocomposite.
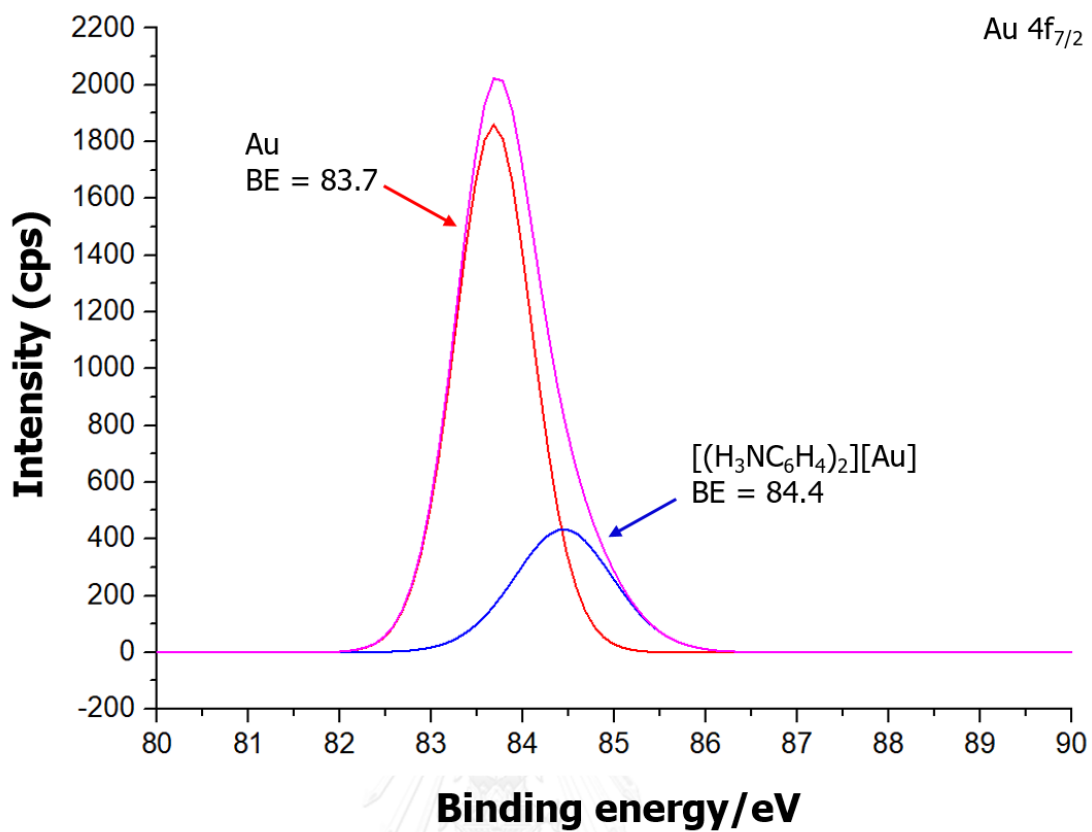
Figure 4.2 Au 4f core level spectra recorded from modified gold nanoparticles with 4-aminophenyl sulfone
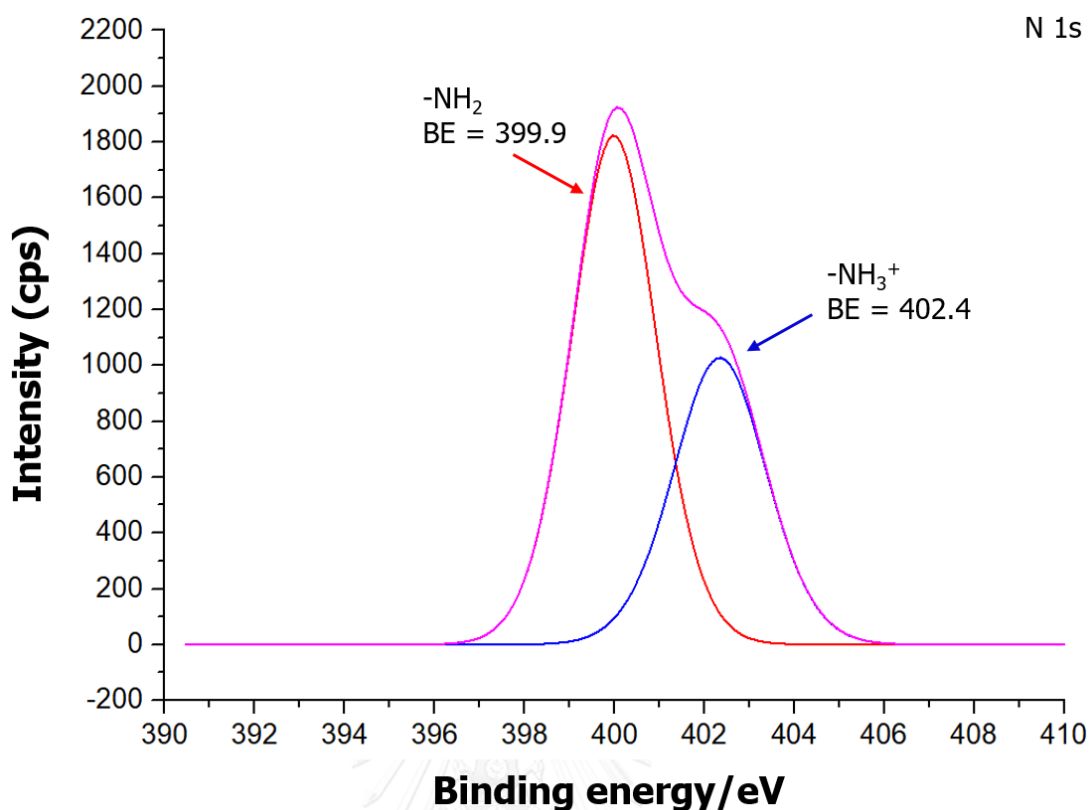
Figure 4.3 N 1s core level spectra recorded from modified gold nanoparticles with 4-aminophenyl sulfone

The localized surface plasmon resonance (LSPR) of AuNP (red line) with the size of 20 nm showed the absorption maxima at 519 nm. The UV-Visible spectra in Figure 4.4 revealed that the localized surface plasmon resonance (LSPR) absorption peak of AuNPs (blue line) was shifted from 519 nm (red line) to 524 nm (blue line) after the addition of 4-aminophenyl sulfone as the modifier. The red-shifted band is mainly caused by the reduction of the plasma oscillation frequency around the nanoparticles due to the binding between amine-containing compounds and the metal nanoparticles [34].
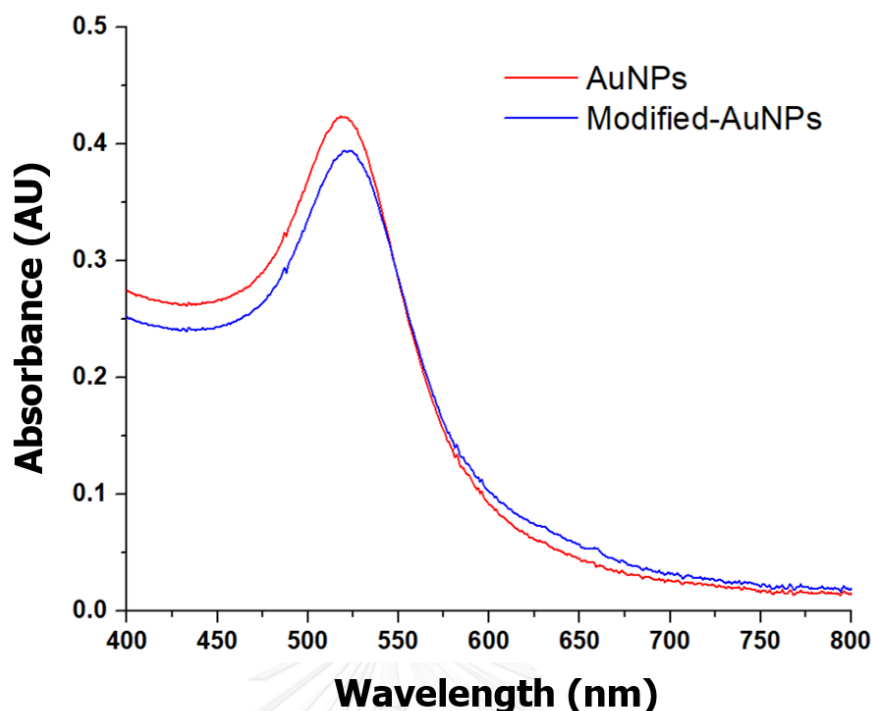
Figure 4.4 Absorption spectra of unmodified AuNPs (red line) and 4-aminophenyl sulfone-AuNPs (blue) in aqueous solution.

From the UV-Visible spectra in figure 4.5, AuNP in aqueous solution showed the maximum absorption at 519 nm as a result of the localized surface plasmon resonance (LSPR) of AuNP (black dot line) and after the modification of AuNPs (black line). The formaldehyde solution was added into the 4-aminophenyl sulfone-AuNPs solution but the maximum absorption at 524 nm did not change (blue line). The formation of 4-aminophenyl sulfone-AuNPs was induced by the addition of formaldehyde and hydroxylamine hydrochloride. It exhibited a decrease in the LSPR absorption peak at 524 nm and formed a new absorption band broadening at 635 nm (red line), and the resulting color and wavelength suggested that the 4-aminophenyl sulfone can induce the aggregation of AuNPs in the presence of formaldehyde and hydroxylamine hydrochloride. In addition, the increasing concentration of formaldehyde affect to the shift of spectrum. When the concentration of formaldehyde was 60 ppm, a little aggregation leading to the absorption peak at 524 nm decreased and a little new absorption band formed at longer wavelength (orange line). Whereas, the higher concentration of formaldehyde at the 100 and 200 ppm caused more aggregation resulting in the absorption peak at 524 nm much more decreased and

a new absorption band formed at longer wavelength with higher absorbance (pink and red line, respectively).
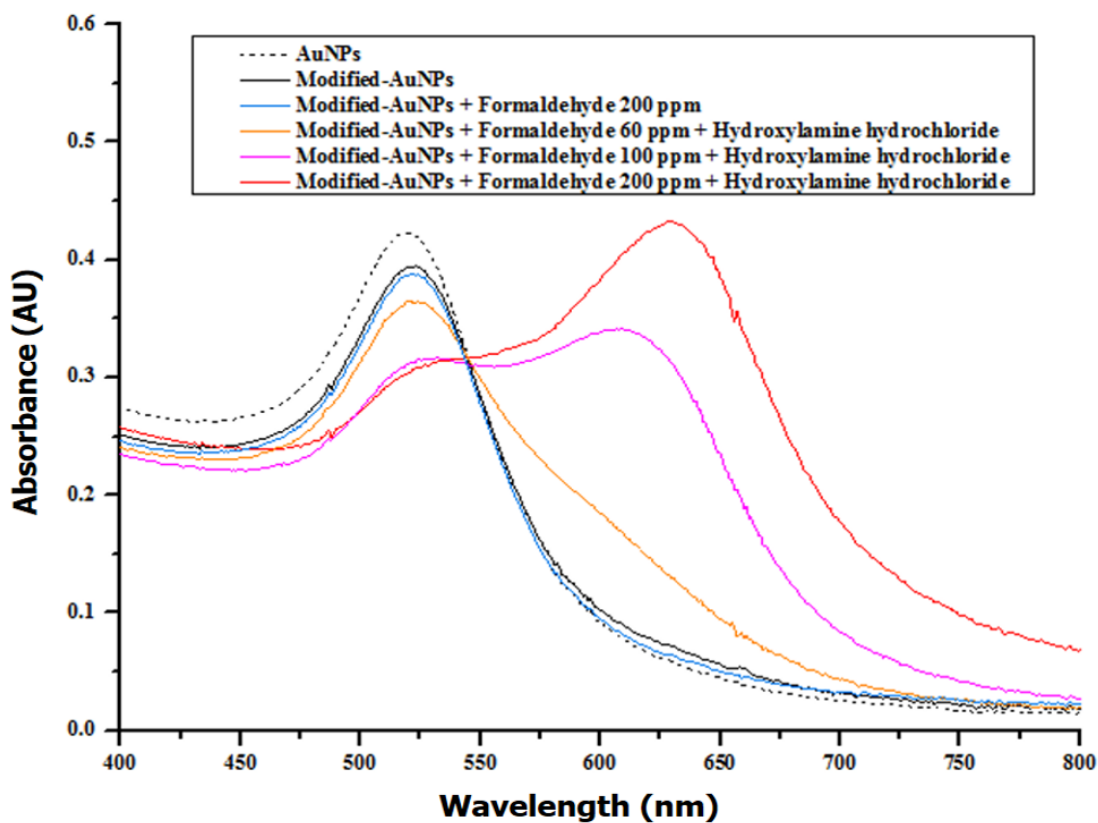
Figure 4.5 Absorption spectra of AuNPs (black dot line), 4-aminophenyl sulfone-AuNPs (black line), 4-aminophenyl sulfone-AuNPs in presence of formaldehyde (blue line) and 4-aminophenyl sulfone-AuNPs in presence of 60, 100 and 200 ppm of formaldehyde after hydroxylamine hydrochloride was added (orange, pink and red line, respectively).

The absorption data by UV-Vis method confirmed to the change of color by naked eyes and it was ascribed to the aggregation process of AuNPs modified with 4-aminophenyl sulfone. When 4-aminophenyl sulfone was added in AuNPs solution, AuNPs were interacted with only one amino position ($-NH_2$) of 4-aminophenyl sulfone and it has the other to react with formaldehyde. The color of 4-aminophenyl sulfone-AuNPs solution can be changed only in the system involved both of formaldehyde and hydroxylamine hydrochloride as schematically demonstrated in figure 4.6.
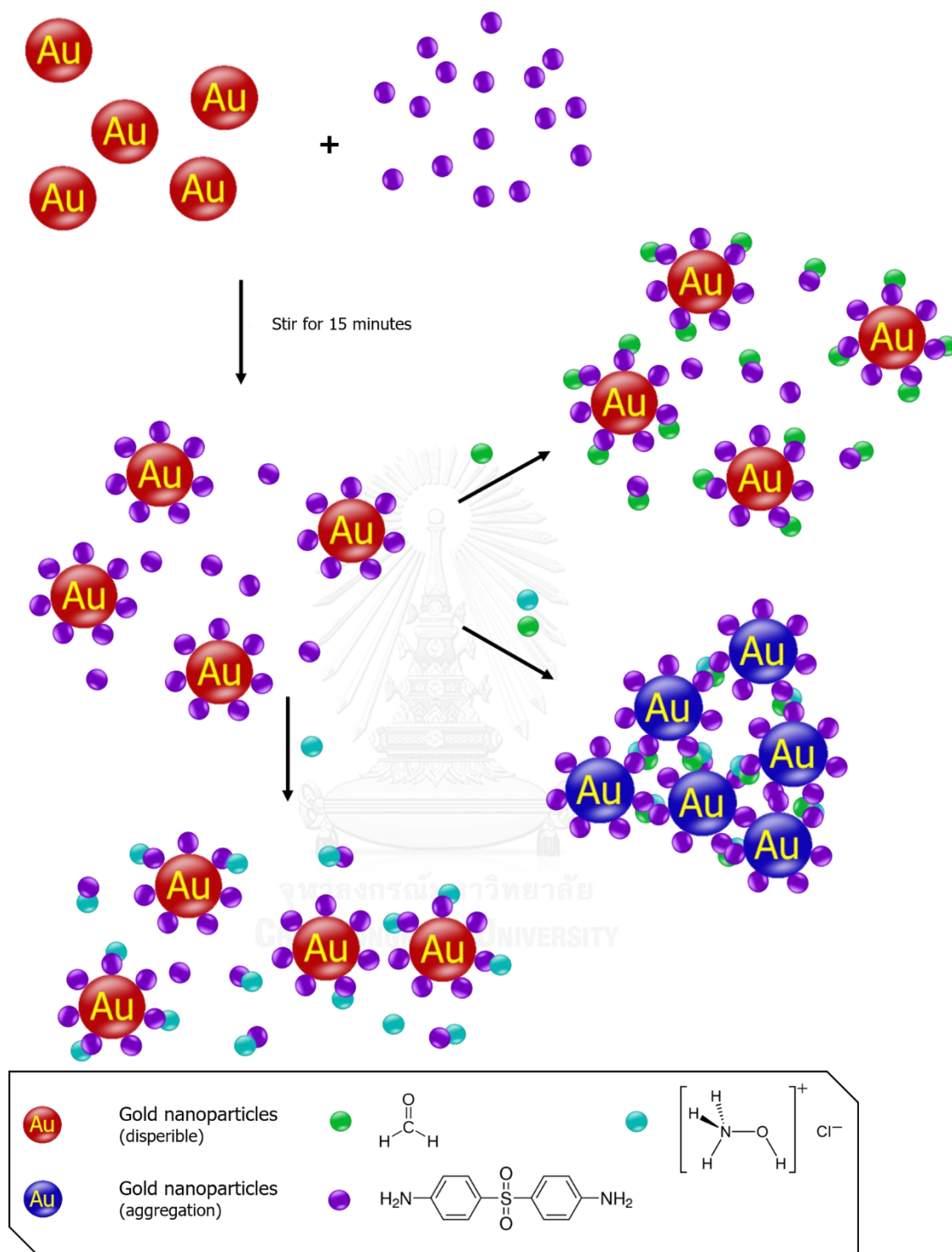
Figure 4.6 Schematic of modification and aggregation process of AuNPs.

4.2 Detection of formaldehyde using paper-based colorimetric device.

After the modification of AuNPs, the colorimetric detection of formaldehyde was performed. In the beginning, 4-aminophenyl sulfone-AuNPs was well dispersed in red color solution. If only formaldehyde or hydroxylamine hydrochloride was added in 4-aminophenyl sulfone-AuNPs solution, the color did not change. When added the both of formaldehyde and hydroxylamine hydrochloride were added, the color changed from red to blue immediately presumably due to the aggregation of 4-aminophenyl sulfone-AuNPs induced by formaldehyde and hydroxylamine as schematically demonstrated in figure 4.6. and figure 4.7

Modified-AuNPs

Modified-AuNPs with Formaldehyde

Modified-AuNPs with Hydroxylamine hydrochloride

Modified-AuNPs with Formaldehyde and Hydroxylamine hydrochloride
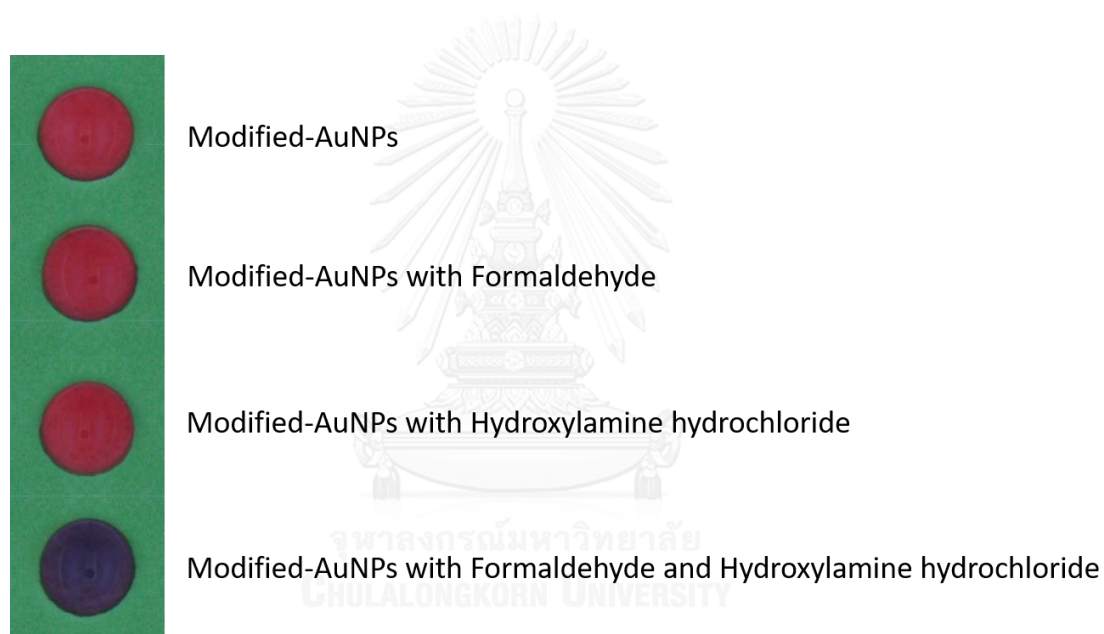
Figure 4.7 The colors of modified-AuNPs; modified-AuNPs in aqueous solution, modified-AuNPs after formaldehyde were added, modified-AuNPs after hydroxylamine hydrochloride were added and modified-AuNPs after formaldehyde and hydroxylamine hydrochloride were added.

4.3 The morphology of 4-aminophenyl sulfone-AuNPs

AuNPs, 4-aminophenyl sulfone-AuNPs, 4-aminophenyl sulfone-AuNPs after the addition of formaldehyde, 4-aminophenyl sulfone-AuNPs after addition of hydroxylamine hydrochloride and 4-aminophenyl sulfone-AuNPs after addition of formaldehyde and hydroxylamine hydrochloride were investigated using Transmission electron microscopy (TEM). The TEM images in figure 4.8 show the overall distribution of AuNPs and the TEM image with high magnification in figure 4.9 show the distribution and behavior of AuNPs in various condition, respectively. The unmodified AuNPs were nearly spherical and uniformly distributed with the average particle size roughly 20 nm as shown in figure 4.8 (a) and 4.9 (a). After the modification AuNPs with 4-aminophenyl sulfone, 4-aminophenyl sulfone-AuNPs were maintained the uniformly distribution showed in figure 4.8 (b) and 4.9 (b). The shape and size of modified AuNPs remained relatively unchanged after the addition of formaldehyde as exhibited in figure 4.8 (c) and 4.9 (c). In case of adding only hydroxylamine hydrochloride into the solution of 4-aminophenyl sulfone-AuNPs also provided the same result as adding only formaldehyde in the solution as shown in figure 4.8 (d) and 4.9 (d). However, after the addition both of the formaldehyde and hydroxylamine hydrochloride into 4-aminophenyl sulfone-AuNPs solution can cause the aggregation of 4-aminophenyl sulfone-AuNPs as shown in figure 4.8 (e) and 4.9 (e). This result indicated the increasing particle size postulated earlier by the change of color and the red shift of absorption wavelength was happened.
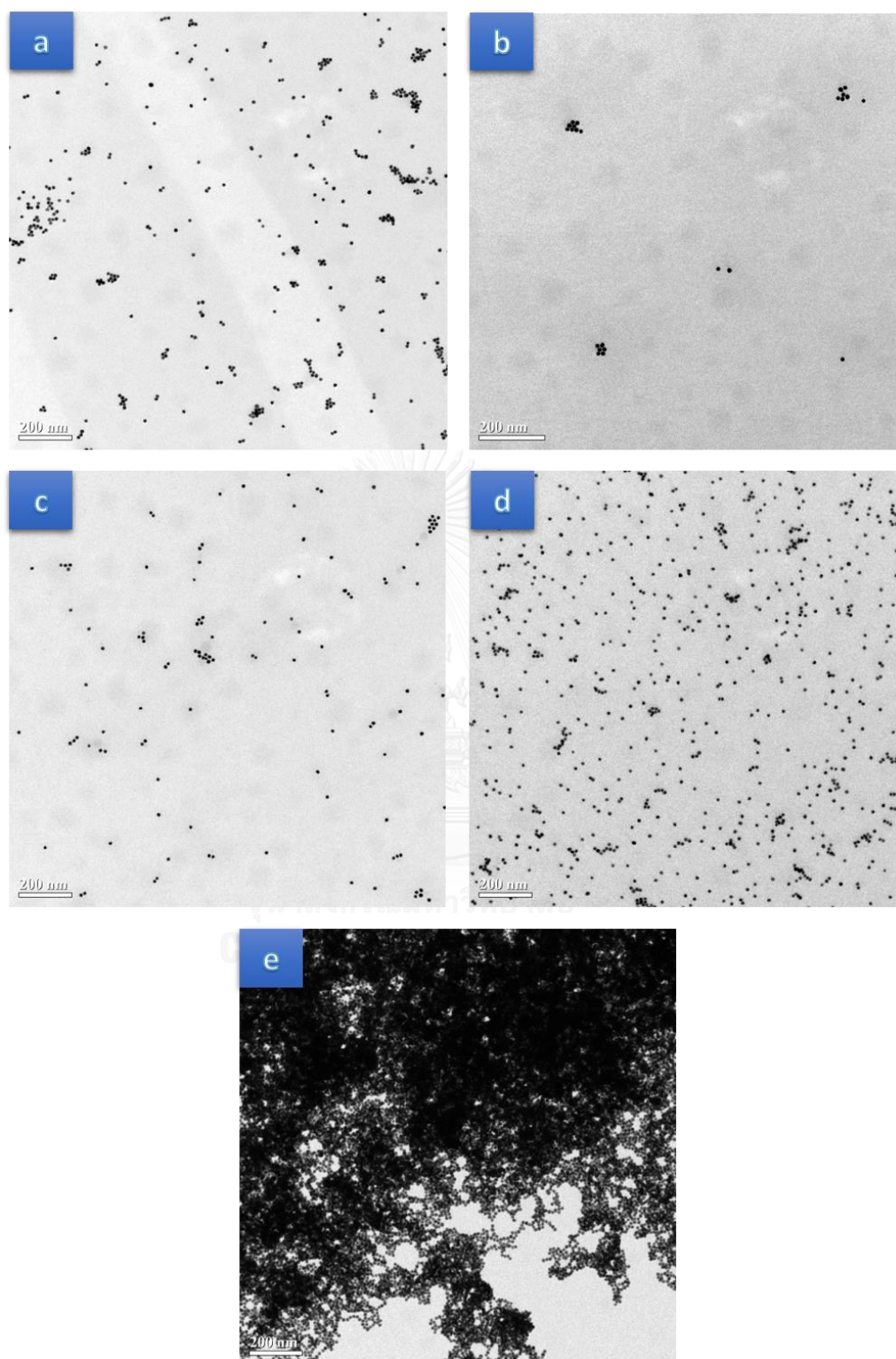
Figure 4.8 TEM images of [a] AuNPs [b] modified-AuNPs [c] modified-AuNPs with formaldehyde [d] modified-AuNPs with hydroxylamine hydrochloride and [e] modified-AuNPs with formaldehyde and hydroxylamine hydrochloride.
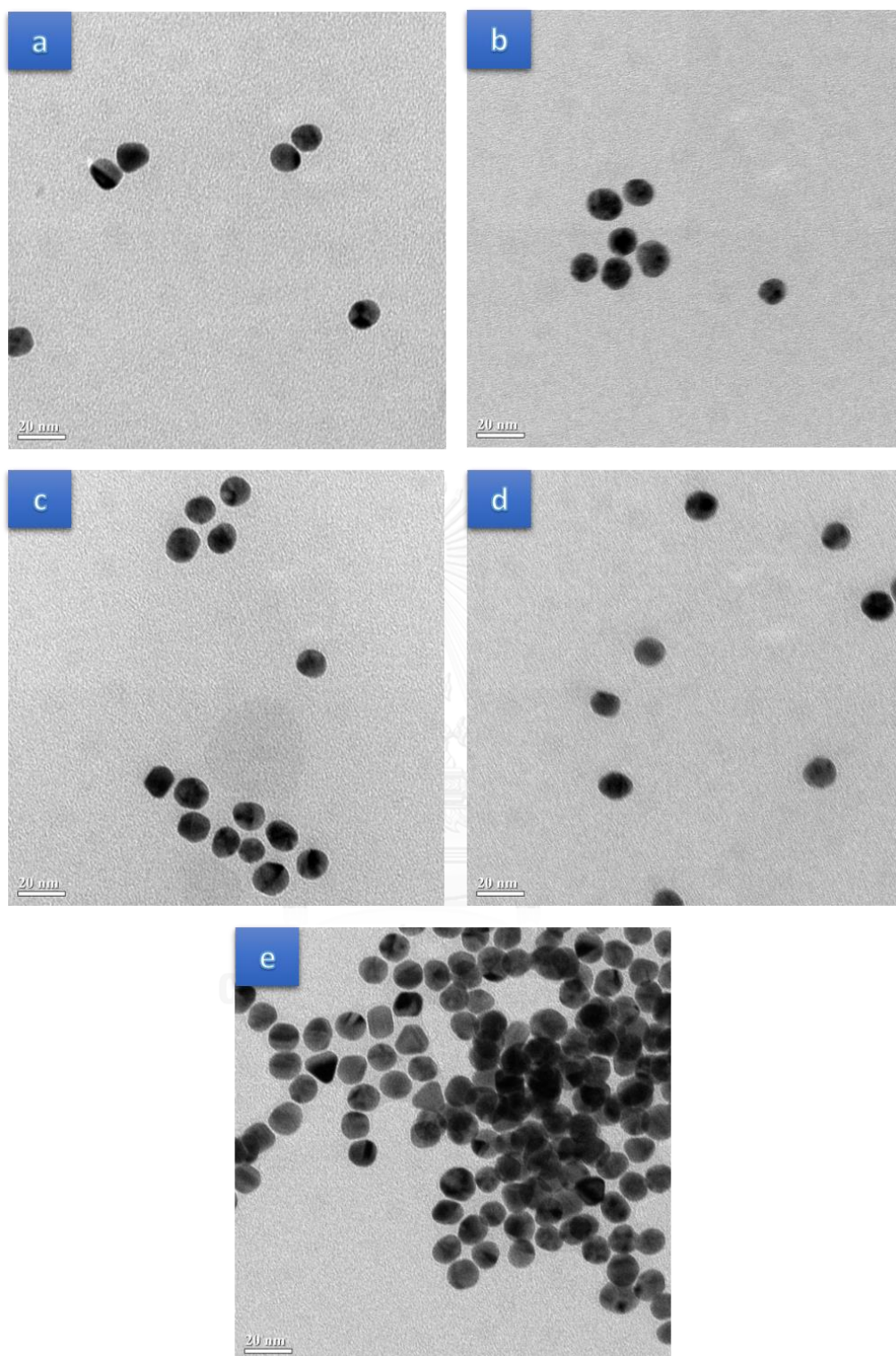
Figure 4.9 TEM images with high magnification of [a] AuNPs [b] modified-AuNPs [c] modified-AuNPs with formaldehyde [d] modified-AuNPs with hydroxylamine hydrochloride and [e] modified-AuNPs with formaldehyde and hydroxylamine hydrochloride.

4.4 Optimization of the AuNPs concentration and incubation time

To obtain a significant change of color between 4-aminophenyl sulfone-AuNPs and formaldehyde in the presence of hydroxylamine hydrochloride, the AuNPs concentration in the range of 0.01-0.10 %w/w and the incubation time in the range of 3 to 15 minutes were optimized. The picture was captured every minute and the Δ red intensity was calculated by using imageJ software as shown in figure 4.10. The Δ red intensity was increased with increasing concentration of AuNPs and incubation time. The concentration of AuNPs at 0.01, 0.02 and 0.04 %w/w showed the increasing explicit Δ red intensity when incubation time was increased. While, the concentration of AuNPs higher than 0.04 %w/w showed the decrease of Δ red intensity at the incubation time longer than 10 minutes. This is because of the reducing agent, hydroxylamine hydrochloride, leading to high concentration of AuNPs at the long time can self-aggregation a little bit. However, the Δ red intensity increased with increasing the concentration up to 0.06 %w/w AuNPs and remained constant afterwards during the initial incubation time period. In the case of 0.08 and 0.10 %w/w AuNPs, the Δ red intensity exhibited a decreasing tend with increased time because the modified-AuNPs were unstable due to self-aggregation and the camera cannot provide maximum intensity of changing color from this reaction, so the concentration of AuNPs at 0.06 %w/w was chosen. From the results, the Δ red intensity increased with increasing time until 5 minutes after that the Δ red intensity was relatively stable. The optimal concentration of AuNPs and incubation time are thus 0.06 %w/w and 5 minutes, respectively.
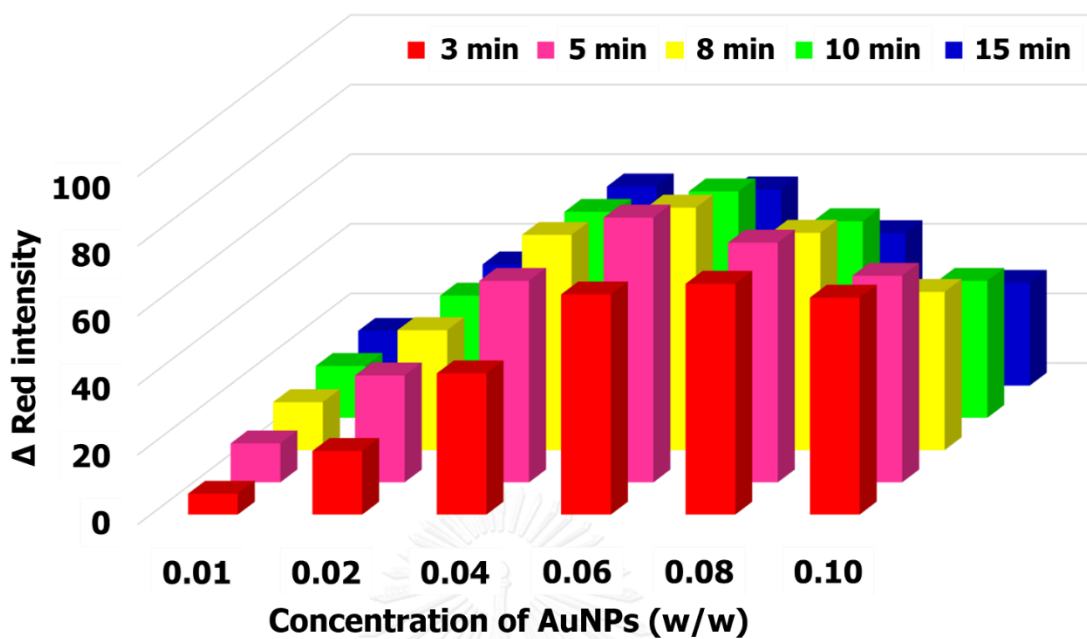
Figure 4.10 The effect of concentration of AuNP modified with 4-aminophenyl sulfone and incubation time on the detection of formaldehyde in the presence of hydroxylamine hydrochloride; red, pink, yellow, green and blue color represent the incubation time at 3, 5, 8, 10 and 15 minutes, respectively.

4.5 Optimization of the modifier concentration

The result of color of various concentration of 4-aminophenyl sulfone modified-AuNPs for formaldehyde detection in the presence of hydroxylamine hydrochloride are clearly distinguished as shown in figure 4.11. The Initial color of modified-AuNPs solution was red. The Δ red intensity was increased by increasing concentration of modifier until 4 mM because the modifier can cause the aggregation of AuNPs after adding formaldehyde in presence of hydroxylamine hydrochloride. The observed color of AuNPs solution can be categorized into 3 colors (red, violet-blue and blue). This is according to the result of UV-Vis absorption that aggregation process of AuNPs leading to the absorption shift to longer wavelength with band broadening. However, the excess of 4-aminophenyl sulfone concentration can cause the color of AuNPs solution changing from red to garnet red and decreasing of Δ red intensity. The change of color to cherry red after the modification step suggested that the AuNPs size might be increased. At 5 mM of 4-aminophenyl sulfone the solution turned to garnet red which could be an indication of the self-aggregation of AuNPs without adding formaldehyde and hydroxylamine hydrochloride [48]. An important concept in the surface modification of nanoparticle is that the color of solution after the modification should be similar to those of original nanoparticle solutions. Therefore, only the modified solution of 4 mM 4-aminophenyl sulfone was selected and used for the further experiments because this concentration provided the highest Δ red intensity.
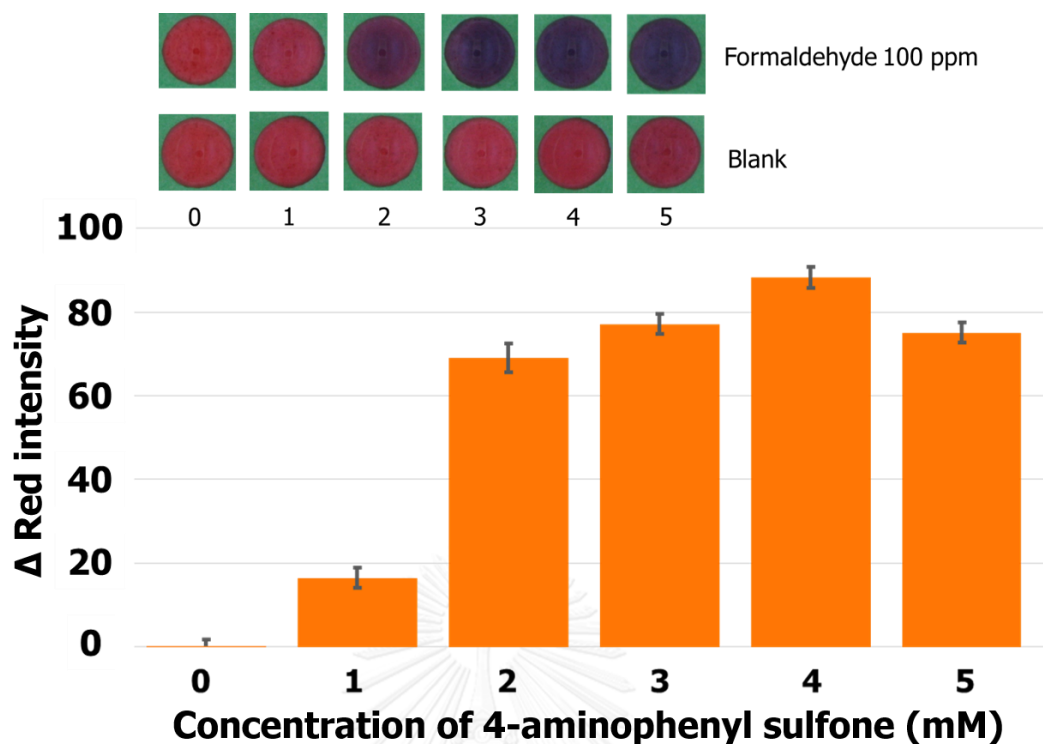
Figure 4.11 Effect of concentration of 4-aminophenyl sulfone as modifier on the detection of formaldehyde in the presence of hydroxylamine hydrochloride using intensity of red color. Inset: the photographic images results of colorimetric determination of formaldehyde detection; with formaldehyde (top) and without formaldehyde (bottom) on paper-based devices.

4.6 Optimization of the hydroxylamine hydrochloride concentration

The influence of hydroxylamine hydrochloride concentration over the range of 0 to 60 mM on the aggregation process was studied as shown in figure 4.12. In the range of 10 to 60 mM of hydroxylamine hydrochloride, the aggregation was presumably attained as clearly indicated by the color change from red to blue. The Δ red intensity was increased with increasing the concentration of hydroxylamine hydrochloride until 20 mM suggesting that the hydroxylamine hydrochloride induce the aggregation of modified-AuNPs in presence of formaldehyde. The hydroxylamine hydrochloride concentration in the range of 20 to 30 mM provided the similar Δ red intensity and the hydroxylamine hydrochloride concentration in the range of 40 to 50 mM provided a slight reduction of Δ red intensity because the excess amount of hydroxylamine hydrochloride affected the stability of modified-AuNPs and caused self-aggregation. At the concentration of hydroxylamine hydrochloride higher than 50 mM, the Δ red intensity was decreased because the modified-AuNPs are aggregated. The 4-aminophenyl sulfone-AuNPs in the presence of hydroxylamine hydrochloride without formaldehyde displayed an obvious change from red wine to cherry red as shown in the Inset of figure 4.12. The concentration of 20 mM hydroxylamine hydrochloride provided the highest different red intensity and thus was chosen as optimal.
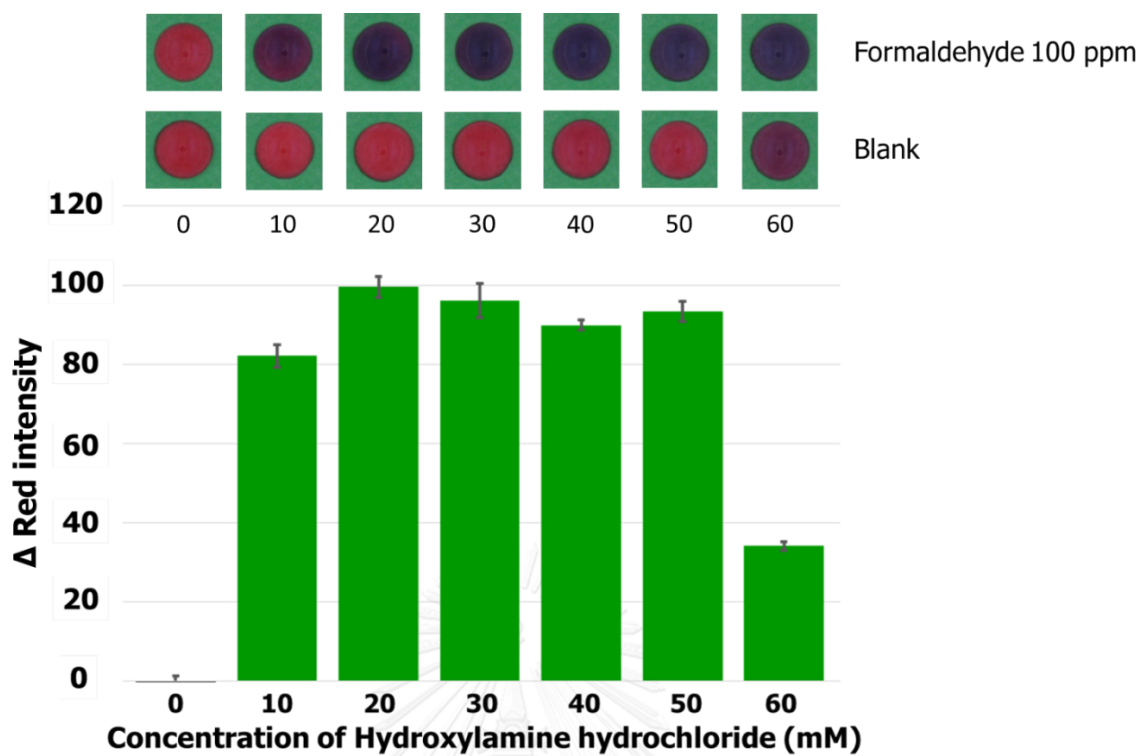
Figure 4.12 Effect of hydroxylamine hydrochloride concentration on the aggregation process of 4-aminophenyl sulfone-AuNPs for the detection of formaldehyde. Inset: the photographic images results of colorimetric determination of formaldehyde detection; with formaldehyde (top) and without formaldehyde (bottom) on paper-based devices.

4.7 Selectivity of 4-aminophenyl sulfone-AuNPs toward formaldehyde detection

The selectivity for formaldehyde detection, it was depended on the functional group of modifiers. The functional groups containing lone pair electron in the structure likes 4-aminophenyl sulfone and hydroxylamine hydrochloride such as $-NH_2$ and $-NH_3$ can easily bind to formaldehyde [42, 43, 49, 50]. However, the specific conditions to achieve the selectivity of formaldehyde's detection including modifier and hydroxylamine hydrochloride concentration might be required.

The investigate the selectivity, it can use various concentrations of other foreign chemicals including 2-propanol, acetaldehyde, acetone, acetylacetone, ammonium acetate, benzaldehyde, calcium chloride, ethanol, ethyl acetate, methanol, potassium chloride, sodium bicarbonate and sodium chloride to study under the optimal conditions and the results are shown in figure 4.13. According to the results, it can be seen that almost all organic compounds and salts did not affect to formaldehyde detection. However, only calcium chloride probably impacted the reliability and sensitivity of the colorimetric sensor because 4-aminophenyl sulfone have a donor groups such as amine group and calcium chloride classified as hard Lewis acid according to the Hard-Soft Acid-Base theory. Therefore, the complex between calcium(II) ion and nitrogen in amine group. In the case of potassium chloride, sodium bicarbonate and sodium chloride, they were classified as hard Lewis acid as same as calcium chloride but the oxidation state of potassium chloride, sodium bicarbonate and sodium chloride equal +1 while calcium chloride equal +2, so the calcium chloride can affect to 4-aminophenyl sulfone-AuNPs sensor cause the positive false because it can easy to polarize than potassium chloride, sodium bicarbonate and sodium chloride.
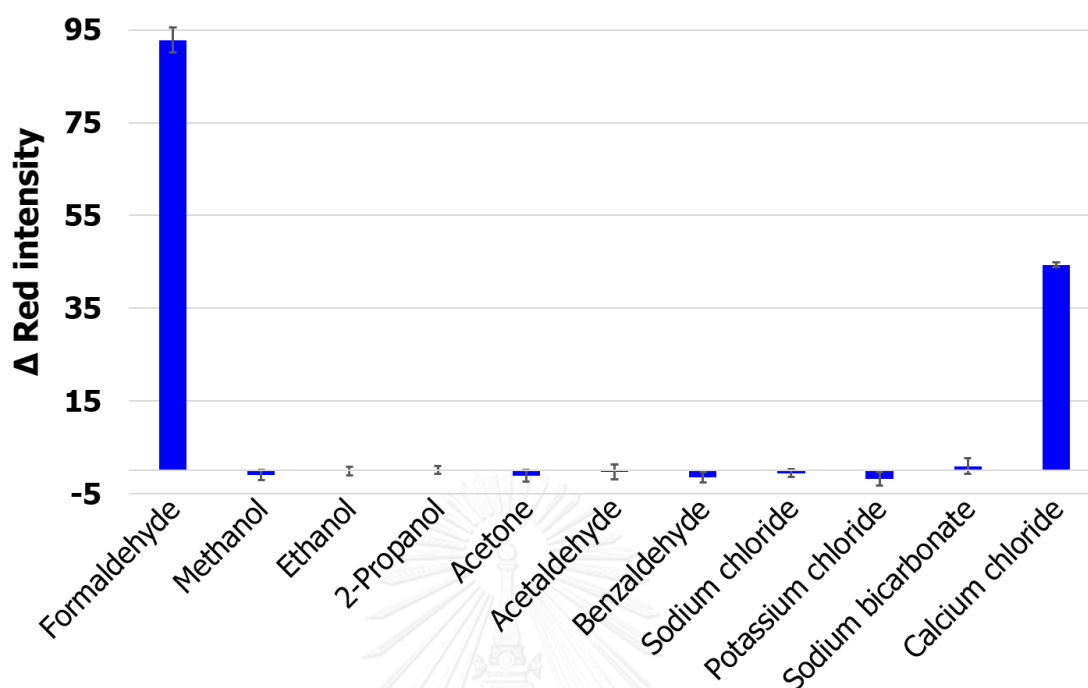
Figure 4.13 The Δ red intensity of 4-aminophenyl sulfone-AuNPs for formaldehyde detection in the presence of hydroxylamine hydrochloride after addition 100 ppm of formaldehyde compare with 200 ppm of other foreign chemicals including 2-propanol, acetaldehyde, acetone, acetylacetone, ammonium acetate, benzaldehyde, calcium chloride, ethanol, ethyl acetate, methanol, potassium chloride, sodium bicarbonate and sodium chloride.

Moreover, the concentrations of interference that is organic compounds and salts on the formaldehyde determination using the proposed colorimetric sensor are shown in the table 4.1. This tolerance limit was defined as the concentration of interfering chemicals including organic compounds and salts that produces in the Δ red intensity of ± 5% of the analyte. According to the results, it can be seen that almost all organic compounds and salts did not affect to formaldehyde detection. However, calcium chloride and sodium bicarbonate probably impacted the reliability and sensitivity of the colorimetric sensor. Sodium bicarbonate can affect to 4-aminophenyl sulfone-AuNPs sensor cause the negative false because it can cause the changing acidic to high pH value. At high pH, this has a bad condition because the gold nanoparticles are pH sensitive. So, it should be noted interfering salts like calcium

chloride and sodium bicarbonate needed to be removed, masked or even diluted to a level that no longer influenced the analytical findings.

Table 4.1 Tolerance ratio of interfering organic compounds and salts in the determination of formaldehyde 100 ppm

Interference	Tolerance concentration of chemicals (ppm)	Tolerance ratio ($C_{Chemicals}/C_{Formaldehyde}$)
Methanol, Ethanol, 2-Propanol	100,000	1,000
Potassium chloride, Acetaldehyde, Benzaldehyde, Sodium chloride	1,000	10
Acetone	500	5
Calcium chloride	75	0.75
Sodium bicarbonate	50	0.5

4.8 Analytical performance

4.8.1 Calibration curve

The study of calibration curve was obtained from red intensity and measured by digital camera using 4-aminophenyl sulfone-AuNPs solution in the presence of hydroxylamine hydrochloride with added concentration of formaldehyde at incubation time of 5 minutes. For the increase of formaldehyde concentration, the red intensity of 4-aminophenyl sulfone-AuNPs was decrease because the 4-aminophenyl sulfone-AuNPs color changed from red to blue and corresponds to results from UV-Vis spectrophotometer in figure 4.5. In figure 4.14, A linear relationship between the red intensity and formaldehyde concentration was established. Red intensity of 4-aminophenyl sulfone-AuNPs is directly proportional to the added formaldehyde concentration. A good linearity was observed in the concentration range of 40 to 110 ppm formaldehyde with a correlation coefficient of 0.9979.
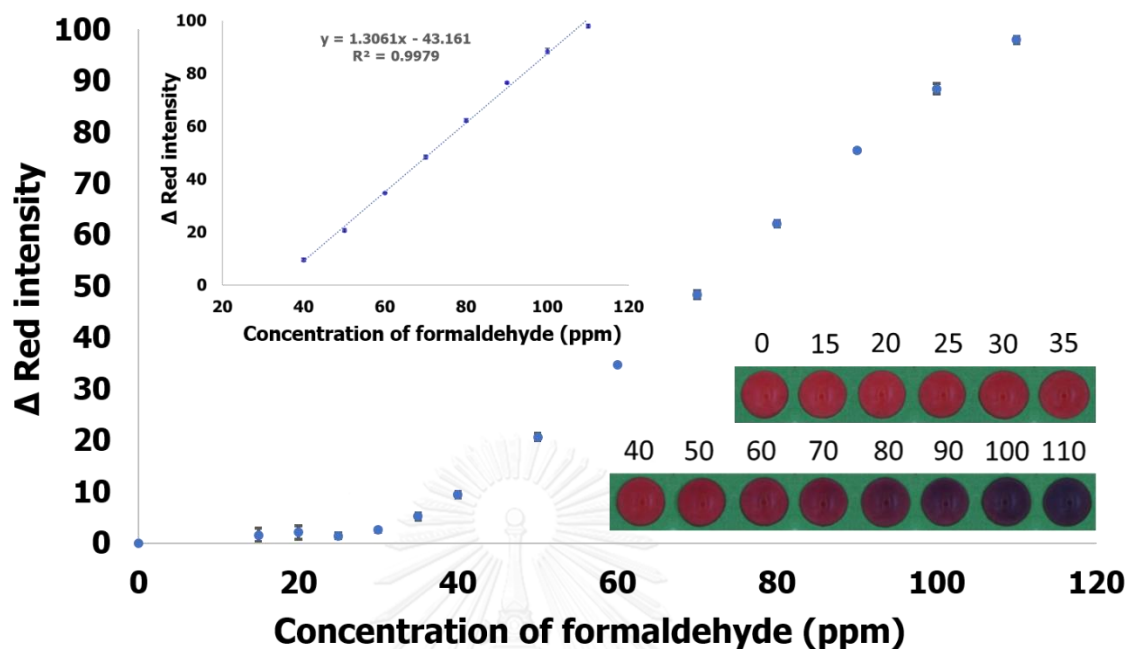
Figure 4.14 Calibration curve plot of the different red intensity versus various formaldehyde concentration including 0, 15, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 and 110 ppm. Inset: the photographic images results of colorimetric determination of formaldehyde detection; with formaldehyde (top) and without formaldehyde (bottom) on paper-based devices.

4.8.2 The limit of detection (LOD) and the limit of quantitation (LOQ)

The limit of detection (LOD) and the limit of quantitation (LOQ) for formaldehyde were found to be 1.92 ppm (S/N=3) and 6.41 ppm (S/N=10), respectively.

4.8.3 Repeatability

In this research, the repeatability was studied by performing eleven repeated measurements of standard solution. The colorimetric method of 4-aminophenyl sulfone-AuNPs sensor were showed high repeatability within 5 % RSD in different concentration, as show in figure 4.15. and table 4.2
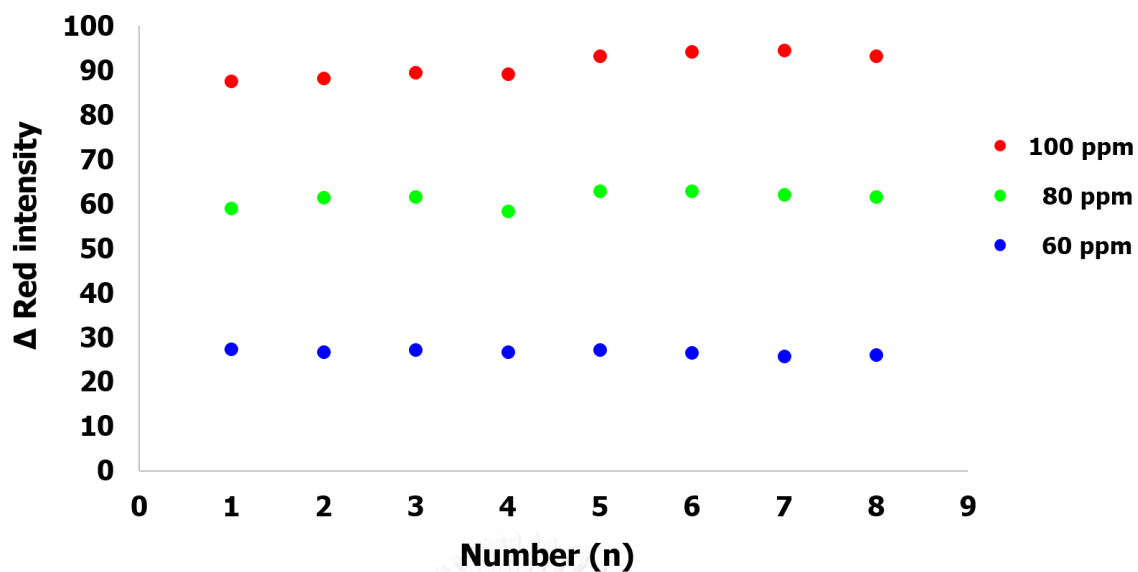
Figure 4.15 The stability of different red intensity using colorimetric 4-aminophenyl sulfone-AuNPs sensor for detecting formaldehyde in optimal condition.

Table 4.2 The relative standard deviations of colorimetric 4-aminophenyl sulfone-AuNPs sensor for detecting formaldehyde *(n=8)*

Concentration of formaldehyde	SD	%RSD
60 ppm	0.558	2.08
80 ppm	1.570	2.56
100 ppm	2.962	3.47

4.9 Analytical application in a real sample

To evaluate the efficiency of our method, the colorimetric sensor was used to detect formaldehyde in food samples including fresh shrimp, frozen shrimp and shiitake mushroom. Under the optimal conditions, the food samples were extracted and filtered before determination of formaldehyde. However, they were not found formaldehyde in food samples. The results of this proposed method were validated by UV-Vis spectrophotometry following AOAC International Method 964.21. The determination of formaldehyde in food samples and spiked samples with upper and lower concentration of formaldehyde were shown in table 4.3. This proposed method and standard method can determine formaldehyde with a good recovery in the range of 85-110 %recovery with satisfied the relative standard deviation. Finally, the statistics was used to verify this propose method. The result from t-test at 90% confidence level indicated that both propose method and standard method are not statistically significant differences. As results, this proposed colorimetric sensor can be applied for the selective formaldehyde determination in food samples with satisfactory results.

Table 4.3 The comparison of the proposed method and standard method for determination of formaldehyde in fresh shrimp, frozen shrimp and shiitake mushroom (n=3).

Samples	Spiked (ppm)	Formaldehyde (ppm)		% Recovery	
		This proposed method	UV-Vis	This proposed method	UV-Vis
Fresh shrimp	0	ND	ND	-	-
	60	64.32 ± 0.28	54.76 ± 0.07	107.19 ± 0.21	91.27 ± 0.13
	90	90.95 ± 1.51	83.19 ± 0.11	101.06 ± 0.90	92.43 ± 0.14
Frozen shrimp	0	ND	ND	-	-
	60	64.72 ± 0.15	57.10 ± 0.09	107.87 ± 0.11	95.16 ± 0.16
	90	91.29 ± 1.48	86.95 ± 0.10	101.43 ± 0.88	96.61 ± 0.12
Shiitake mushroom	0	ND	ND	-	-
	60	60.48 ± 0.79	54.61 ± 0.11	100.80 ± 0.62	91.02 ± 0.21
	90	88.03 ± 1.49	88.15 ± 0.08	97.82 ± 1.03	97.95 ± 0.10

CHAPTER V

CONCLUSIONS AND FUTURE PERSPECTIVE

5.1 Introduction

In this work, 4-aminophenyl sulfone modified onto AuNPs surface was successfully developed for determination of formaldehyde. In the modification step, 4-aminophenyl sulfone can self-assemble on AuNPs surface via the -NH group, resulting in a red-colored solution of 4-aminophenyl sulfone-AuNPs. The color of 4-aminophenyl sulfone-AuNPs solution did not change when adding only formaldehyde or hydroxylamine hydrochloride. When formaldehyde was added into the 4-aminophenyl sulfone-AuNPs and followed with hydroxylamine hydrochloride, the color changed from red to blue. This result indicated that 4-aminophenyl sulfone-AuNPs solution was aggregated induce by formaldehyde in the presence of hydroxylamine hydrochloride. The optimization parameters including concentration of AuNPs, 4-aminophenyl sulfone, hydroxylamine hydrochloride and incubation time were examined. The optimal conditions for surface modification of AuNPs with 4-aminophenyl sulfone are 0.06% w/w of AuNPs and 4 mM of 4-aminophenyl sulfone. For the determination of formaldehyde, the 4-aminophenyl sulfone-AuNPs was fabricated on paper-based device by wax printing method. Then, the formaldehyde solution was applied on paper-based sensor, the color changed from red to blue which can be monitored by the naked-eye after 5 minutes. The calibration curve was generated linear range at 40 to 110 ppm of formaldehyde with a high correlation coefficient of 0.9979. The detection limit and quantification limit (LOD and LOQ) were found to be 1.92 ppm and 6.41 ppm, respectively. Additionally, this method was applied for the quantification of formaldehyde in food samples including fresh shrimp, frozen shrimp and shiitake mushroom. A good agreement between the AOAC International Method 964.21 and 4-aminophenyl sulfone-AuNPs colorimetric sensor for the determination of formaldehyde was achieved. However, this sensor might have a potential to measure formaldehyde in various kinds of real samples as well.

5.2 Future perspective

In the future, this sensor has the potential to be develop as test kit model for determination of formaldehyde in food, water and environment samples. This sensor provides a lot of benefits including easy to produce, easy to use, portable and cheap. Moreover, the sensitivity and selectivity of colorimetric AuNPs sensor can be modified by using another type and concentration of modifier, tending to discover an innovative colorimetric sensor which can be applied for the determination of other chemicals and metal ions.

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APPENDIX

t-Test: Paired Two Sample for Means			
	Variable 1	Variable 2	
Mean	71.70278	76.64111	
Variance	254.1361	220.9389	
Observati	6	6	
Pearson C	0.967481		
Hypothesi	0		
df	5		
t Stat	-2.9714		
P(T<=t) on	0.015553		
t Critical o	3.36493		
P(T<=t) tw	0.031107		
t Critical t	4.032143		

Figure A1. Comparison of this proposed method and UV-Vis spectrophotometry
method using pair t-test at 90% confidence level
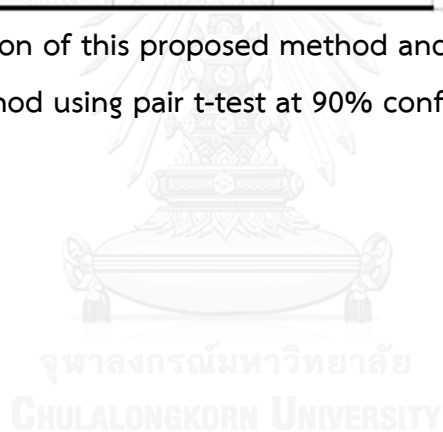
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PROCEEDING

Kritanusorn, A.; Praphairaksit, N.; and Chailapakul, O. (30 November - 2 December, 2016) Paper based sensor for determination of formaldehyde using gold nanoparticles modified with 4-aminophenyl sulfone. Proceedings of The 42nd Congress on Science and Technology of Thailand, Centara Grand at Central Plaza Ladprao, Bangkok, Thailand.