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Paper Strip Based on Nanoemulsion of Curcumin as Boric Acid Detection

Anting Wulandari [a], Titi Candra Sunarti [b,*], Farah Fahma [b], Erliza Noor [b], Toshiharu Enomae [c]

[a] *Graduate School, Study Program of Agroindustrial Technology, IPB University, Dramaga, Bogor, 16680 West Java, Indonesia*
[b] *Department of Agroindustrial Technology, IPB University, Dramaga, Bogor, 16680 West Java, Indonesia*
[c] *Faculty of Life and Environmental Sciences, University of Tsukuba, Japan*

*Corresponding author: *titi-cs@apps.ipb.ac.id*

***Abstract*— Boric acid is a toxic contaminant chemical that is found not only in food but also in the environment, especially the water environment so that its existence needs to be detected. In this work, we design the paper strip using nanoemulsion curcumin for boric acid detection. Curcumin is a bioactive compound that is able to provide a color change response to boron. However, curcumin is not stable to certain environmental conditions, so it needs to be encapsulated. Since it has a low solubility so that the proper encapsulation technique is nanoemulsion. This study investigates nanoemulsion curcumin paper strips' performance as a colorimteric biosensor for the detection of boric acid. The results showed that nanoemulsion curcumin reagent (CURNnsr) as a boric acid detection had a smooth spherical shape with a size of 25.70 nm. Interaction between created curcumin paper strips and boric acid led to a color change from yellow to red. Curcumin paper strip was selective towards sole boric acid after being reacted with various chemicals such as Pb^{2+}, Zn^{2+} , Fe^{2+}, Mg^{2+}, NaCl, sodium nitrite, monosodium glutamate, sodium benzoate, and formalin with a concentration of 10000 ppm, respectively. The detection limit (LOD) for curcumin paper strips was 105.56 ppm in the range 200-700 ppm of boric acid. This research results are pledging to develop disposable biosensors that are sensitive, selective, and stable, low cost, easy to use and detect quickly.**

***Keywords*— Biosensor; boric acid; curcumin; nanoemulsion; paper strip.**

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I. INTRODUCTION

Boric acid is often used as a fungicide, antiseptic, and pesticide. It is usually used to kill mites, insects, and algae fungi, such as ticks, cockroaches, termites, and wood decay fungi [1]. Boric acid is used to manufacture glass (fiberglass, borosilicate glass, enamel, frit, and glaze), soaps and detergents, fire retardants, and neutron absorbers nuclear installations. It has also been used in mild antiseptics, cosmetics, medicines (as a pH buffer), neutron boron capture therapy (for cancer treatment), and agricultural fertilizer. The use of this chemical often leaves a residue. The boric acid residue is a contaminant source for the environment, especially the groundwater environment [2]. Besides, in developing countries such as Indonesia, boric acid or borax is widely misused as food preservatives [3]. This chemical can also control the gelatinization of starch and improve the color, flavor, and texture of food [4]. Boric acid in food can be found in meatballs, crackers, tofu, and noodles. Borax or boric acid is very dangerous, even if only in small amounts. It causes symptoms of anorexia, indigestion, and exfoliative dermatitis [5]. Besides, boric acid cause degeneration of the spermatogonia epithelium by inhibiting DNA formation in sperm cells. Therefore, it causes infertility in men. Boric acid reduces metabolic concentrations such as glucose, glycogen, and lactate associated with boron and hydroxyl complexes. It also causes poisoning if the level reaches 2g/kg in liver and brain tissue, and it is lethal if it exceeds 5g/kg of in adults and 3g/kg in neonates [6], whereas according to Saparinto and Hidayati [7] borax poisoning considering safe if the limit does not exceed 10g/kg-20 g/kg of body weight for adults, and 5g/kg of body weight for children.

Since it is a hazardous and toxic chemical, boric acid contamination in the water environment and food needs to be detected. Some methods commonly used to detect boric acid include spectrophotometric [8], [9], gas chromatography-mass spectrometry [10], and titrimetry [9]. However, these methods have limitations such as multi-stage processes, requiring specialized experts, can only be used on

a laboratory scale, time-consuming, require sophisticated, complicated, and relatively expensive equipment [11], so it is not suitable for daily analysis. Thus, a new method for detecting boric acid in a simple, fast, cheap, and easy to use is needed. Colorimetric biosensors have been proved are easy to use, inexpensive, and can be applied on-site [12]. Paper as a matrix has porous and flexible properties [13], and as an analytical tool, the paper has many advantages such as cost savings, high portability, ease to be fabricated, and use of minimum reagents and samples [14].

The diversity of natural plant resources in Indonesia is a good source for dye and bioactive compounds that will offer the opportunity to become a biosensor with unique specificity and sensitivity. Bioactive compounds in the form of curcumin had the potential to detect borax [15]. So based on that, we developed a paper strip biosensor using curcumin for boric acid detection. Curcumin was extracted from the dried root of the rhizome *Curcuma longa*. Curcumin acts as an antioxidant, anti-inflammatory, anticarcinogenic, and antibacterial [16]

However, curcumin has low solubility and bioavailability in water [17], and it is quickly hydrolyzed by physiological pH [18]. To increase the phytochemical solubility, stability, and bioactivity can be done by nanoencapsulation, which is by nanoemulsion [19]. Nanoemulsion of oil in water (O/W) is the most appropriate encapsulation method for curcumin. This is because curcumin has a low solubility; forming it into nanoemulsions can increase its solubility [20].

Therefore, in this study, we developed a biosensor for boric acid detection based on nanoemulsion of curcumin in the form of paper strips. Curcumin and boric acid interaction can occur when curcumin is in protonated conditions, so it is necessary to add strong acids in curcumin nanoemulsion. In this study, concentrated hydrochloric acid was used. Besides, oxalic acid was also added in order to increase the sensitivity of detection. This study aimed to develop a biosensor paper strip using nanoemulsion of curcumin and investigate its performance in boric acid detection.

II. Materials and Methods

A. Materials

Turmeric (*Curcuma longa* (L)) was obtained from a local supplier in Bogor, Indonesia. The paper strip was developed by using Whatman No.1 filter paper. Tween 80 was used as an emulsifier, and maltodextrin DE 10-15 as encapsulating agent (matrix) and stabilizer in the formation of curcumin nanoemulsion was obtained from the nearest chemical store. Chemicals used in this research were sodium nitrite, zinc sulfate, acetate leads, ammonium iron sulfate, magnesium sulfate, zinc sulfate, boric acid (Merck) in pro analysis grade, while sodium chloride (NaCl), monosodium glutamate (MSG), sodium benzoate were food grade.

B. Preparation of Curcumin Extract

A total of 100 g of turmeric powder was suspended in 700 mL of 70% ethanol (1: 7 (w /v)). Furthermore, it was macerated for 2 days with a stirring speed of ± 400 rpm at room temperature. And then, the maserat was filtered with a muslin cloth. The filtrate was re-filtered with Whatman paper No. 41 by using a vacuum filter and then was centrifuged (IEC Clinical Centrifuge, USA) at 3000 rpm for 15 min. Soluble ethanol fraction (CURN) was evaporated at 50 ºC waterbath and was kept in a dark colored glass bottle in the refrigerator [21], [22] and was used as curcumin extract for further analysis.

C. Encapsulation of Curcumin

Encapsulation of curcumin was prepared by the nanoemulsion method with an oil in water (O/W) system referred to Jusnita et al. [23] with slight modifications. 30 mL of curcumin extract (50.99 mg/L) was diluted with 67 mL of pH 7 phosphate buffer solution, and then 3 mL of Tween 80 solution was added. The mixture was stirred at 800 rpm for 10 min, followed by the addition of 30 g maltodextrin. Then the blend was re-stirred at 800 rpm for about 20 min, and it was homogenized using an Ultra-Turrax homogenizer (HG-15D Wise-Tis) at 20000 rpm for 80 min to obtain curcumin nanoemulsion (CURNns). Thermal stability of the encapsulated curcumin extract in maltodextrin matrix was determined by Thermogravimetric Analysis (TGA) at 25-500 ºC with a temperature rise of 10 ºC/min. Microstructure and particle size distribution of CURNns were measured by Transmission Electron Microscopy (TEM) (Hitachi, H-7650) and zetasizer (Malvern), respectively.

As a reagent used for biosensor paper strips, curcumin nanoemulsion was added with oxalic acid and concentrated hydrochloric acid. Curcumin nanoemulsion reagent (CURNnsr) preparation referred to Hayes and Metcalfe [24] and APHA et al. [25]. About 15 mL of 50.99 mg/L CURNns was added with 15 mL of 6.25% oxalic acid (w/v). The mixture of oxalic acid and CURNns solution was added with concentrated HCl of 5.5% (v/v) of the total volume and kept in the dark glass bottle for further analysis.

D. Boric Acid Detection by Curcumin

The principle of boric acid detection by curcumin is determined based on the interactions between both analyzed based on functional groups and microstructure formed between boric acid and curcumin. Study of functional groups between curcumin and boric acid was performed using Fourier-Transform Infrared Spectroscopy (FTIR) and microstructure of CURNnsr and its mixture with boric acid were analyzed using Transmission Electron Microscopy (TEM) (Hitachi, H-7650). The sample analyzed was a red solid CURNnsr-boric acid resulting from heating the CURNnsr-boric acid solution. Then it was compared with powder of turmeric and boric acid samples.

E. Preparation of Curcumin Paper Strip

Filter paper Whatman No.1 (diameter 9 cm) was used as a medium. One piece of filter paper was placed in a petri dish. Subsequently, CURNnsr was poured on the paper's surface, and it was immersed for 30 min. Afterward, it was dried in an oven drying at 50 ºC for 15-20 min. CURNnsr paper was cut into 1.5 cm x 1.5 cm sizes and then was kept in a plastic vacuum bag at room temperature, and it was called a curcumin paper strip. Attachment of CURNnsr on filter paper was observed by Scanning Electron Microscope (SEM). The paper samples analyzed were curcumin paper and curcumin paper which had been reacted with 10000 ppm

boric acid. The parts of the paper observed were the surface and inner edges. It was in dry conditions.

F. Application of CURNnsr Paper Strips as Biosensor for Boric Acid Detection

For single chemicals detection, curcumin paper strips were dripped with 0.25 µL of 10000 ppm of each chemical to examine its selectivity. To investigate the interference of boric acid detection, in this work, 0.25 µL of each chemical was dripped on the curcumin paper strip and then followed by 0.25 µL of 10000 ppm boric acid. The concentration of boric acid was in the range 100 to 10000 ppm for the curcumin paper strip sensitivity determination. Color changes in examinations of selectivity, interference study, and sensitivity were measured by using colorimeters following the CIELAB system (L^*, a^*, b^*, c^{**}, Hue, ΔE^*) where L^* indicates brightness (0 = black, 100 = white), a^* [(Greenness (-) to reddish (+)], b^* [(blueness (-) to yellowness (+)]. The color of sample was calculated as the Hue value, Hue = $\tan^{-1} b^*/a^*$ (0º or 360º = red, 90º = yellow, 180º = green, and 270º = blue), while saturation of color was calculated from chroma value (c^*), $c^* = (a^{*2} + b^{*2})^{½}$. ΔE^* indicates the color differences and calculated as $\Delta E^* = ((L_{ti}^* - Lt_0^*)2 + (a_{ti}^* - a_{t0}^*)^2 + (b_{ti}^* - b_{t0}^*))^{1/2}$; while L_{ti}^*, a_{ti}^*, b_{ti}^* are the color coordinates after treatment, and before treatment/control (t_0) [26], [27]. The morphology of the curcumin paper strip in boric acid detection was observed by Scanning Electron Microscope (SEM) and CURNnsr absorption into the filter paper was observed using a light microscope (CH10MOMF Olympus).

G. Statistical analysis

Statistical analysis was performed using IBM SPSS version 22, where the significance differences inter-treatments were tested with the Tukey method ($\alpha = 0.05$).

III. Result and Discussion

A. Characteristic of Encapsulated Curcumin

1) Thermogravimetric Analysis (TGA): Curcumin as a bioactive compound was a soluble fraction of turmeric in ethanol solvent extraction. Natural curcumin in turmeric powder is a volatile compound which susceptible to temperature. Therefore, it must be encapsulated in a matrix. In this research, maltodextrin was used as an encapsulating agent and stabilizer for curcumin extract. To determine the thermal stability of curcumin extract through changes in its weight, it was carried out using thermogravimetric analysis (TGA). Figure 1 shows that TGA (thermogravimetric analysis) of encapsulated curcumin. Turmeric, maltodextrin, and encapsulated curcumin (CURNns) has three stages of decomposition. Turmeric had three main stages of decomposition. The first stage was obtained in the range of 37.19ºC-92.68ºC. The weight loss might be caused by the loss of volatile compounds [28]. The second stage of decomposition existed in the range 135.22ºC-191.91ºC. Losing weight in the second stage might relate to the process of dehydration (evaporation process of free and bound water in the polymer turmeric) and dihydroxylation of OH groups [29]. While the third stage of decomposition began at 217.66ºC and ended at 340.17ºC. In this third stage, a complete decomposition was obtained. Until the final stage of this degradation, the turmeric lost the weight of 57.07%. Turmeric polymer decomposition took place at this stage. Delgado et al. [29] reported that turmeric polymer decomposition began at 193ºC. Samindra and Kottegoda [30] reported that the complete polymer decomposition of curcumin occurred in the range 200-400ºC.

Maltodextrin decomposition was also found in three stages. The first stage existed in the range of 55.72ºC-73.62ºC, which is related to first-order transitions such as evaporation. The second stage of decomposition occurred in the range 204.02ºC-223.58ºC. A weight loss at this stage confirmed the presence of small decomposition of polymers in low molecular weight oligosaccharides with DP (degree of polymerization) about 5-6. That was as reported by Saavedra-Leos et al. [31]. Complete polymer decomposition was obtained at the third stage, which began at 241.2ºC and ended at 331.25ºC. The weight loss is associated with thermal decomposition of long molecular chains, polymerization processes, and isomerization reactions associated with dehydration [32].

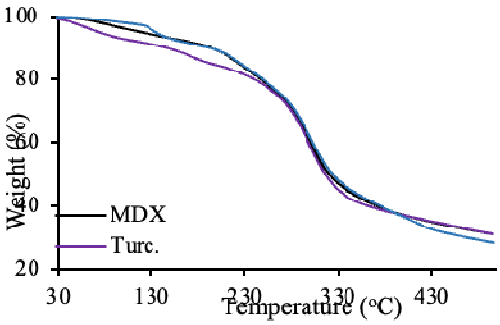

Fig. 1 TGA curve of of turmeric, maltodexktrin and maltodextrin-ethanolic curcumin extract

Maltodextrin-curcumin had three stages of decomposition as well. The first and second stages occurred in the range 119.59ºC-151.59ºC and 206.29ºC-240.44ºC, respectively. Polymer degradation occurred at 240.44ºC-336.79ºC. There were water loss and small decomposition in the first and second stages with a weight loss of up to 18.04%. In this study, the degradation of turmeric polymers containing curcumin began at 217.66ºC. Meanwhile, after curcumin was encapsulated in the matrix, polymer degradation began at 240.44ºC. This indicated that the encapsulation process would increase the thermal stability of curcumin extract. This corresponded with the works of Laczkowski and Sousdaleff [33] and Parize et al. [34]. They explained that polymer degradation of encapsulated turmeric in maltodextrin matrix began at 228ºC. While turmeric without encapsulation was degraded at 201ºC. Similarly, Laczkowski and Sousdaleff [33] exhibited that better turmeric stability was obtained in the form of encapsulation in the maltodextrin matrix.

2) Particle Size Analyzer and Polydispersive Index: Zetasizer analyzed the size and dispersion of curcumin nanoemulsion. Figure 2 presents the particle size distribution of curcumin nanoemulsion (CURNns) before and after mixed oxalic acid and concentrated hydrochloric acid. The distribution of CURNns was bimodal with a droplet size

average of 59.99 nm (Figure 2a). Meanwhile, after added with concentrated hydrochloric acid and oxalic acid (CURNnsr), particle size became smaller, which was 25.70 nm with bimodal distribution (Figure 2b). The presence of concentrated hydrochloric acid might hydrolyze the curcumin hydrogen bonds so that the size of CURNnsr becomes smaller.

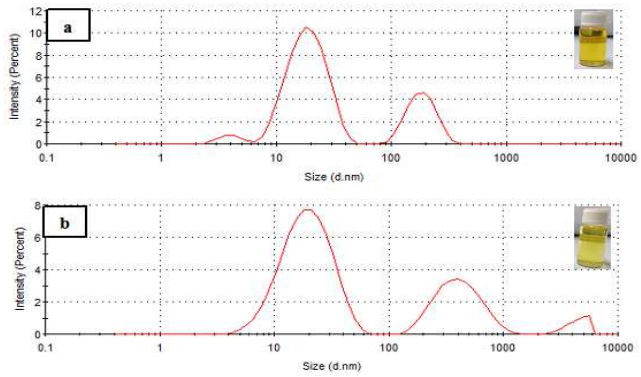

Fig. 2 Curve of particle size distribution for CURNns (a), and CURNnsr (b)

Jusnita et al. [23] used a homogenizer with various mixing speeds and times to produce nanocurcumin with droplet sizes below 100 nm. They reported that the stirring speed and time affected the droplet size. It was obtained below 100 nm using 30% of curcumin with stirring speed of 12.879 g during 40 min. According to Solans et al. [35] nanoemulsion has better stability for particle aggregation and gravity separation due to its small droplet size.

Sari et al. [19] prepared curcumin nanoemulsion using Tween 80 emulsifier and stabilizer of whey protein concentrate with ultrasonication technique. Their work resulted droplets size of 141.6 ± 15.4 nm. Yadav et al. [36] showed that curcumin encapsulated in chitosan nanoparticles with the addition of Tween 80 obtained a droplet size range of 20-50 nm. Hu et al. [37] reported that the average particle size was around 250 nm from curcumin fortified zein-pectin nanoparticles. The minimum size of droplet that can be obtained depends on several different factors. Reducing particle size using high energy depends on the type and operating conditions of the homogenizer (e.g., energy intensity, time and temperature), sample composition (for example oil type and concentration and emulsifier) and physicochemical properties of component phases (e.g., interface voltage and viscosity) [38]

A good homogeneity of curcumin nanoemulsion is needed to get a uniform color change response in boric acid detection, which is related to its sensitivity. The homogeneity of the CURNns and CURNnsr distribution were described by the polydispersion index (PDI). According to Galindo-Rodriguez et al. [39], PDI describes the particle size distribution width and usually ranges from 0 to 1, where higher values indicate a less homogeneous particle size distribution. The polydispersity index (PDI) also provides information about the stability of the emulsion. According to Ahmed et al. [40] nanoemulsion is stable from the possibility of particle collision and gravity separation if the particle size is < 200 nm with a polydispersity index of 0.2 <PDI <0.6.

In this work showed that CURNns had a PDI value of 0.168. While the PDI of CURNnsr was 0.580. In previous studies, curcumin fortified zein-pectin nanoparticles had a PDI of ~ 0.24 [37]. Sari et al. [19] reported that curcumin nanoemulsion in a whey protein concentrate had a PDI of 0.273. A relatively lower PDI value for nanoemulsion is associated with higher storage stability [41]. This research had a PDI of 0.2 <PDI <0.6, so it has good homogeneity and stability.

B. Boric Acid Detection by Curcumin

1) Functional Group of Curcumin in Boric Acid Detection: Functional group examination and structural description of compounds were observed using the Fourier-Transform Infrared Spectroscopy (FTIR). Analysis of this functional group is needed to determine the bonds formed between curcumin and boric acid. Figure 3(a) showed the IR spectra of curcumin powder. Peak of 3510 cm^{-1} confirmed the OH-phenolic stretch of curcumin [42]. Peak of 1626 cm^{-1} was the stretch attribute of -C = C and -C = O of the inter ring chain, peak of 1606 cm^{-1} confirmed the -C = C stretch of aromatic ring, and peak of 1506 cm^{-1} indicated of –C = C, -C = O, and –CC = O stretching vibrations in plane bending [43].

Based on Figure 3(b), O-H stretching appeared at 3191 cm^{-1}. Peak 2259 and 2516 cm^{-1} were assigned as asymmetric B-O bands in BO_2. While asymmetric B-O bands in BO_3 and O-H bands appeared at peaks of 1404 cm^{-1} and 1190 cm^{-1}, respectively. Peak of 883 cm^{-1} confirmed the asymmetric B-O bands in BO_4, peak of 704 cm^{-1} was responsible as symmetric B-O bands in BO_4, and the peak of 544 cm^{-1} belongs to boric acid of H_3BO_3. This is in accordance with the report of Öge and Keskiner [44].

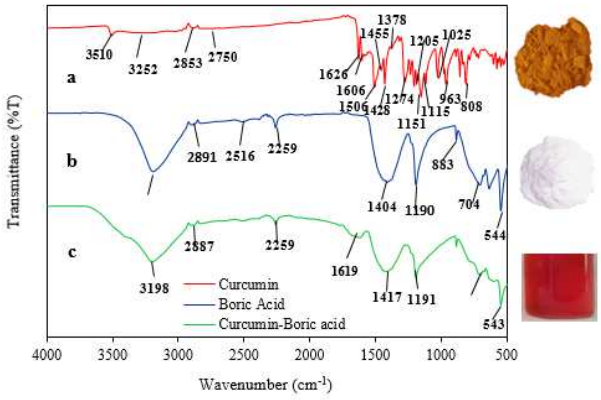

Fig. 3 FTIR spectra of curcumin (a), boric acid (b), and curcumin-boric acid (c)

After curcumin was reacted with boric acid, some changes in IR band occurred. There was a shift in the O-H and C = O groups from 3510 cm^{-1} and 1626 cm^{-1} to 3198 cm^{-1} and 1619 cm^{-1}, and O-H band became broad (Figure 3c). This indicates that O-H and C=O groups are involved in the formation of curcumin and boric acid complexes. Thus, it can be assumed that the formation of curcumin-boric acid complex occurs through intermolecular hydrogen bonds. This similar result also reported by previous researchers. According to Dible et al. [45], the curcumin-boric acid (rosocyanine) complex might be form due to the

combination of boron with one of the hydroxy groups of the curcumin molecule. Yoe and Sarver [46] explained that the complexes were formed due to ring formation by coordinating boron with the methoxy and hydroxy curcumin groups.

The curcumin and boric acid complex caused the absorption intensity of asymmetric B-O bands in BO_3 at peak 1417 cm^{-1} and O-H bands at peak 1191 cm^{-1} to be decreased. Besides that, the decrease in band intensity also existed at 700 cm^{-1} and 543 cm^{-1}. While the IR band at 2259 cm^{-1} was relatively stable. These conditions indicate that boric acid is strongly bound to curcumin so that IR spectra could still detect its presence.

2) Microstructure of Curcumin Nanoemulsion Reagent (CURNnsr) in Boric Acid Detection: Microstructural determination of CURNnsr was carried out using the Transmission Electron Microscope. Figure 4 shows the TEM micrographs of CURNnsr and their interactions with boric acid with different magnifications. CURNnsr had a spherical shape with a smooth surface in sizes of 25-60 nm. Granular particles of curcumin were not mutually bonded to each other. Hu et al. [37] and Raj and Dhesingh [42] reported that curcumin nanoparticles were spherical.

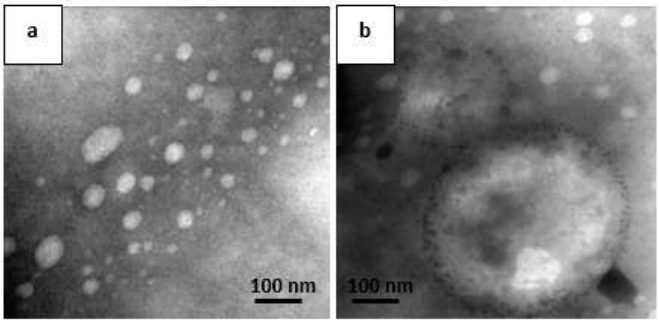

Fig. 4 TEM image ofCURNnsr (a) and aggregation of CURNnsr-boric acid mixture (b and c)

Figure 4(b) shows TEM micrograph of CURNnsr upon contact with boric acid. It appeared that the interaction between boric acid and curcumin formed a fine unified aggregate forming a large circle with a range of 200-500 nm. The formation of these aggregates confirmed the color changes of curcumin from yellow to red. A similar result was also explained by Raj and Dhesingh [42] and Shi et al. [47]. They described that the color change in the colorimetric sensor occurred due to an aggregate formation between the sensor reagent and the targeted chemical analyte.

C. Application of CURNnsr Paper Strips as Biosensor for Chemicals Detection

1) Physical Appearance and its Microscopy Studies: The morphology of the curcumin paper strip for boric acid detection was observed by Scanning Electron Microscope (SEM), and CURNnsr absorption into the filter paper was observed with a light microscope. Figure 5(a) showed a visualization of the curcumin paper strip. It appeared yellow with an even color distribution on the surface of the filter paper. CURNnsr solution can be absorbed into the filter paper evenly (Figure 5b). The color of the curcumin paper strip changed from yellow to red homogeneously upon contact with boric acid (Figure 5c). The color homogeneity was obtained because the CURNnsr droplets were nanometer-sized so that the surface area was large; therefore, the ability to adsorb onto the filter paper surfaces was higher [42]. Nanoparticles are more active because they have a larger surface area than micrometer-sized particles [48]. Therefore, when it was reacted with boric acid, the response of color change was homogeneous. Boric acid solution adsorbed onto fibers of a curcumin paper strip so that the red color resulted homogeneous (Figure 5d).

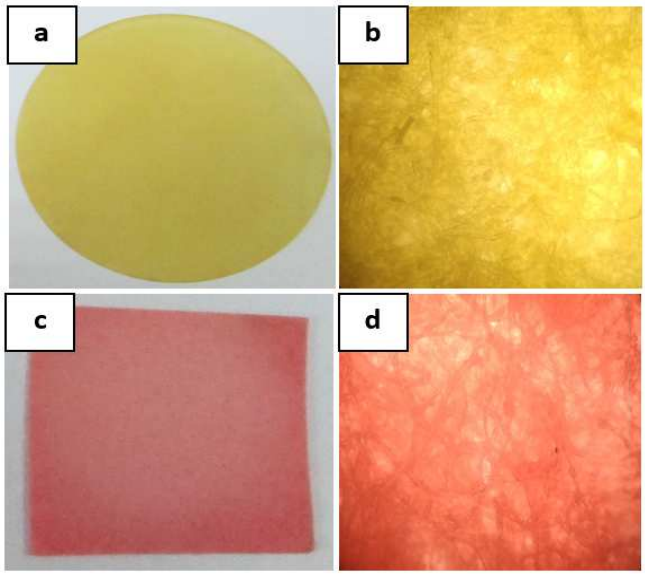

Fig. 5 Appearance of curcumin paper strip (a), optical microscope image of curcumin paper strip (b), curcumin paper strip upon contact with boric acid (c), optical microscope image of curcumin strip-boric acid (d)

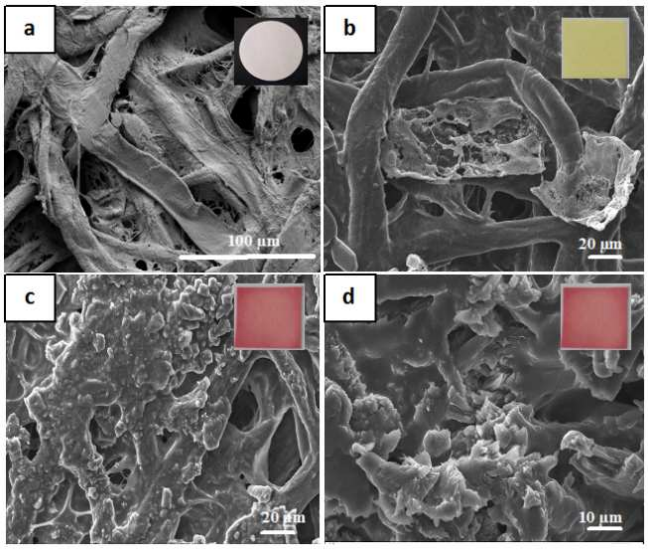

Fig. 6 SEM images of filter paper (a), curcumin paper strip surface (b), curcumin paper strip-boric acid surface (c) curcumin paper strip-boric acid, cross section (d)

The morphological and microstructure determination of the curcumin paper strip by SEM were presented in Figure 6. The filter paper consisted of a long fiber that were confirmed as cellulose (Figure 6a). The filter paper was coated with CURNnsr solution, and it was used as a sensor strip for boric acid. Figure 6(b) described the surface morphology of the

curcumin paper strip. When compared to the filter paper, on the surface of the curcumin paper strip, layers were covering the filter paper fibers. The layers are suspected as maltodextrin contained within CURNnsr. Figure 6(c) showed the surface of the curcumin paper strip after interacting with boric acid. Aggregates were formed on the surface of the curcumin paper strip. It was almost no visible air cavity on its surface. This is because the CURNnsr has thoroughly coated the filter paper until it was absorbed into the filter paper. Thick aggregates also covered the filter paper fibers in a cross-section of the curcumin paper strip-boric acid. The aggregates appeared as an irregular and thick layer (Figure 6d). They were estimated due to the interaction of CURNnsr with boric acid, which also confirmed the color change of curcumin paper strips from yellow to red (Figure 6d, inserted picture). In another study, Pourreza and Golmohammadi [49] reported that the aggregate which was formed between nano curcumin and alkaline solution in pH sensing indicated the color change.

2) Selectivity of CURNnsr Paper Strip and the Interferences of the Chemicals in Boric Acid Sensing: Selectivity and interference examinations of curcumin paper strips were carried out to ensure that its performance for boric acid detection is only selective to boric acid. It is not interfered with by other chemicals (Pb^{2+}, Zn^{2+}, Fe^{3+}, Mg^{2+}, NaCl, monosodium glutamate (MSG), sodium benzoate, formalin, and sodium nitrite). The interaction of curcumin paper strips with boric acid gave a red color change. While its interactions with other chemicals (Pb^{2+}, Zn^{2+}, Fe^{3+}, Mg^{2+}, NaCl, monosodium glutamate (MSG), sodium benzoate, formalin, and sodium nitrite) did not show color changes (remain yellow color), however there was minor loss of color (color fading) when interacting with sodium nitrite (Figure 7a). The values of b^* and c^* of curcumin paper strip-nitite differed significantly ($p < 0.05$) towards control (curcumin paper strip) (Table 1). Curcumin paper strip interaction with nitrite caused the b^* and c^* values drop as a sign of a decline in the yellow color intensity to colorless. This is due to the presence of curcumin which can reduce the formation of nitrite (NO_2) from NO oxidation [50], which occurs due to sequestration of NO_2 intermediate reactions [51]. Unnikrishnan and Rao [51] explained that curcumin could also inhibit the oxidation of NO_2 from hemoglobin to methemoglobin. So, the interaction of the curcumin and nitrite caused the curcumin paper strip to lose color.

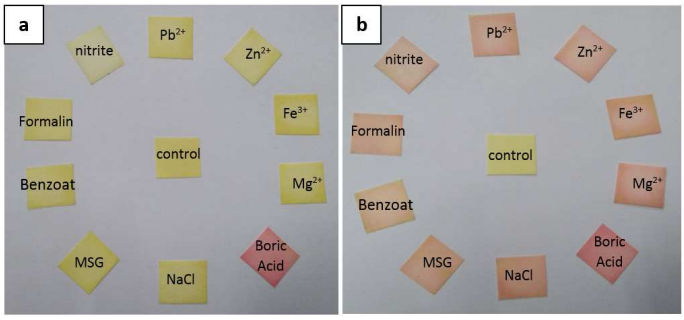

Fig. 7 Detection of curcumin paper strip towards 10000 ppm of various sole chemicals (a), chemicals + boric acid mixture (b).

TABLE I
COLORIMETRIC CHARACTERISTIC OF CURCUMIN PAPER STRIP AGAINST 10000 PPM OF CHEMICALS

Chemical treatment	Color parameter					
	L^*	a^*	b^*	c^*	Hue	ΔE^*
Control	97.50 ± 1.77^{cd}	-19.57 ± 4.64^{cde}	43.45 ± 0.49^{fg}	47.76 ± 2.40^{cde}	114.09 ± 4.76^{bcd}	
Pb^{2+}	97.30 ± 2.34^{cd}	-16.44 ± 7.87^{ef}	40.16 ± 0.89^{de}	43.81 ± 2.78^{bcde}	111.86 ± 9.89^{bc}	5.81 ± 2.60^{ab}
Zn^{2+}	97.54 ± 0.89^{cd}	-17.09 ± 3.21^{def}	37.01 ± 0.66^{d}	40.82 ± 1.91^{bc}	114.66 ± 3.78^{bcde}	7.82 ± 1.06^{ab}
Fe^{3+}	92.44 ± 1.10^{b}	-17.71 ± 5.89^{def}	32.62 ± 1.21^{c}	37.38 ± 2.81^{b}	118.15 ± 8.03^{bcde}	13.77 ± 1.83^{bc}
Mg^{2+}	99.98 ± 0.01^{d}	-31.97 ± 6.67^{bc}	40.56 ± 2.12^{ef}	51.74 ± 5.83^{e}	127.93 ± 4.19^{efg}	13.17 ± 1.79^{bc}
Boric acid	82.16 ± 0.93^{a}	40.61 ± 1.35^{g}	10.41 ± 0.44^{a}	41.93 ± 1.41^{bcd}	14.37 ± 0.14^{a}	70.37 ± 4.53^{f}
NaCl	99.23 ± 0.66^{d}	-43.30 ± 2.55^{ab}	44.44 ± 1.29^{g}	62.05 ± 2.71^{f}	134.23 ± 0.83^{fg}	23.85 ± 5.99^{cd}
MSG	99.99 ± 0.00^{d}	-54.43 ± 5.35^{a}	48.76 ± 1.70^{h}	73.10 ± 5.10^{g}	138.06 ± 1.82^{g}	35.39 ± 6.09^{e}
Benzoate	99.98 ± 0.00^{d}	-29.77 ± 2.33^{cd}	40.52 ± 0.71^{ef}	50.29 ± 1.83^{de}	126.27 ± 1.84^{def}	10.95 ± 3.59^{ab}
Formalin	99.79 ± 0.21^{d}	-26.50 ± 2.77^{cde}	40.77 ± 0.77^{ef}	48.64 ± 2.16^{cde}	122.96 ± 2.20^{cdef}	8.51 ± 5.62^{ab}
Nitrite	95.78 ± 0.13^{c}	-6.24 ± 0.43^{f}	21.00 ± 0.45^{b}	21.91 ± 0.54^{a}	106.54 ± 0.84^{b}	26.39 ± 3.42^{de}

Table 1 shows that the values of a^*, b^*, Hue and ΔE^* on CURNnsr paper strip-boric acid were significantly different ($p<0.05$) toward control and curcumin paper strip-other chemicals. Meanwhile, on curcumin paper, strip-other chemicals did not differ significantly ($p > 0.05$). The value of a^* on curcumin paper strip-boric acid increased, while b^* value decreased. Where a^* and b^* value of 40.61 ± 1.35 and 10.41 ± 0.44, respectively. And the value of ^{o}Hue and ΔE^* on the curcumin paper strip was in the first quadrant on the CIELAB scale with values of 14.37 ± 0.14 and 70.37 ± 4.53, respectively. The Hue value from 0 to < 45^{o}C indicates red [52]. This confirmed that the interaction of boric acid with CURNnsr led to the color change from yellow to red. Similarly, the ΔE^* value of curcumin paper strip-boric acid was significantly different ($p < 0.05$) to the others with a value of 70.37 ± 4.53 ($\Delta E^* > 5$), the value $\Delta E^* > 5$ indicates the color difference that can be seen evidently by the human eye. According to Óbon et al. [53], the values of $0.0 < \Delta E^* < 1.5$ confirm undistinguishable color differences by the human eye. When $1.5 < \Delta E^* < 5.0$ color differences perhaps discernible and become evident when $\Delta E^* > 5.0$. The interaction of curcumin paper strips with other chemicals was stable at yellow. So that curcumin paper strips have good selectivity towards sole boric acid. Figure 7(b) shows

curcumin paper strips' performance in detecting boric acid when it interacted with various chemicals simultaneously (interfering chemicals). Visually, the boric acid detection by curcumin paper strips remained red color even though it was added with various interfering chemicals such as Pb^{2+}, Zn^{2+}, Fe^{3+}, Mg^{2+}, NaCl, monosodium glutamate (MSG), sodium benzoate, formalin, and sodium nitrite. Table 2 showed the color characteristics with parameters of L^*, a^*, b^*, Hue, and ΔE^* values on the biosensor paper strips to various interfering chemicals. Curcumin paper strips-boric acid/chemicals had L^*, a^*, c^*, Hue, and ΔE^* values that were significantly different ($p < 0.05$) (Table 2), where the smallest L* value was 81.66 ± 0.63.

TABLE II
COLORIMETRIC CHARACTERISTIC OF BORIC ACID SENSING BY CURCUMIN PAPER STRIP UPON CONTACT WITH 10000 PPM CHEMICALS INTERFERENCE

Chemicals interference	Color parameter					
	L^*	a^*	b^*	c^*	°Hue	ΔE^*
Control	99.99 ± 0.00^{e}	-69.74 ± 8.03^{a}	54.45 ± 1.87^{g}	88.55 ± 7.42^{d}	141.90 ± 2.31^{e}	
Pb^{2+}	86.10 ± 0.95^{b}	25.38 ± 0.45^{bc}	19.66 ± 0.44^{cde}	30.38 ± 3.41^{ab}	40.81 ± 4.86^{c}	102.25 ± 7.71^{ab}
Zn^{2+}	88.61 ± 0.44^{bcd}	17.43 ± 0.37^{b}	19.31 ± 0.25^{cd}	26.02 ± 0.28^{ab}	47.93 ± 0.77^{d}	94.69 ± 9.51^{a}
Fe^{3+}	88.47 ± 0.61^{bcd}	18.10 ± 1.43^{b}	16.96 ± 0.42^{bc}	24.81 ± 1.30^{a}	43.18 ± 1.67^{cd}	96.23 ± 7.29^{a}
Mg^{2+}	88.65 ± 1.02^{cd}	25.03 ± 1.99^{bc}	15.97± 0.38^{ab}	29.71 ± 1.47^{ab}	32.64 ± 2.71^{b}	102.92 ± 8.93^{ab}
Boric acid	81.66 ± 0.63^{a}	40.95 ± 0.79^{d}	13.74 ± 0.41^{a}	43.19 ± 0.68^{c}	18.55 ± 0.75^{a}	119.36 ± 9.68^{ab}
NaCl	87.40 ± 1.34^{bcd}	28.51 ± 2.96^{bc}	18.06 ± 0.14^{bc}	33.78 ± 2.45^{b}	32.48 ± 2.77^{b}	105.55 ± 8.62^{b}
MSG	89.31 ± 0.74^{cd}	23.10 ± 0.61^{bc}	22.51 ± 1.66^{ef}	32.26 ± 1.47^{ab}	44.22 ± 1.72^{cd}	98.78 ± 9.37^{ab}
Benzoate	89.50 ± 0.45^{d}	22.33 ± 1.54^{bc}	21.72 ± 0.29^{def}	31.20 ± 1.38^{ab}	44.17 ± 1.70^{cd}	98.29 ± 8.36^{ab}
Formalin	86.93 ± 1.03^{bc}	21.96 ± 0.57^{bc}	23.21 ± 0.65^{f}	31.96 ± 0.49^{ab}	46.59 ± 1.27^{cd}	97.76 ± 7.99^{ab}
Nitrite	88.36 ± 0.11^{bcd}	21.12 ± 0.66^{bc}	22.77 ± 0.86^{f}	31.06 ± 0.97^{ab}	47.33 ± 0.71^{cd}	96.96 ± 8.95^{ab}

This result presented that the red color of curcumin paper strip-boric acid was darker than others, indicating that a* and c^* values were higher. It could also be seen that from its Hue value of 18.55 ± 0.75, which indicated the dark red color because it approached 0 [52]. While the value of Hue curcumin paper strip-other chemicals was in the range of 32.48 ± 2.77 to 47.93 ± 0.77, which indicated a red-orange color. Thus, chemicals such as Pb^{2+}, Zn^{2+}, Fe^{3+}, Mg^{2+}, NaCl, monosodium glutamate (MSG), sodium benzoate, formalin, and sodium nitrite in boric acid detection caused the response of color change to became a reddish-orange (red color to fade slightly). This is probably due to CURNnsr solution having a very small size droplet. So, when it was dripped with a chemical solution, curcumin dye became soluble and decays. Consequently, the curcumin concentration in the paper strip reduced and caused the binding with boric acid became decline, so the intensity of the red color decreased. However, these chemicals' presence maybe not interfered with boric acid-sensing because it still responds to a similar color change (no contrast in color differences).

3) Sensitivity of CURNnsr Paper Strip to Boric Acid: The sensitivity of curcumin paper strips to boric acid was examined with different boric acid concentrations from 100 to 10000 ppm. The curcumin paper strip color response scale for various concentrations of boric acid was presented in Figure 8. There was a change in the color of the curcumin paper strip from yellow to red. The color change began from 200 ppm, so the visual limit of detection (LOD) value of 200 ppm where the detection time was about 1 hour. The detection time needs a long time because the interaction between boric acid and curcumin paper strip occurs in dry condition, so it needs about 1 hour to dry the paper strip at ambient temperature.

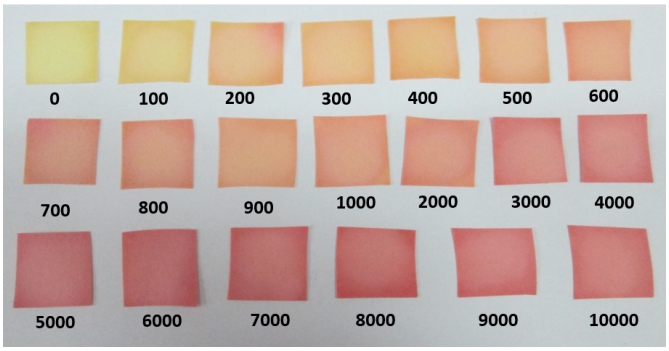

Fig. 8 Color scale of the curcumin paper strip response to various concentration of boric acid solution from 100-10000 ppm

Based on Table 3, it was seen that a^* value of curcumin paper strips-boric acid from 100 to 10000 ppm of boric acid increased in the range of 10.34 ± 0.08 to 38.03 ± 0.17. Similarly, ΔE^* increased in the range of 7.5 ± 0.27 to 46.89 ± 0.23. This showed that the red color intensity of the curcumin paper strip-boric acid increased. However, the increase was relatively not a significant different ($p > 0.05$). While the values of Hue (Figure 8) and b^* decreased from the range 72.42 ± 0.14 to 11.71 ± 0.12 and 32.63 ± 0.04 to 10.43 ± 0.08, respectively. But the decrease that occurred was relatively insignificant too ($p > 0.05$). When it contacts with 100-600 ppm boric acid, the curcumin paper strip color changed from yellow to reddish yellow. That was evidenced by the Hue value ranging from 43.04 ± 0.23–72.42 ± 0.14. Nevertheless, it was in red color with higher intensity upon interacted with 700-10000 ppm of boric acid, where the Hue values ranged from 11.71±0.12–35.93±2.98. According Camgöz [52], Hue values ranging 0-45 and 45-90 correspond to red-yellow and yellow green, respectively.

TABLE III
COLORIMETRIC CHARACTERISTIC OF CURCUMIN PAPER STRIP UPON CONTACT WITH BORIC ACID FROM 100-10000 PPM

Concentration of boric acid (ppm)	Color parameter					
	L^*	a^*	b^*	c^*	°Hue	ΔE^*
0	89.48 ± 0.29^{l}	3.64 ± 0.25^{a}	34.62 ± 0.20^{l}	34.81 ± 0.18^{bcd}	84.00 ± 0.45^{j}	
100	86.78 ± 0.12^{k}	10.34 ± 0.08^{b}	32.63 ± 0.04^{k}	34.23 ± 0.02^{ab}	72.42 ± 0.14^{i}	7.5 ± 0.27^{a}
200	83.95 ± 0.25^{j}	17.95 ± 0.38^{c}	27.76 ± 0.13^{j}	26.26 ± 0.67^{a}	31.81 ± 0.35^{d}	16.80 ± 0.04^{b}
300	84.09 ± 0.19^{j}	18.72 ± 0.32^{cd}	27.76 ± 0.13^{j}	33.48 ± 0.08^{ab}	56.02 ± 0.57^{h}	17.41 ± 0.77^{b}
400	82.03 ± 0.05^{i}	20.61 ± 0.15^{de}	28.16 ± 0.02^{j}	35.63 ± 0.96^{cde}	39.34 ± 1.67^{ef}	19.62 ± 0.55^{b}
500	82.08 ± 0.06^{i}	21.98 ± 0.11^{e}	25.09 ± 0.16^{i}	33.36 ± 0.05^{b}	48.78 ± 0.33^{g}	21.95 ± 0.58^{bc}
600	80.96 ± 0.20^{hi}	24.98 ± 0.16^{f}	23.32 ± 0.04^{h}	34.18 ± 0.09^{ab}	43.04 ± 0.23^{f}	25.60 ± 0.18^{cd}
700	79.85 ± 0.86^{gh}	26.92 ± 0.83^{fg}	19.51 ± 1.54^{ef}	33.27 ± 0.23^{b}	35.93 ± 2.98^{de}	29.38 ± 2.13^{def}
800	80.19 ± 0.29^{gh}	27.16 ± 0.08^{fgh}	21.11 ± 0.50^{fg}	34.40 ± 0.38^{ab}	37.85 ± 0.58^{e}	28.67 ± 0.48^{de}
900	80.96 ± 0.66^{fg}	27.56 ± 1.40^{fgh}	22.58 ± 0.19^{gh}	35.63 ± 0.96^{cde}	39.34 ± 1.67^{ef}	28.98 ± 1.08^{ef}
1000	79.35 ± 0.01^{fgh}	28.74 ± 0.08^{gh}	18.71 ± 0.01^{e}	34.30 ± 0.08^{ab}	33.06 ± 0.06^{d}	31.40 ± 0.46^{efg}
2000	77.57 ± 1.16^{ef}	29.75 ± 1.95^{h}	18.72 ± 0.58^{e}	35.16 ± 1.34^{bcde}	32.23 ± 2.49^{d}	32.81 ± 2.66^{fg}
3000	76.14 ± 0.28^{de}	34.25 ± 0.48^{i}	14.46 ± 0.20^{c}	37.18 ± 0.37^{efg}	22.89 ± 0.57^{c}	39.00 ± 0.17^{g}
4000	75.26 ± 0.18^{bcd}	34.71 ± 0.15^{i}	12.20 ± 0.06^{b}	36.79 ± 0.16^{def}	19.37 ± 0.01^{bc}	40.87 ± 0.42^{hi}
5000	75.39 ± 0.28^{cd}	35.01 ± 0.28^{i}	11.68 ± 0.31^{ab}	36.91 ± 0.16^{def}	18.45 ± 0.59^{b}	41.33 ± 0.08^{hij}
6000	73.59 ± 0.35^{ab}	36.81 ± 0.49^{ij}	10.26 ± 0.06^{a}	38.21 ± 0.49^{fgh}	15.58 ± 0.11^{ab}	44.11 ± 0.87^{ijk}
7000	73.74 ± 0.11^{abc}	36.84 ± 0.22^{ij}	10.28 ± 0.10^{a}	38.25 ± 0.19^{fgh}	15.60 ± 0.23^{ab}	44.07 ± 0.14^{ijk}
8000	72.54 ± 0.45^{a}	37.80 ± 0.72^{j}	11.32 ± 0.03^{ab}	39.46 ± 0.69^{h}	16.67 ± 0.25^{b}	44.69 ± 1.11^{ijk}
9000	72.60 ± 0.72^{a}	37.83 ± 0.80^{j}	10.43 ± 0.08^{a}	39.24 ± 0.80^{gh}	15.42 ± 0.19^{ab}	45.15 ± 1.2^{jk}
10000	72.14 ± 0.08^{a}	38.03 ± 0.17^{j}	7.88 ± 0.04^{d}	38.84 ± 0.16^{fgh}	11.71 ± 0.12^{a}	46.89 ± 0.23^{k}

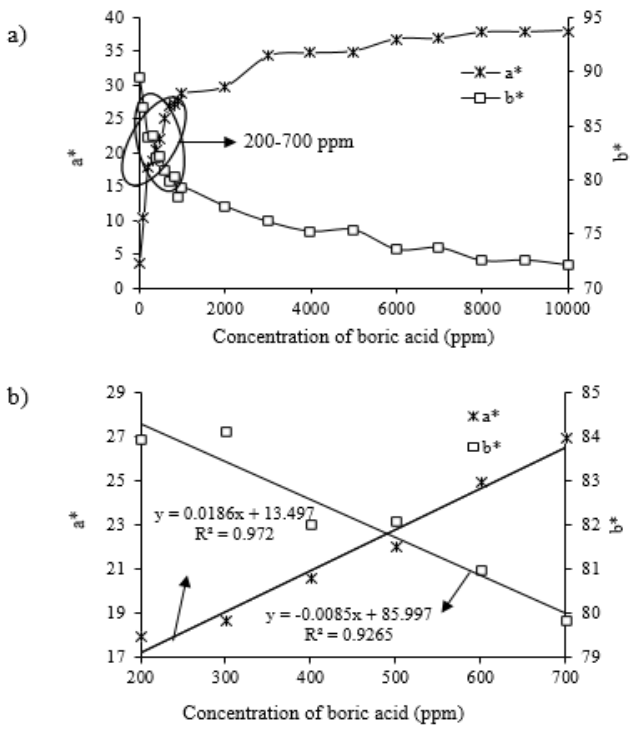

Fig. 9 Relationship between a* and b* values of curcumin paper strip-boric acid and concentration of boric acid from 100 to 10000 ppm (a) calibration line drawn for boric acid sensing by curcumin paper strip based on a* and b* (b)

The red color change of the curcumin paper strip against boric acid increased. In contrast, the intensity of the yellow color decreased to a certain concentration; then it became constant. This was shown based on the values of a^* and b^*, respectively (Figure 9a). Increasing the intensity of the red color based on the value of a^* led to a linearity curve in the range of 200-700 ppm of boric acid where the linear regression equation was expressed as $y = 0.0186x + 13.497$ and the correlation coefficient (R^2) was 0.972 (Figure 9b).

The linear graph obtained the limit of detection (LOD) value of curcumin paper strips for boric acid-sensing of 105.56 ppm. A decrease in the intensity of the yellow color based on the linear b^* value was also occurred at 200-700 ppm, resulting in a linear equation $y = -0.0085 + 85.997$ and $R^2 = 0.927$.

D. The Future Applications of CURNnsr Paper Strips in Food Product

In the future, this paper strip will be applied to detect boric acid in food. Its use is preceded by the preparation of a food sample containing borax. The food samples containing borax are extracted by crushing them with a bit of water added. The food extract about 0.25 µL is then dripped onto the paper strip's surface, then let dry until the color changes. The color change is matched with a color series of paper strips of 0-10000 ppm borax concentration. It is conducted to estimate the borax concentration in the food.

IV. CONCLUSION

Curcumin encapsulation in the form of nanoemulsion is successfully carried out. Curcumin nanoemulsion reagent (CURNnsr) for boric acid detection has a smooth spherical shape with a size of 25.70 nm. After CURNnsr is applied as a paper strip, it can detect boric acid with good sensitivity,

selectivity, and stability. Interaction with boric acid causes the color of the curcumin paper strip to change from yellow to red with the visual LOD of 200 ppm. The color change intensity of the curcumin paper strip increased proportionally to the concentration of boric acid, forming a good linear graph at 200-700 ppm. The linear graph results from the LOD of 105.56 ppm with the detection time of about 1 hour. Curcumin paper strip is one form of colorimetric biosensor development that provides practicality in use. In the future, it is also promising to apply it in societies by use of advantages including low cost, environmentally friendly, easy to use, sensitive, selective, stable, and quick in detecting.

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