

# of chlorpromazine

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**Abstract** We are presenting a simple, low-cost and rapid solid-state optical probe for screening chlorpromazine (CPZ) in aquacultures. The method exploits the colourimetric reaction between CPZ and Fe(III) ion that occurs at a solid/liquid interface, the solid layer consisting of ferric iron entrapped in a layer of plasticized PVC. If solutions containing CPZ are dropped onto such a layer, a colour change occurs from light yellow to dark pink or even light blue, depending on the concentration of CPZ. Visual inspection enables the concentration of CPZ to be estimated. The resulting colouration was also monitored by digital image collection for a more accurate quantification. The three coordinates of the hue, saturation and lightness system were obtained by standard image processing along with mathematical data treatment. The parameters affecting colour were assessed and optimized. Studies were conducted by visible spectrophotometry and digital image acquisition, respectively. The response of the optimized probe towards the concentration of CPZ was tested for several mathematical transformations of the colour coordinates, and a linear relation

was found for the sum of hue and luminosity. The limit of detection is 50  $\mu\text{M}$  (corresponding to about 16  $\mu\text{g}$  per mL). The probe enables quick screening for CPZ in real water samples with prior sample treatment.

**Keywords** Chlorpromazine · Colourimetry · Optical probe · Aquaculture

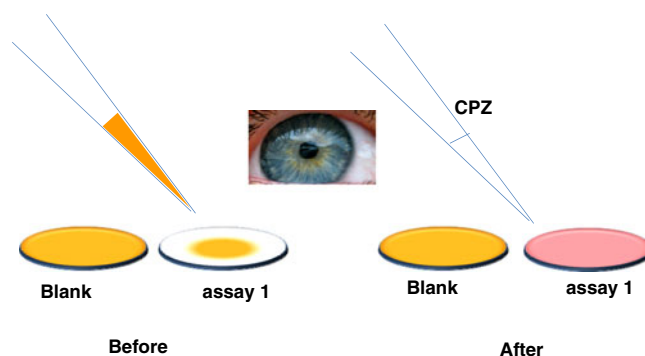
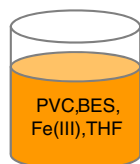
## Introduction

Aquaculture is a vital food source around the world. It provides nutritious and healthy fish and fishery products at low cost. Strong safety policies are applied to these products given that a small mistake may pose a serious risk to an entire population, of acute or long-term effects [1]. Several hazards have been already associated to aquaculture production, including environmental contaminants, unapproved food additives, and improper use of growth hormones or veterinary drugs.

Veterinary drugs employed in aquaculture ensure higher rate benefits within intensive production. They prevent or treat diseases, control parasites, aid reproductive processes, tranquilize fish and promote growth. Some of the drugs are potentially carcinogenic, can cause allergic reactions and may lead to antibiotic resistance in humans [2]. As a consequence, the EU has established regulations that limit or prohibit their use [3].

Chlorpromazine (CPZ) is an example of that. It is phenothiazine derivative employed as an antiemetic, pre-anaesthetic and muscle relaxant, although it is widely used in humans to treat various mental and personality disorders

**Fig. 1** Schematic illustration for the development of the colour product in the probe



[4]. It is today banned from EU although it is still being used in some occasions [3]. Facing today's regulations, it is important to have methods for on-site screening, as a measure of control of its application.

Several methods have been reported in the literature for CPZ determination. These include spectrofluorimetry [5], chemiluminescence [6], high performance liquid chromatography [7–10], voltammetry [11–13], differential pulse stripping voltammetry [14–17], polarography [18, 19], and electrophoresis [20–24], visible spectrophotometry [25–29] and a combination of the previous ones [30]. These methods exhibit excellent selectivity, but require expensive instrumentation and are unsuitable for screening in the local under survey. An alternative procedure for field evaluations could be a small sensing strip, based on an optical probe (for an easy transportation) and low cost materials (allowing its disposable after use).

In general, the major goals of a possible new method rely on the low cost, easy performance and quick response for a specific target analyte. Although not simple, the idea of developing a “simple” colour screening stick for a home-detection of several drugs is indeed very attractive. This concept has been started here for CPZ.

An important characteristic of phenothiazine derivatives is their easy oxidation in acidic medium and subsequent formation of coloured oxidation products [31]. Several oxidants such as  $\text{Fe}^{3+}$ ,  $[\text{Fe}(\text{CN})_6]^{3-}$ ,  $\text{Cr}_2\text{O}_7^{2-}$ ,  $\text{IO}_3^-$ ,  $\text{IO}_4^-$ ,  $\text{BrO}_3^-$ ,  $\text{H}_2\text{O}_2$ , have been reported for this purpose, being iron and its anionic complexes the most used ones [32–34].  $\text{FeCl}_3$  is the elected reagent due to the high stability of the intermediate radicals formed. The optical probe is designed by immobilizing iron on a PVC membrane containing *bis*(2-ethylhexyl)sebacate (BES) as plasticizer, deposited over a polycarbonate solid support. The contact of CPZ with the immobilized iron grants its oxidation and the subsequent formation of a coloured product detected by human eye. This principle may guide to a new generation of portable colourimetric sensing strips for rapid drug screening in real samples, capable of a routine environmental use.

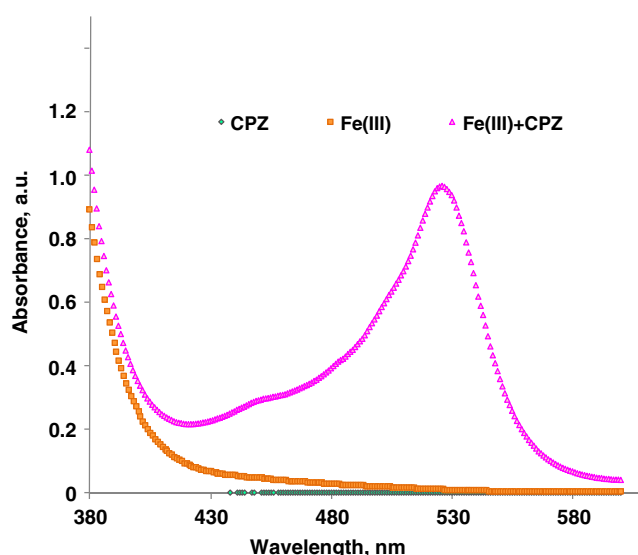
## Experimental

### Apparatus

All spectrophotometric measurements were carried out at room temperature using a double beam Spectrophotometer Thermo Evolution 300 UV-Visible with 1 cm length plastic cells. The digital image of solid surfaces was acquired by a digital camera Olympus C-480 with 4 megapixels, and 3× optical zoom lens. The Paint program of windows 2007 was used for gaining the three coordinates of the HSL model system. Polycarbonate plates (Kartell) of eight cavities and of 200  $\mu\text{L}$  each were used for deposition of the sensory material.

### Reagents

All chemicals were of analytical grade and de-ionized water (conductivity  $<0.1 \mu\text{S cm}^{-1}$ ) was employed. CPZ, *bis*(2-ethylhexyl)sebacate (BES) and poly (vinyl chloride) (PVC) of high molecular weight were purchased from Fluka



**Fig. 2** Spectra of CPZ, Fe(III) and the formation product between both

([www.sigmaaldrich.com](http://www.sigmaaldrich.com)). Tetrahydrofuran (THF) was obtained from Panreac ([www.panreac.es](http://www.panreac.es)). Iron (III) chloride hexahydrate was purchased by Merck ([www.merck-chemicals.com.pt](http://www.merck-chemicals.com.pt)) and HEPES from Sigma ([www.sigmaaldrich.com/chemistry.html](http://www.sigmaaldrich.com/chemistry.html)).

#### Optical single-short probe preparation

The optical single-short probe was prepared by mixing variable amounts of  $\text{FeCl}_3$  with 0.050 g of PVC, and 0.100 g of plasticizer BES. The mixture was stirred until the PVC was well moistened, and dispersed in 2 mL of THF. A volume of 50  $\mu\text{L}$  of each of these solutions was casted on each cavity of the polycarbonate plate and let dry for 30 min (Fig. 1).

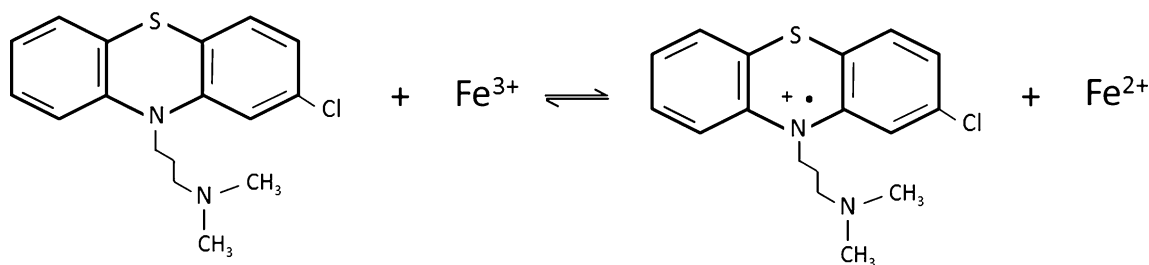
#### Procedures in liquid phase

##### Wavelength selection

The coloured complex formed between Fe and CPZ was investigated by recording the spectra of individual and mixed components. Solutions of  $6.7 \times 10^{-3} \text{ mol L}^{-1}$  Fe(III),  $3.0 \times 10^{-4} \text{ mol L}^{-1}$  CPZ and a mixture of both (1:1) were used for this purpose. These solutions were prepared in variable pHs (acidic, neutral and alkaline) by addition of a few drops of saturated sodium hydroxide or hydrochloric acid solutions. Maximum absorbancies were obtained for 526 nm, in acidic medium, and further quantification studies were carried out in this wavelength.

##### pH effect

The CPZ and Fe(III) solutions were prepared in  $1.00 \times 10^{-2}$  and  $1.00 \times 10^{-3} \text{ mol L}^{-1}$  HEPES buffer solutions, respectively. The final pH of this solution was adjusted from 1 to 12, by the addition of suitable amounts of saturated sodium hydroxide or concentrated hydrochloric solutions. A calibration curve from  $1.66 \times 10^{-5}$  to  $5.81 \times 10^{-4} \text{ mol L}^{-1}$  CPZ was traced for each pH condition. The concentration of Fe (III) was kept constant in all experiments, always  $3.35 \times 10^{-3} \text{ mol L}^{-1}$ .



**Scheme 1** Oxidation of Chlorpromazine in presence of ferric chloride

#### $\text{FeCl}_3/\text{CPZ}$ ratio

The Fe(III) concentration was studied for pHs 3 and 9 and a  $3.04 \times 10^{-4} \text{ mol L}^{-1}$  CPZ solution. The concentration of Fe (III) was varied between  $6.67 \times 10^{-4}$  to  $2.00 \times 10^{-2} \text{ mol L}^{-1}$ . All absorbances were measured for 526 nm.

#### Complex stability

The stability of the colour oxidation product was investigated by measuring the absorbance for 16 h. The solutions were prepared at pH 3 and 9. The CPZ concentration was  $3.04 \times 10^{-4} \text{ mol L}^{-1}$  and the Fe(III) concentration ranged from  $3.35 \times 10^{-4}$  to  $3.35 \times 10^{-2} \text{ mol L}^{-1}$ , respectively.

#### Procedures in solid phase

##### Analytical procedure

A volume of 150  $\mu\text{L}$  of CPZ standards ranging from  $5.00 \times 10^{-5}$  to  $1.00 \times 10^{-1} \text{ mol L}^{-1}$  or samples was added to each probe on the polycarbonate plate. The blank was the buffer solution and used as control. The colour of the probes were measured by taking their picture with a digital camera and treating the results with the PAINT program of Windows, using the three coordinates of the HSL model: hue, saturation and lightness. These three values were manipulated in order to obtain a linear or second degree function against the CPZ concentration. All measurements corresponded to the average of, at least, three trials.

##### Optimization procedures

The study of the amount of Fe(III) in the membrane was carried out similarly to that described in “ $\text{FeCl}_3/\text{CPZ}$  ratio”. The amount of Fe(III) studied was 0.5 or 0.1 g for pH 3 or 9, respectively.

The time required to achieve a constant colour on the surface of the optical probes was studied by monitoring the analytical response for one hour and thirty minutes. The stability to the complex was also evaluated by means of this study.

**Table 1** pH effect in liquid phase

Parameters	pH								
	1	2	3	4	5	7	9	11	
Slope, L mol <sup>-1</sup> cm <sup>-1</sup>	2229.44	1444.13	1270.87	803.52	804.34	1519.47	942.42	933.23	
LLLR, mol L <sup>-1</sup>	8.21×10 <sup>-5</sup>	1.67×10 <sup>-4</sup>	8.42×10 <sup>-5</sup>	8.47×10 <sup>-5</sup>	8.26×10 <sup>-5</sup>	1.65×10 <sup>-5</sup>	8.21×10 <sup>-5</sup>	8.56×10 <sup>-5</sup>	
LSRL, mol L <sup>-1</sup>	4.92×10 <sup>-4</sup>	5.84×10 <sup>-4</sup>	5.05×10 <sup>-4</sup>	5.08×10 <sup>-4</sup>	4.13×10 <sup>-4</sup>	4.94×10 <sup>-4</sup>	5.75×10 <sup>-4</sup>	5.14×10 <sup>-4</sup>	
r <sup>2</sup>	0.9964	0.9936	0.9978	0.9945	0.9956	0.9966	0.9924	0.9921	
O.O.	0.207	0.237	0.123	0.179	0.141	0.105	0.210	0.266	

The effect of pH was tested by calibrating the optical probe with CPZ stock solutions of pH 3 or 9.

#### Determination of CPZ in aquaculture water

The optical probe was used for the direct determination of CPZ in water from aquaculture activities. Colour measurements were made by applying the test solution directly over the probe. The results were recorded with a digital camera and the CPZ concentration was calculated using the calibration data.

## Results and discussions

### Formation of coloured complex in aqueous media

The formation of the coloured complex was confirmed by recording the visible spectra of single and mixed solutions of Fe(III) and CPZ (Fig. 2). The CPZ solution was unable to absorb radiation from 360 to 750 nm. The Fe(III) solution displayed a light yellow colour, producing little absorbancies within the higher wavelengths; this light colour indicated the presence of Fe(OH)<sup>2+</sup> or Fe(OH)<sub>2</sub><sup>+</sup> species.

A single and strong peak was detected on the spectra of the mixed solution, displaying maximum absorbing properties in 526 nm. The compound behind this peak was probably the radical cation of CPZ, as a result of its oxidation and subsequent Fe (III) reduction in a 1:1 molar ratio. This mechanism of the redox reaction is shown in Scheme 1.

The obtained absorbancies increased with the CPZ concentration, suggesting a successful application of this system in quantification studies.

### pH effect

This parameter is very important given that the colour of a specific compound is intrinsically connected to its protonation state. The extent of the reaction leading to the

formation of the coloured product and the stability of the formed compound also depend on the pH [33]. In addition, previous studies using FeCl<sub>3</sub> as oxidizing agent indicate an acidic media as the optimal condition for the formation of coloured products [34,35].

The pH effect was tested by calibrating the system in different buffers, ranging from pH 1 to 11, with a fixed amount of Fe(III) and varying concentrations of CPZ (Figure S1, Electronic Supplementary Material). The resulting calibration data is presented in Table 1. pHs 1 and 2 provided average slopes of 2229 and 1444 L mol<sup>-1</sup> cm<sup>-1</sup>, respectively, the highest ones obtained. In terms of lower limit of linear range the behavior was about 8.0×10<sup>-5</sup> mol L<sup>-1</sup> in all pHs, except for pHs 2 and 7. However, high intercepts with Y-axes were obtained for pHs ranging from 3 to 7. This resulted from the light yellow colour from iron (III), but this solution could not be used as reference because the concentration of iron (III) varied along each calibration as it was being reduced by CPZ. The higher correlation coefficients were obtained for pH 3, suggesting that the product of the reaction was more stable under this condition. Thus, as a compromise, pH 3 was selected as the best condition in the acidic range.

In alkaline media, both pH 9 and 11 presented similar results however, although smooth, pH 9 display better sensitivity and lower limit of linear range. Compared with the last two pH, pH 7 presented higher value of lower limit of linear range. For all pH, different behaviors were obtained as show figure S1. According to the results, pH 3 in acid and pH 9 in alkaline media were selected for further experiments, once in solution it could exist different ferric species according to pH that could affect the results.

**Table 2** Membrane composition for the optical probe

Compound	25% Iron (g/g)	40% Iron (g/g)
Fe(III) (g)	0.0509	0.1004
PVC (g)	0.0496	0.0531
BES (g)	0.1069	0.1031
THF (mL)	2	2

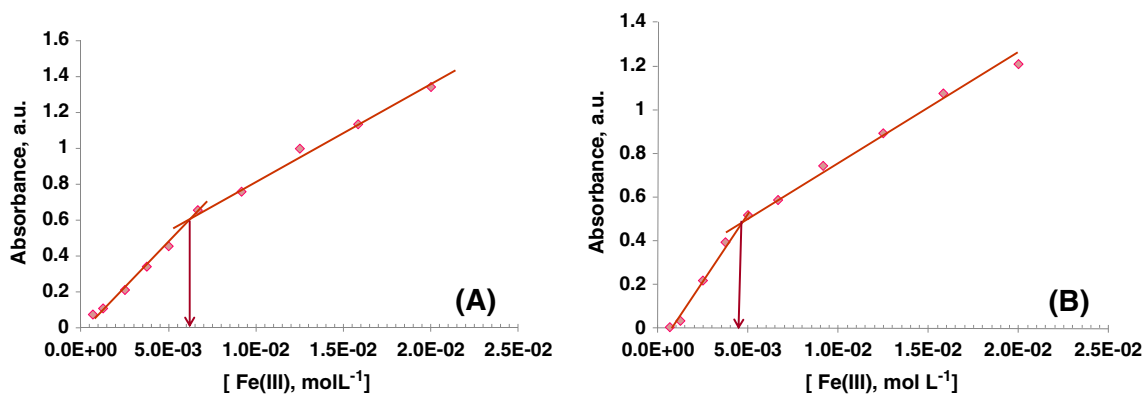


Fig. 3 Effect of molar ratio Fe(III)/CPZ on the coloured complex formation in solution media: (a) pH 3; (b) pH 9

#### Ratio of $\text{FeCl}_3$ /CPZ

All solutions should carry a sufficient amount of Fe(III) to react with all CPZ molecules present in the solution, up to the maximum CPZ concentration tested. If the reaction taking place was incomplete, an exceeding amount of reactant would favour the formation of the coloured product. This procedure increases the cost of the determination, for which the amount of Fe(III) should be set to the minimum required to produce the desired sensitivity.

In the present study, a solution of  $3 \times 10^{-4} \text{ mol L}^{-1}$  in CPZ was added of different Fe(III) concentrations, buffered to the previously selected pHs. Fe(III) concentrations ranged from  $3 \times 10^{-4}$  to  $2.0 \times 10^{-2} \text{ mol L}^{-1}$ , corresponding to Fe(III)/CPZ ratios from 1 to 67. In all cases, the colour formation was immediate and quite stable along time. Not at all expected, Fe(III)/CPZ ratios up to 4 gave light blue solutions that changed to pink with higher amounts of Fe(III). Thus, the kind of colour obtained could work as an indicator of the concentration level present in a given sample.

The experimental data showed that an increasing amount of Fe(III) increased the absorbance of the resulting solution

up to a maximum of about 1200 m.a.u. (Fig. 3). This plateau was never observed for lower concentration ratios, down to 0.1.

The intercept of the two linear regions displayed in Fig. 3 is the best concentration for Fe(III). For pH 3 a  $5.8 \times 10^{-3} \text{ mol L}^{-1}$  concentration was selected, corresponding to a molar ratio Fe(III)/CPZ of 20. For pH 9 the Fe(III) concentration was set to  $4.5 \times 10^{-3} \text{ mol L}^{-1}$ , corresponding to a molar ratio Fe(III)/CPZ of 14. These great excess of iron required confirmed that the reaction was incomplete. Similar results were obtained for different times up to 30 min after mixing the reagents, thus suggesting that the reaction was in equilibrium or that the formed product was stable for a long time.

#### Complex stability

The stability of the complex was studied by measuring the absorbances of all calibrating solutions (from  $3.35 \times 10^{-4}$  to  $3.35 \times 10^{-2} \text{ mol L}^{-1}$ ) for 16 h. Studies were conducted for pHs 3 and 9 and the results are plotted in Fig. 4.

A similar behaviour was obtained in both pHs. The colour was formed immediately after mixing Fe(III) and

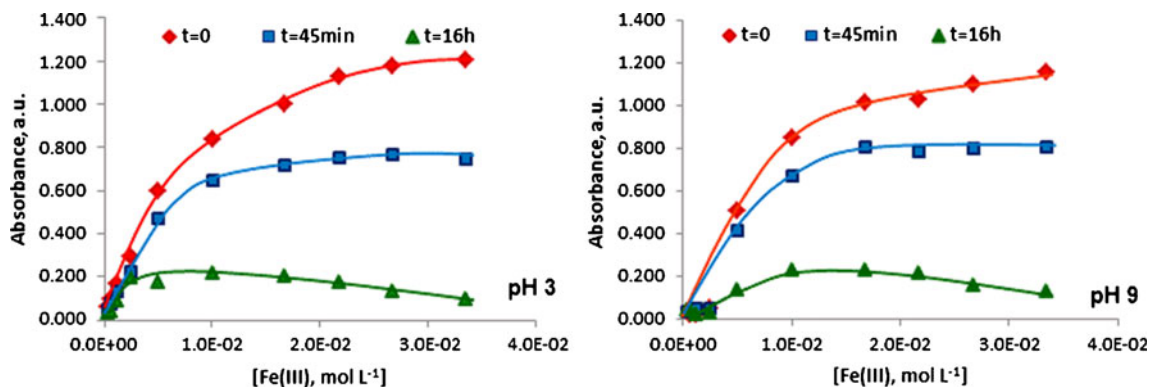
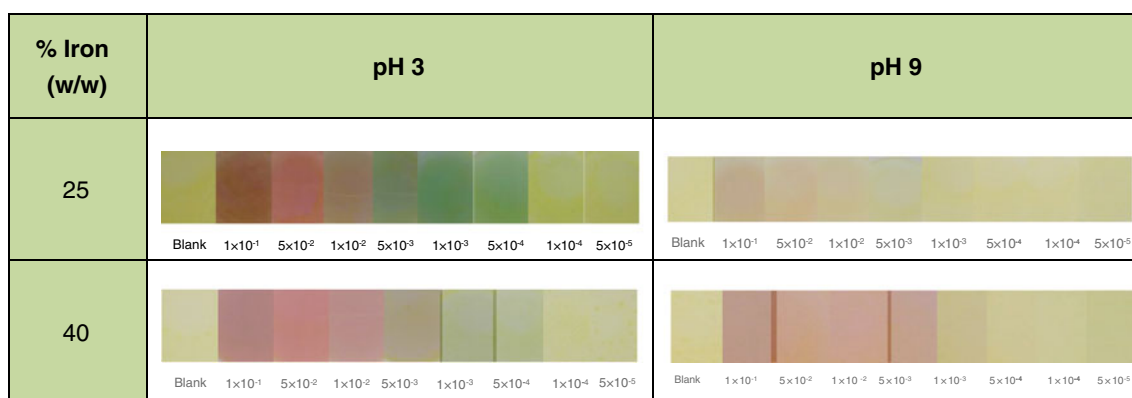


Fig. 4 Stability of the coloured complex during 16 h in solution media



**Fig. 5** Influence of pH and Fe(III) amount on the coloured complex formation in a solid matrix

CPZ. Maximum absorbances were therefore obtained at time zero. The absorbance was not stable for 30 min, decreasing with a slow rate. A faster decrease was observed afterwards and by the end of 16 h the absorbance of the complex was very low.

Curiously, the product formed in a pH 3 environment was a little less stable within time than that obtained in pH 9.

#### Preparation of the optical single-short probe

The optical probe was prepared by entrapping Fe(III) on a polymeric matrix. Plasticized PVC was selected for this purpose because it is inert to both CPZ and iron and allows ion-exchange on the solid/liquid interface. In addition, it is of low cost and compatible with most materials that may constitute the physical support of the probe, such as ceramics and regular plastics.

Knowing that the amount of Fe(III), pH and time may turn out crucial parameters, these were finely studied under solid state.

#### Fe(III) load and pH

The previous studies have indicated the need to control the pH and ensure an exceeding amount of Fe(III), conditions with great impact on the detection limit of the probe. There

is however a physical limit for doping a PVC membrane with a solid species and preserving its mechanical integrity and exchange capability. In addition, the higher the iron amount, the more intense was the yellow colour of the blank membrane.

Two doping levels of Fe(III) for pHs 3 and 9 were tested (Table 2): 25% or 40% (w/w), the later being the maximum loading percentage possible. Visual inspection indicated that the membrane with higher amount of Fe(III) presented more intense colours, including that of the blank membrane. Each membrane was used to make a calibration curve with stock solutions of CPZ ranging from  $5 \times 10^{-5}$  to  $1 \times 10^{-1} \text{ mol L}^{-1}$  and was also made a membrane as a blank. For the higher concentrations of CPZ the membrane changed to dark pink colour while the low concentrations gave a light blue (Fig. 5).

The colour gradient was more intense for membranes with a higher amount of Fe(III). This was confirmed by both visual and digital inspections, in pHs 3 and 9. Regarding digital acquisition, several three-dimensional representations of a specific colour could represent useful properties of that colour, but only the application determines which would be the most reliable. In the present study, and with the purpose of giving a simple way of measuring in almost any place, the HSL model in programs from Windows was selected. Several mathematical approaches were made over the three coordinates to reach

**Table 3** Influence of pH and ion(III) amount in the probe

Parameters	25% Iron (g/g)		40% Iron (g/g)	
	pH 3	pH 9	pH 3	pH 9
Slope	13.64	10.17	24.02	15.67
LLLR, $\text{mol L}^{-1}$	$5.01 \times 10^{-5}$	$5.01 \times 10^{-4}$	$5.01 \times 10^{-5}$	$1.00 \times 10^{-4}$
LSRL, $\text{mol L}^{-1}$	$1.00 \times 10^{-1}$	$1.00 \times 10^{-1}$	$1.00 \times 10^{-1}$	$1.00 \times 10^{-1}$
$r^2$	0.8820	0.8592	0.9529	0.9170
Intercept, a.u.	66.12	40.24	113,91	69,68

**Table 4** Stability results according to pH and Fe(III) amount during 90 min

	25% Iron (g/g)						40% Iron (g/g)					
	pH 3			pH9			pH 3			pH9		
Time, s	0	45	90	0	45	90	0	45	90	0	45	90
Slope	13.64	28.07	23.55	10.17	15.57	24.02	24.02	23.04	24.04	15.67	17.85	13.28
LLLR, mol L <sup>-1</sup>	5.01 × 10 <sup>-5</sup>	5.01 × 10 <sup>-5</sup>	5.01 × 10 <sup>-5</sup>	5.01 × 10 <sup>-4</sup>	5.01 × 10 <sup>-5</sup>	1.00 × 10 <sup>-4</sup>	5.01 × 10 <sup>-5</sup>	5.01 × 10 <sup>-5</sup>	5.01 × 10 <sup>-5</sup>	1.00 × 10 <sup>-4</sup>	1.00 × 10 <sup>-4</sup>	1.00 × 10 <sup>-4</sup>
LSLR, mol L <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	1.00 × 10 <sup>-1</sup>	5.01E-02
r <sup>2</sup>	0.8820	0.9320	0.9696	0.8592	0.9725	0.9695	0.9529	0.9403	0.9223	0.9170	0.9891	0.8981
Intercept, a.u.	66.12	117.04	105.83	40.24	69.73	96.51	113.91	99.67	105.78	69.68	95.30	70.80

a simple correlation between the true and known variable (concentration, in X axis) and the analytical signal (in Y axis). In almost all cases, this was achieved by plotting the sum of hue and luminosity against logarithm concentration. The Y axis was considered as arbitrary units while the concentration was expressed in mol L<sup>-1</sup>.

The general analytical features of the prepared optical single-short probe are indicated in Table 3. The membranes working in pH 3 displayed linear ranges from  $5 \times 10^{-5}$  to  $1 \times 10^{-1}$  mol L<sup>-1</sup>. The 40% load in Fe(III) gave the highest slopes, double to those observed in 25%. Similar behaviour was observed for pH 9, with the membranes of higher Fe (III) load giving higher sensitivity and better linear ranges ( $1 \times 10^{-4}$  against  $5 \times 10^{-4}$  mol L<sup>-1</sup>).

In general terms, the highest load in Fe(III) favoured the analytical features of the sensing membrane for increasing the amount of reaction product. The best analytical performance was reached when CPZ was prepared in acid media. This was confirmed by the literature, because the radical products from the iron/CPZ redox reaction were stabilized by acidic conditions.

#### Reading time

Although the complex is stable for a long period, the CPZ molecule in a liquid phase must meet Fe(III) on a solid phase for reaction to take place. CPZ has to reach the solid membrane where the iron is entrapped or find leached iron

in the liquid phase. This means that some additional time may be required to achieve maximum colour. The intensity of the colour of the optical single-short probe was tested for 90 min.

Membranes with lower amounts of Fe(III) covered with solutions of pH 3 showed colours of increased intensity up to 45 min, and after that time the colour started fading away. For pH 9 the colour intensity kept increasing until the 90 min. This increase was not however proportional in all standards, narrowing the linear range.

Membranes of higher iron load and tested in solutions of pH 3 displayed almost immediately their final colour. This colour was stable along the 90 min. For pH 9, the colour intensity of the complex increased slightly until 45 min, decreasing after that. Thus, colour measurement should be conducted before 45 min for the present membranes.

#### Determination of CPZ in aquaculture water

The best optical probe was applied to determine CPZ in aquaculture water: higher iron loads (40% g) and tested in pH 3. Blank water samples were spiked of  $5.0 \times 10^{-4}$ . Visual inspection allowed confirming the low concentration because the colour formed was light blue. The analytical results confirmed the accuracy and precision of the screening probe for the lower concentration range (Table 4). Thus, the probe may be used to screen CPZ in low concentrations ( $\approx 150 \mu\text{g mL}^{-1}$ ) (Table 5).

**Table 5** Colourimetric determination of CPZ in aquaculture samples with the optical probe

Sample	CPZ, mol L <sup>-1</sup>	log Conc. CPZ	Found, mol L <sup>-1</sup>			
			Solid sensor	Average	Standard deviation	Relative Error, %
Aquaculture 1	$5.00 \times 10^{-4}$	-3.30	$5.72 \times 10^{-4}$	$6.10 \times 10^{-4}$	$8.67 \times 10^{-9}$	12.56
			$6.86 \times 10^{-4}$			27.11
			$5.72 \times 10^{-4}$			12.56

## Conclusions

In this work an optical probe for quick screening CPZ was developed by incorporating iron in a PVC plastic membrane. Surface colour change was easily achieved by naked eye. The resulting colour intensity observed by a digital camera was directly proportional to log of CPZ concentration. The use of Fe(III) in higher amounts, as well as the preparation of CPZ solution in pH 3 enhanced the intensity of the determination. Measurements should be conducted before 45 min after the beginning of the reaction to assure high signals.

This work allowed the rapid screening of CPZ and shows strong potential for field applications. However its detection limit is not low enough for a direct analysis of the samples. Therefore, further tests should be conducted to improve this parameter. This should start by attaching Fe (III) to nanoparticles bound to the outer layer of a polymeric membrane, increasing the contact area and, consequently, decreasing the detection limit.

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