Spectrophotometric determination of triclosan based on diazotization reaction: response surface optimization using Box–Behnken design

Inderpreet Kaur, Sonal Gaba, Sukhraj Kaur, Rajeev Kumar and Jyoti Chawla

ABSTRACT

A spectrophotometric method based on diazotization of aniline with triclosan has been developed for the determination of triclosan in water samples. The diazotization process involves two steps: (1) reaction of aniline with sodium nitrite in an acidic medium to form diazonium ion and (2) reaction of diazonium ion with triclosan to form a yellowish-orange azo compound in an alkaline medium. The resulting yellowish-orange product has a maximum absorption at 352 nm which allows the determination of triclosan in aqueous solution in the linear concentration range of 0.1–3.0 μM with $R^2 = 0.998$. The concentration of hydrochloric acid, sodium nitrite, and aniline was optimized for diazotization reaction to achieve good spectrophotometric determination of triclosan. The optimization of experimental conditions for spectrophotometric determination of triclosan in terms of concentration of sodium nitrite, hydrogen chloride and aniline was also carried out by using Box–Behnken design of response surface methodology and results obtained were in agreement with the experimentally optimized values. The proposed method was then successfully applied for analyses of triclosan content in water samples.

Key words | Box–Behnken design (BBD), diazotization reaction, optimization, response surface methodology (RSM), spectrophotometric determination, triclosan

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INTRODUCTION

Triclosan (2,4,4′-trichloro-2′-hydroxydiphenylether), also known as Irgasan DP 300, is an antibacterial and antifungal agent found in consumer products, including toothpaste, soaps, detergents, toys, and surgical cleaning treatments (Marques *et al.* 2017). Triclosan is also incorporated into fabrics and plastics, including toothbrush handles, cutting boards, pizza-cutters and mop handles as well as surgical drapes and hospital over-the-bed table tops (Schweize 2001). Depending on the formulation and application, triclosan is recognized by the United States Food and Drug Administration (FDA) as either an over-the-counter or a prescription drug. In addition, it is FDA-accepted for use as an antimicrobial pesticide for fungicide/fungistat and bacteriostat applications. The last decade has seen a rapid increase in the use of triclosan-containing products. Due to its extensive use and stability, triclosan and its derivatives can now readily be detected in the environment and some food sources (Okumura & Nishikawa 1996). Triclosan has also been detected in breast milk, urine and plasma, with levels of triclosan in the blood correlating with consumer use patterns of the antimicrobial products (Dann & Hontela 2011). Nevertheless recent reports also demonstrated that triclosan can combine with chlorine in tap water to form chloroform, which is classified by the United States Environmental Protection Agency as a probable human carcinogen (Sioufi *et al.* 1977). Additionally, triclosan is lipophilic, and can bio-accumulate in fatty tissues (Miller *et al.* 1983). Over 95% of the uses of triclosan are in consumer products that are disposed off in residential drains (Reiss *et al.* 2002). Since wastewater treatment plants fail to remove triclosan from the water and the compound is highly stable for long periods of time, a huge amount of triclosan is expected to be emitted into waterways (Adolfsson-Erici *et al.* 2002; Kolpin *et al.* 2002; Lindstrom *et al.* 2002; Nakada *et al.*

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2010; Kookana *et al.* 2011; Lyndall *et al.* 2017). Triclosan has been widely found in rivers, lakes and open sea water at mg/L levels (Kolpin *et al.* 2002; Thomas & Foster 2004). With exposure to UV radiation at 254 nm, triclosan can photodegrade to 2,7- and 2,8-dichlorodibenzo-p-dioxin (2,7/2,8-DCDD) (Lorres *et al.* 2005). In addition, 2,4-dichlorophenol (DCP), which is not a dioxin, has been identified as a major degradation product under artificial conditions and it was reported that 93.8–96.6% of the applied triclosan degrades to DCP within 240 minutes post treatment. Studies on the health effects of triclosan indicated that it is endocrine (hormonally) active and has the potential to affect the liver, blood, thyroid and reproductive systems. So, it is necessary to monitor the triclosan content in various water bodies.

Although many techniques such as gas chromatography atomic emission detection (Rasmussen *et al.* 1996), gas chromatography–ion trap mass spectrometry (Wu *et al.* 2007; Canosa *et al.* 2008), liquid chromatography with ultraviolet detection (LC-UVD) (Silva *et al.* 2005), liquid chromatography–mass spectroscopy (LC-MS) (Chu & Metcalfe 2007) and electrochemical methods (Pemberton & Hart 1999; Safavi *et al.* 2003; Montaseri & Forbes 2016) and chemiluminescence (CL) (Song *et al.* 2007) are available for determination of triclosan even at very low concentration (mg/mL), these techniques require expensive, heavy and sophisticated instrumentation, which might not be available in many laboratories. Therefore, it is necessary to develop a sensitive, selective and convenient method for the determination of triclosan in order to monitor its content in water bodies as they provide the main route of its entrance into the environment.

So, it is necessary to explore methods for the determination of triclosan which are relatively economic and involve simple instrumentation. Keeping this in mind, a simple, reliable, economic and rapid spectrophotometric method based on the diazotization reaction between sodium nitrite, aniline and triclosan has been proposed (Figure 1). The reaction conditions and the concentration of hydrochloric acid (HCl), sodium nitrite ($NaNO_2$), and aniline ($C_6H_5NH_2$) were optimized for the diazotization reaction to achieve good spectrophotmetric determination of triclosan. Furthermore, the optimization of experimental conditions was also carried out for spectrophotometric determination of triclosan in terms of concentration of sodium nitrite, HCl, and aniline by using Box–Behnken design of response surface methodology (RSM). RSM is a collection of statistical and mathematical tools that has been recognized as helpful for multifactor optimization of various processes and is extensively used for experimental design (Vining & Myers 1991; Singh *et al.* 2005). Box–Behnken design (BBD) was customized for three levels (-1, 0, and +1). This method was then successfully applied for determination of triclosan content in various water samples.

MATERIALS AND METHODS

Chemicals and instruments

AR grade chemicals used in the present study were triclosan (Sigma-Aldrich), sodium nitrite (Spectro Chem. Pvt. Ltd), aniline (SD Fine Chem. Ltd, HCl (SD Fine Chem. Ltd), NaOH (Fischer Scientific), glycine (New India Chemical Enterprises), NaCl (Sisco Chem. Pvt. Ltd). All solutions were prepared with double distilled water. Working standard solutions were prepared daily by appropriate dilution of the stock solution with double distilled water. An electrical oven (Universal), UV–visible (UV-Vis) spectrophotometer

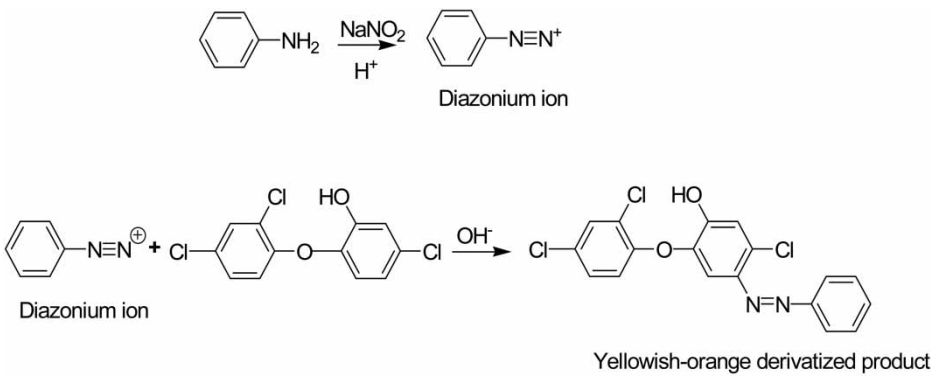

Figure 1 | Proposed reaction mechanism of diazotization reaction.

(UV-1800, Shimadzu), and ultrasonic cleaner (KQ218) were used in the present study.

Preparation of stock solutions

A triclosan stock solution of 1×10^{-5} M was prepared by dissolving 0.00028 g of triclosan in 20 mL of 0.01 M NaOH and diluting to 100 mL with deionized water, which was stored in a refrigerator. Sodium nitrite stock solution with a concentration of 0.50 M was prepared by dissolving 3.45 g $NaNO_2$ in 100 mL water and diluted to 0.020 M with water before use. Aniline solution (1×10^{-2} M) was prepared by dissolving an appropriate amount of aniline (0.1 mL) in 0.1 M hydrochloric acid (100 mL). An alkaline glycine buffer of pH 12 was used to maintain alkaline pH of the solution.

Methods

Diazotization reaction

To a mixture of 1.5 mL of 0.02 M nitrite solution was added 1.0 mL of 0.01 M aniline solution in 0.1 M hydrochloric acid, 3.5 mL of triclosan standard (or sample solution) and 2.0 mL of glycine buffer solution step by step with careful mixing after each addition. Finally, the contents were diluted with deionized water to 10.00 mL. The intense yellowish-orange colored solution so obtained was analyzed for absorbance using a UV-Vis spectrophotometer.

Absorption maxima for derivatized triclosan solution

The UV-Vis spectrum was recorded by measuring the absorbance of derivatized triclosan solution at various wavelengths in the range of 320–600 nm. The plot between wavelength and absorbance so obtained is shown in Figure 2. From the plot, it is clear that an absorption maximum is at 352 nm. Hence, $\lambda_{max} = 352$ nm and it was then chosen for all further recordings.

Optimization of concentration of HCl, $NaNO_2$ and $C_6H_5NH_2$ for diazotization reaction

The reaction conditions for the derivatization process were optimized systematically, by studying the effect of concentration of sodium nitrite, aniline, and HCl on the sensitivity of the method.

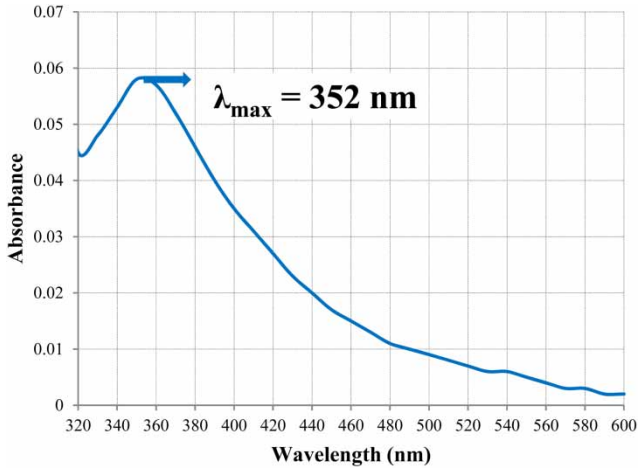

Figure 2 | Plot between absorbance and wavelength showing $\lambda_{max} = 352$ nm of derivatized triclosan.

Optimization of triclosan determination using RSM

The reaction conditions for the derivatization process, i.e. concentration of sodium nitrite, aniline, and HCl, were optimized systematically by RSM. RSM is an experimental approach focused specifically on finding the role of individual process parameters and also the effect of their interaction with each other in bringing out the responses. In this study, the experiments were conducted according to a Box–Behnken type response surface design. For applying the approach, Design-Expert® software (Version 7.0.0, Stat-Ease Inc., Minneapolis, USA) was used.

The course of action of the RSM was as follows:

(i) Designing of experiments for measurement of the absorbance as response and developing a mathematical model with the best fittings.
(ii) Finding the optimal set of concentrations of HCl, $NaNO_2$ and $C_6H_5NH_2$ that produces a maximum value of absorbance.
(iii) Representing the direct and interactive effects of concentration of HCl, $NaNO_2$ and $C_6H_5NH_2$ by two- and three-dimensional plots.

Mathematical modeling. The second order response surface representing the absorbance can be expressed as a function of concentration of HCl, $NaNO_2$ and $C_6H_5NH_2$, being the input variables (Davim & Francisco 2005). A regression model can also be used for the same purpose (Draper & Smith 1981). Analysis of variance was used to check the adequacy of the model. It is a statistical assessment tool that uses sum of squares and F statistics to find out the relative

significance of affecting parameters, measurement errors and uncontrolled parameters (Montgomery 1991).

Practical application

Determination of triclosan content in water samples was carried out using this spectrophotometric method based on the diazotization reaction with optimized reaction conditions. The procedure adopted for sample preparation was as: 100 mL volume of each sample collected from various locations was first filtered and treated with 1 g of NaOH. Subsequently, the pH of the sample was adjusted in the range of 2–3 using 6 M HCl. The pH-adjusted water sample was extracted three times using hexane (10 mL). The hexane phase was dehydrated using anhydrous Na_2SO_4. The dehydrated hexane phase was concentrated up to 3–5 mL by heating it slowly on a water bath and further evaporated to dryness. The sample was dissolved in 5 mL of 0.01 M NaOH and derivatization of triclosan present in the water sample was carried out using optimum reaction conditions. The colored solution so obtained was analyzed spectrophotometrically at $\lambda_{max} = 352$ nm and triclosan content was determined with the help of the calibration curve.

RESULTS AND DISCUSSION

This is a simple diazotization reaction which involves the reaction of sodium nitrite with aniline in an acidic medium to form diazonium ion, which further reacts with triclosan to form an azo compound in an alkaline medium (proposed mechanism is given in Figure 1). The reaction conditions for the derivatization process were optimized systematically, by studying the effect of concentration of sodium nitrite, aniline, and HCl on the sensitivity of the method.

Effects of concentration of HCl, $NaNO_2$ and $C_6H_5NH_2$

Effect of hydrochloride concentration

The effect of concentrations of HCl on the sensitivity of the method was investigated by carrying out diazotization of triclosan over the range of 0.025–0.50 M. The results are shown in Figure 3. It shows that absorbance increases initially with increase in concentration of HCl up to 0.25 M and then becomes constant. So, 0.25 M HCl was chosen for the derivatization process to achieve good response.

Effect of sodium nitrite concentration

The effect of sodium nitrite concentration on the sensitivity of the method was also studied over the range 0.005–0.05 M. The results obtained are shown in Figure 4. The absorbance increased gradually with increase in concentration of sodium nitrite and remained constant after 0.03 M. Therefore, 0.03 M sodium nitrite was chosen for further study.

Effect of aniline concentration

The effect of aniline concentration on the sensitivity of the method was also studied over the range 0.0025–0.02 M. The results are shown in Figure 5. The absorbance increased gradually with increase in aniline concentration and remained constant after 0.01 M. Therefore, 0.01 M aniline was chosen for further study.

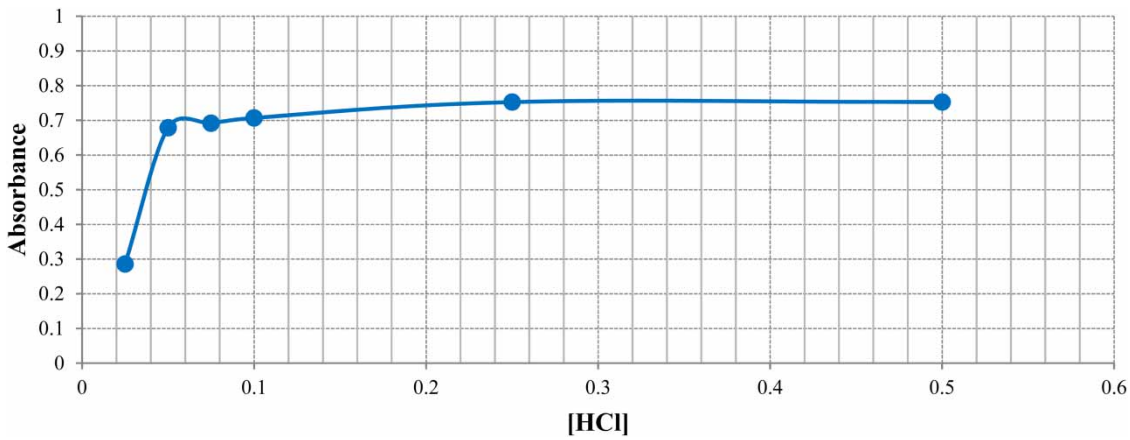

Figure 3 | Effect of HCl concentration on the sensitivity of spectrophotometric determination. [Triclosan] = 1.5 μM.

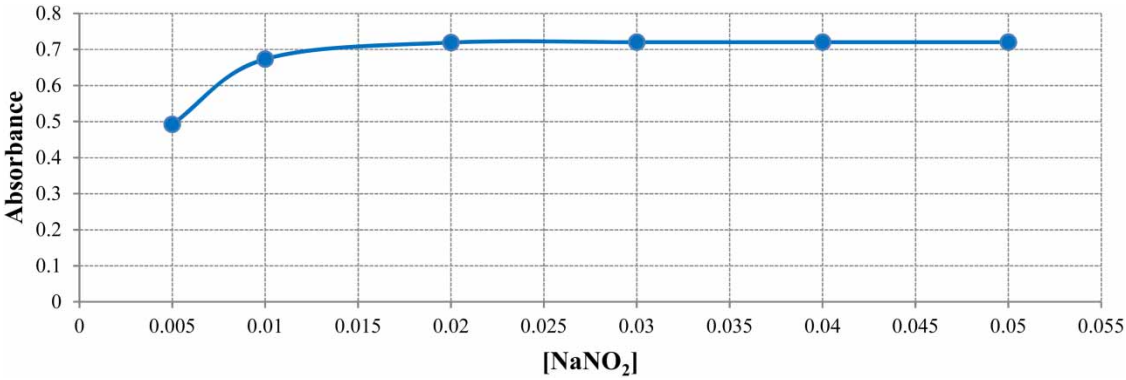

Figure 4 | Effect of $NaNO_2$ concentration on the sensitivity of spectrophotometric determination. [Triclosan] = 1.5 μM.

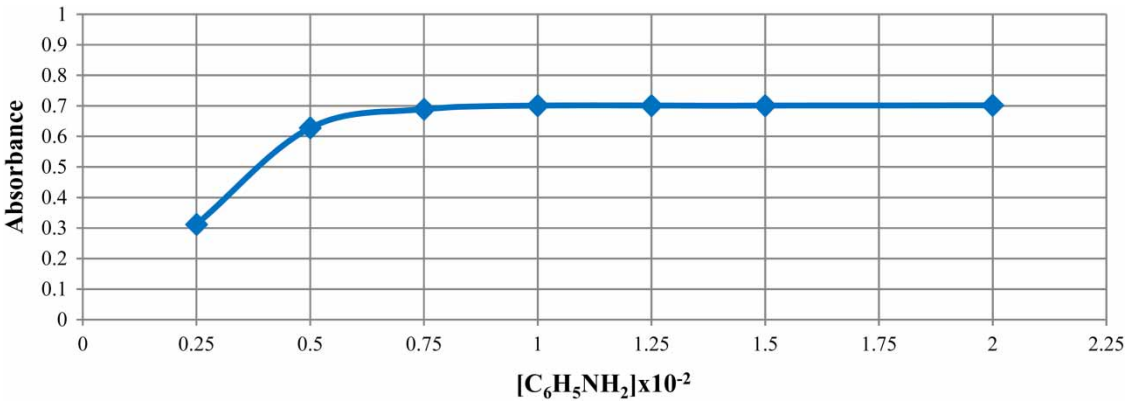

Figure 5 | Effect of aniline concentration on the sensitivity of spectrophotometric determination. [Triclosan] = 1.5 μM.

It can been seen that the set of optimized conditions which gave the best response for triclosan determination was as follows:

0.25 M HCl, 0.03 M $NaNO_2$, 0.01 M $C_6H_5NH_2$

Optimization of reaction conditions using RSM

Optimization of experimental conditions was conducted in terms of concentration of sodium nitrite, HCl, and aniline by using BBD of RSM process parameters at three levels as given in Table 1. The levels were fixed based on the preliminary experiment trials. The proposed BBD requires 17 runs for modeling a response surface. Details of the experimental runs with the set of input parameters that were conducted are given in Table 2 with measured absorbance value as the response.

A second order RSM representing the relationship between absorbance and concentration of HCl, $NaNO_2$ and $C_6H_5NH_2$ as the input process parameters was generated using the values of the experimental data. The final equation in terms of actual factors is as follows:

$$\begin{aligned}\text{Absorbance} = &-0.23772 + 1.72843[\text{HCl}] + 20.54827[\text{NaNO}_2] \\ &+ 52.52315[\text{C}_6\text{H}_5\text{NH}_2] - 9.87135[\text{HCl}][\text{NaNO}_2] \\ &- 10.8271[\text{HCl}][\text{C}_6\text{H}_5\text{NH}_2] - 275.556[\text{NaNO}_2][\text{C}_6\text{H}_5\text{NH}_2] \\ &- 1.5938[\text{HCl}]^2 - 172.148[\text{NaNO}_2]^2 - 1285.22[\text{C}_6\text{H}_5\text{NH}_2]^2\end{aligned}$$

The 'Pred R-Squared' of 0.9536 is in reasonable agreement with the 'Adj R-Squared' of 0.9932. 'Adeq Precision' measures the signal to noise ratio. A ratio greater than 4 is

Table 1 | Selection of process parameters

Process parameters	Reagent	Level 1	Level 2	Level 3
A	[HCl]	0.025	0.2625	0.5
B	[$NaNO_2$]	0.005	0.0275	0.05
C	[$C_6H_5NH_2$]	0.0025	0.01125	0.02

Table 2 | Box–Behnken design for the experiment with response values

Run	[HCl]	[$NaNO_2$]	[$C_6H_5NH_2$]	Absorbance
1	0.2625	0.0275	0.01125	0.776
2	0.5	0.0275	0.0025	0.630
3	0.2625	0.0275	0.01125	0.782
4	0.2625	0.005	0.0025	0.286
5	0.2625	0.0275	0.01125	0.782
6	0.5	0.0275	0.02	0.796
7	0.2625	0.05	0.0025	0.654
8	0.2625	0.005	0.02	0.645
9	0.5	0.05	0.01125	0.780
10	0.2625	0.0275	0.01125	0.782
11	0.025	0.005	0.01125	0.322
12	0.2625	0.05	0.02	0.796
13	0.2625	0.0275	0.01125	0.782
14	0.025	0.05	0.01125	0.653
15	0.5	0.005	0.01125	0.660
16	0.025	0.0275	0.0025	0.344
17	0.025	0.0275	0.02	0.600

desirable. The ratio of 45.666 indicates an adequate signal. The model F-value of 262.58 implies the model is significant (Table 3).

In order to analyze the effects of concentration of HCl, $NaNO_2$ and $C_6H_5NH_2$ on the absorbance more instinctively, three-dimensional response surfaces are shown in Figure 6(a)–6(c) with concentration of one reagent being kept constant at the optimal statistic and the other two concentrations varied within the experimental range. A rounded ridge running diagonally along the plot indicated that the three key parameters had slight interactive effects on the response value, and each of the factors showed a great effect on the response value. It is clear that the maximum absorbance of 0.851 is achieved at the peak of the surface at the corresponding experimental conditions:

$$[HCl] = 0.349\ M,\ [NaNO_2] = 0.043\ M$$
$$[C_6H_5NH_2] = 0.016\ M$$

Table 3 | Model summary statistics

R-Squared	0.997047
Adj R-Squared	0.993250
Pred R-Squared	0.953610
Adeq Precision	45.66571

The optimized conditions obtained experimentally were compared with those obtained by using BBD of RSM and both results were found in good agreement as summarized in Table 4. The results clearly showed that the BBD could be effectively applied to optimize the concentration of reagents to get the desired response and reduce the time and efforts required for experiments.

Calibration curve for triclosan solution

For obtaining calibration curve for triclosan solution, initially triclosan stock solution of 10^{-5} M was prepared and further this solution was used to prepare other triclosan solutions with 3, 2.5, 1.5, 1.0, 0.5 μM concentration and absorbance of all solutions were recorded by UV-Vis spectrophotometer at $\lambda_{max} = 352$ nm. The calibration curve so obtained by plotting absorbance versus concentration at λ_{max} is shown in Figure 7 and it allows the determination of triclosan in the measuring range of 0.5–3.0 μM.

Analysis of water samples for triclosan content

The method developed was used for analysis of the triclosan in a variety of environmental water samples. Samples were collected from various locations in Punjab and samples were prepared as mentioned in the 'Practical application' section. Triclosan contents were determined in these water samples and results so obtained are summarized in Table 5. The accuracy of the proposed spectrophotometric method based on the diazotization reaction for determination of triclosan was further evaluated by testing all four samples with an already established technique, high-performance liquid chromatography (HPLC). All samples were spiked with 0.2 ppm triclosan after the extraction and appropriate dilution. All measurements were performed in triplicate. The results obtained by the proposed method were found to be in good agreement with those obtained with HPLC. These results could be helpful to check the quality of water as far as the triclosan content is concerned. The Minnesota Department of Health developed a guidance value of 0.05 ppm for triclosan in drinking water. A person drinking water at or below this level would have little or no risk of any health effects from triclosan. Based on the levels of triclosan detected in water samples from different locations in Punjab, India, all the samples were found to be safe except the water from Gang Canal. Its value is above 0.05 ppm and hence can pose a threat to human health.

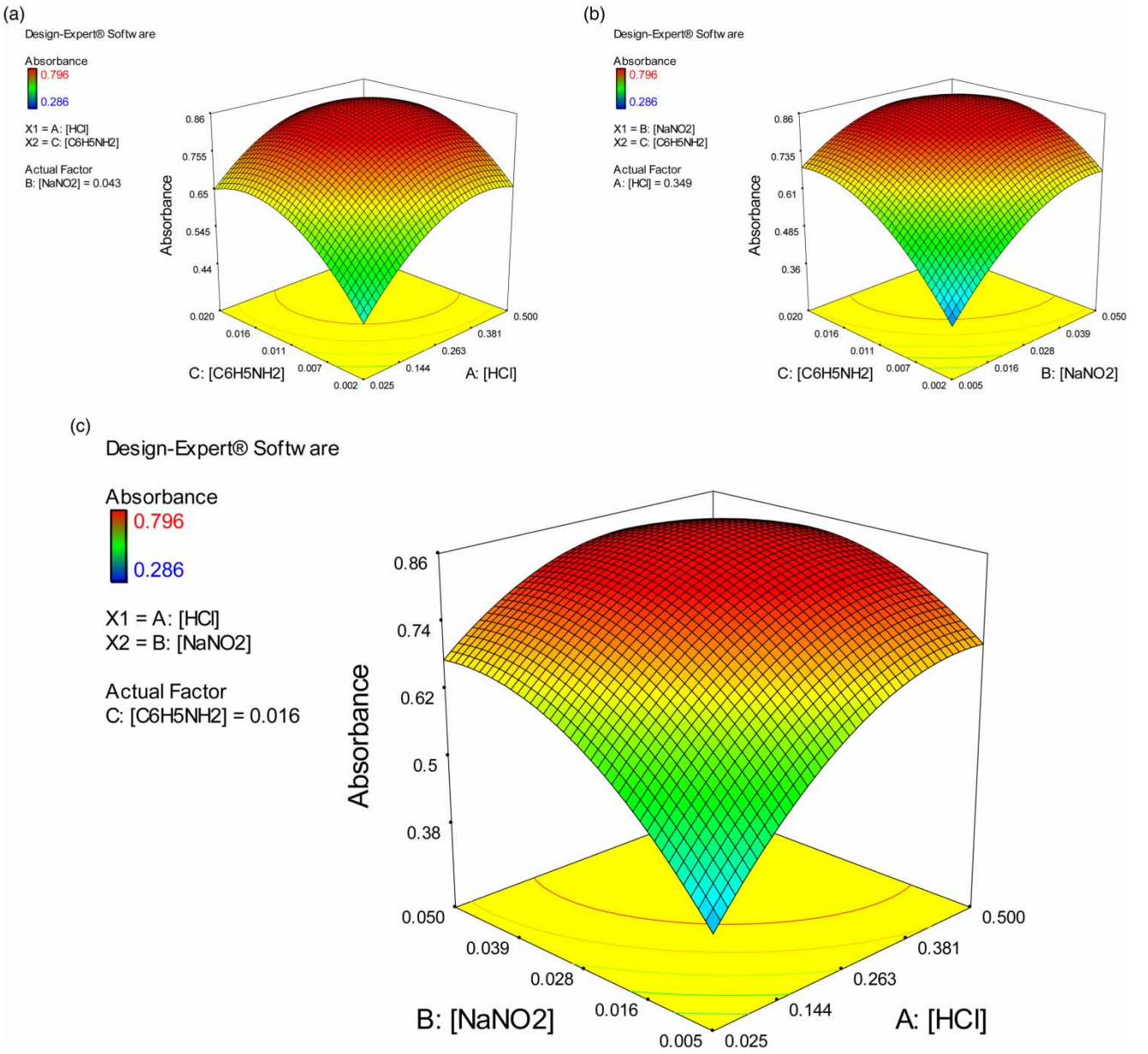

Figure 6 | Response surface plot for the effects of (a) concentration of $C_6H_5NH_2$ and HCl (b) concentration of $C_6H_5NH_2$ and $NaNO_2$ (c) concentration of $NaNO_2$ and HCl on the absorbance.

Table 4 | Comparison of optimized conditions obtained experimentally and by using Box–Behnken design of response surface methodology (RSM)

Reagent	Optimized conditions obtained with	
	Experiment	BBD (RSM)
[HCl]	0.250 M	0.349 M
[$NaNO_2$]	0.030 M	0.043 M
[$C_6H_5NH_2$]	0.010 M	0.016 M

CONCLUSION

A simple, reliable and rapid spectrophotometric method based on the diazotization reaction between sodium nitrite, aniline and triclosan under optimized conditions was developed. Optimized concentrations of reactants were chosen to achieve the highest response, i.e. 0.25 M HCl, 0.03 M sodium nitrite, and 0.01 M aniline. The calibration curve so obtained was in the range of 0.5–3.0 μM. The maximum

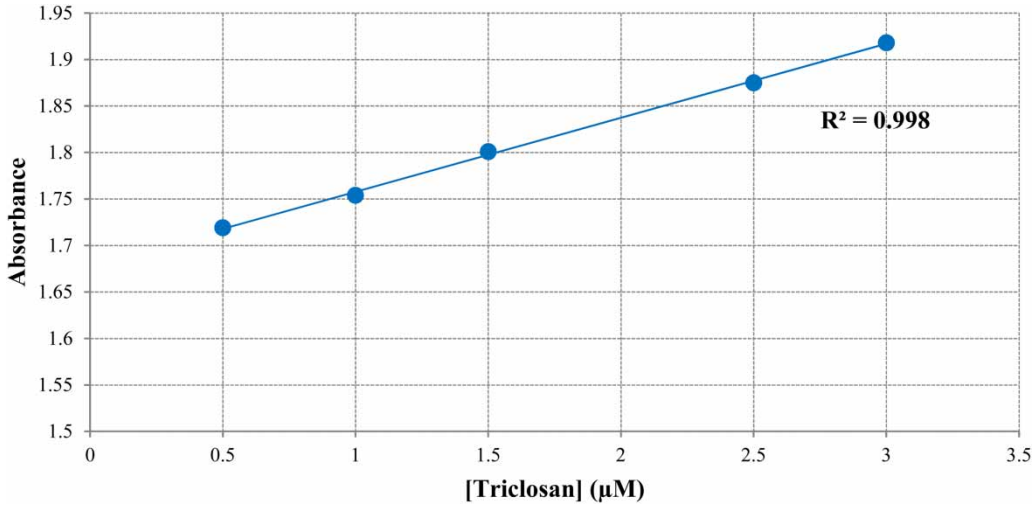

Figure 7 | Calibration curve for spectrophotometric determination of derivatized triclosan.

Table 5 | Analytical results of triclosan determination in environmental water samples using proposed method and HPLC

		Triclosan content (ppm)	
S. no.	**Samples**	**Present method**	**HPLC method**
1	Guru Nanak Dev University, Amritsar	0.017 ± 0.002	0.018 ± 0.001
2	Sirhind Peter, Faridkot	0.029 ± 0.001	0.031 ± 0.001
3	Upper Bari Doab Canal, Pathankot	0.057 ± 0.001	0.059 ± 0.001
4	Gang Canal	0.173 ± 0.003	0.174 ± 0.003

Note: All samples were spiked with 0.2 ppm triclosan after the extraction and appropriate dilution. All measurements were performed in triplicate.

value of absorbance of 0.851 is achieved at the peak of the surface; the corresponding experimental conditions of $[HCl] = 0.349$ M, $[NaNO_2] = 0.043$ M, $[C_6H_5NH_2] = 0.016$ M using BBD design are found to be in agreement with experimentally optimized values. This method was then successfully applied for determination of triclosan content in various environmental water samples.

REFERENCES

Adolfsson-Erici, M., Pettersson, M., Parkkonen, J. & Sturve, J. 2002 Triclosan, a commonly used bactericide found in human milk and in the aquatic environment in Sweden. *Chemosphere* **46**, 1485–1489.

Canosa, P., Rodríguez, I., Rubí, E., Ramil, M. & Cela, R. 2008 Simplified sample preparation method for triclosan and methyltriclosan determination in biota and foodstuff samples. *J. Chromatogr. A* **1188**, 132–139.

Chu, S. G. & Metcalfe, C. D. 2007 Simultaneous determination of triclocarban and triclosan in municipal biosolids by liquid chromatography tandem mass spectrometry. *J.Chromatogr. A* **1164**, 212–218.

Dann, A. B. & Hontela, A. 2011 Triclosan: environmental exposure, toxicity and mechanisms of action. *J. Appl. Toxicol.* **31**, 285–311.

Davim, J. P. & Francisco, M. 2005 Optimisation of surface roughness on turning fibre reinforced plastics (FRPs) with diamond cutting tools. *Int. J. Adv. Manufact. Technol.* **26**, 319–323.

Draper, N. R. & Smith, H. 1981 *Applied Regression Analysis*, 3rd edn. John Wiley & Sons, New York.

Kolpin, D. W., Furlong, E. T., Meyer, M. T., Thurman, E. M., Zaugg, D. S., Barber, L. B. & Buxton, H. T. 2002 Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams. *Environ. Sci. Technol.* **36**, 1202–1211.

Kookana, R. S., Ying, G.-G. & Waller, N. J. 2011 Triclosan: its occurrence, fate and effects in the Australian environment. *Water Sci. Technol.* **63** (4), 598–604.

Lindstrom, A., Buerge, I. J., Poiger, T., Berqvist, P., Muller, M. D. & Buser, H. R. 2002 Occurrence and environmental behavior of the bactericide triclosan and its methyl derivative in surface waters and in wastewater. *Environ. Sci. Technol.* **36**, 2322–2329.

Lorres, M., Llompart, M., Prado, L. S., Jares, C. G. & Cela, R. 2005 Confirmation of the formation of dichlorodibenzo-p-dioxin in the photodegradation of triclosan by photo-SPME. *Anal. Bioanal. Chem.* **381**, 1294–1298.

Lyndall, J., Barber, T., Mahaney, W., Bock, M. & Capdevielle, M. 2017 Evaluation of triclosan in Minnesota lakes and rivers: part I – ecological risk assessment. *Ecotoxicol. Environ. Saf.* **142**, 578–587.

Marques, I., Mota, G. M., Pires, F., Serio, S., Ribeiro, P. A. & Raposo, M. 2017 Detection of traces of triclosan in water. *Appl. Surf. Sci.* **421**, 142–147.

Miller, T. L., Lorusso, D. J., Walsh, M. L. & Deinzer, M. L. 1983 The acute toxicity of penta-, hexa-, and heptachlorohydroxydiphenyl ethers in mice. *J. Toxicol. Environ. Health* **12**, 245–253.

Montaseri, H. & Forbes, P. B. C. 2016 A review of monitoring methods for triclosan and its occurrence in aquatic environments. *TrAC Trends Anal. Chem.* **85**, 221–231.

Montgomery, D. C. 1991 *Design and Analysis of Experiments*, 8th edn. John Wiley & Sons, New York.

Nakada, N., Yasojima, M., Okayasu, Y., Komori, K. & Suzuki, Y. 2010 Mass balance analysis of triclosan, diethyltoluamide, crotamiton and carbamazepine in sewage treatment plants. *Water Sci. Technol.* **61** (7), 1739–1747.

Okumura, T. & Nishikawa, Y. 1996 Gas chromatography-mass spectrometry determination of triclosans in water, sediment and fish samples via methylation with diazomethane. *Anal. Chim. Acta* **325**, 175–184.

Pemberton, R. M. & Hart, J. P. 1999 Electrochemical behaviour of triclosan at a screen-printed carbon electrode and its voltammetric determination in toothpaste and mouthrinse products. *Anal. Chim. Acta* **390**, 107–115.

Rasmussen, H. T., McDonough, R., Gargiullo, R. J. & McPherson, B. P. 1996 Determination of triclosan in human dental plaque by gas chromatography with atomic emission detection. *J. High Resolut. Chromatogr.* **19**, 359–361.

Reiss, R., Mackay, N., Habig, C. & Griffin, J. 2002 An ecological risk assessment for triclosan in lotic systems following discharge from wastewater treatment plants in the United States. *Environ. Toxicol. Chem.* **21**, 2483–2492.

Safavi, A., Maleki, N. & Shahbaazi, H. R. 2003 Electrochemical determination of triclosan at a mercury electrode. *Anal. Chim. Acta.* **494**, 225–233.

Schweize, H. P. 2001 Triclosan: a widely used biocide and its link to antibiotics. *FEMS Microbiol. Lett.* **202**, 1–7.

Silva, A. S., García, R. S., Hernandez, J. L. & Losada, P. P. 2005 Determination of triclosan in foodstuffs. *J. Sep. Sci.* **28**, 65–72.

Singh, B., Dahiya, M., Saharan, V. & Ahuja, N. 2005 Optimizing drug delivery systems using systematic design of experiments. Part II: retrospect and prospects. *Crit. Rev. Ther. Drug Carrier Syst.* **22**, 215–293.

Sioufi, A., Caudal, F. & Grimault, D. 1977 GLC determination of free and conjugated triclosan in human plasma and urine. *J. Pharmaceut. Sci.* **66**, 1166–1168.

Song, S. J., Song, Q. J. & Chen, Z. L. 2007 Online phototransformation-flow injection chemiluminescence determination of triclosan. *Anal. Bioanal. Chem.* **387**, 2917–2922.

Thomas, P. M. & Foster, G. D. 2004 Determination of nonsteroidal anti-inflammatory drugs, caffeine and triclosan in wastewater by gas chromatography–mass Spectrometry. *J. Environ. Sci. Health A* **39**, 1969–1978.

Vining, G. G. & Myers, R. H. A. 1991 Graphical approach for evaluating response surface designs in terms of the mean squared error of prediction. *Technometrics* **33**, 315–326.

Wu, J. L., Lama, N. P., Martens, D., Kettrup, A. & Cai, Z. W. 2007 Triclosan determination in water related to wastewater treatment. *Talanta* **72**, 1650–1654.

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