



Green and real-time detection of GHB in soft drinks and alcoholic beverages using an eco-friendly cellulose paper-based fluorescent probe

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ABSTRACT

Chemical submission, a nefarious tactic increasingly employed in criminal activities, has spurred urgent calls for innovative countermeasures. GHB, often dubbed “liquid ecstasy,” stands out as a favoured agent for its surreptitious nature and seamless solubility in water and alcoholic beverages. Addressing this menace head-on, a groundbreaking study delves into the development of advanced chemosensors, leveraging 2-aminonaphthoxazole- and benzoxazole-based compounds adorned with fluorescein, to construct a cellulose paper-based detection system. This ingenious setup not only detects GHB in water but extends its vigilance to real alcoholic and non-alcoholic beverages, illuminating a pathway to thwart potential assailants. With a fluorescence enhancement mechanism at play, the system boasts a dynamic range from 0 to 125 mM GHB in water, exhibiting a commendable limit of detection (LOD) at 7.3 mM. Crucially, its eco-friendly nature, devoid of solvent residuals, underscores its suitability as a proactive shield against chemical submission, embodying a beacon of hope in the fight against such insidious threats to public safety.

1. Introduction

Chemical Submission refers to the administration of psychoactive substances to a person, without their consent and knowledge, causing them to become incapacitated or unconscious, and enabling criminal activity [1,2]. This practice has become increasingly prevalent in recent times, particularly in cases involving alleged sexual assault [3]. Typically, the perpetrator places the drug in the drink of the unsuspecting victim. γ -Hydroxybutyric acid (GHB), also known as liquid ecstasy, is one of such drugs [4]. This chemical substance is colorless, odorless, and tasteless, and highly soluble in water, which makes it undetectable when added to beverages [5,6]. Furthermore, since GHB is a naturally occurring inhibitory neurotransmitter, it is rapidly metabolized and

excreted from the body, which makes its detection very difficult after a certain time after consumption. Even though an ingestion of approximately 50–60 mg of GHB per kg of body weight is necessary to achieve chemical submission effects, only about 3–5 % of the original ingestion of GHB can be detected in urine samples within 6–10 h [7,8].

Various instrumental, enzyme- and metabolomics-based methodologies for detecting GHB in forensic samples have been described [9–12]. However, these techniques require the use of expensive instruments and trained personnel, and the samples generally require pre-treatment. In this sense, the use of optical chemosensors for the detection of drugs of abuse is an undeniable advantage, as they allow the rapid and *in situ* detection of these drugs in beverages or biological fluids, by means of a change in color or fluorescence, that can be observed with the naked eye

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or with help of relatively inexpensive instruments [13].

Concerning GHB detection, some recent examples of colorimetric and/or fluorescent chemosensors and probes have been reported, that are able to detect the presence of this drug in beverages [14–19]. However, some of these approaches still have certain disadvantages, such as the need of organic solvents, smartphones to obtain an accurate readout, need to carry out several consecutive chemical reactions or high limits of detection in aqueous media. For all this, the use of solid state-based sensing devices is highly desirable [20–23].

We have recently reported two new 2-aminonaphthoxazole derivatives which, in DMSO solution, are able to detect the presence of GHB in beverages through either color or fluorescent changes [16]. Following these studies, and with the aim of developing a safer and easy-to-use detection device, we report herein an eco-friendly cellulose paper-based sensor for the *in situ* fluorescent detection of GHB in water, soft drinks, and alcoholic beverages, at concentrations that are known to produce chemical submission effects.

2. Materials and methods

2.1. Materials

All reagents employed were purchased from Sigma Aldrich and used without further purification. The solvents were ACS reagent grade or better quality and were purchased from Scharlab S.L. Compound **1** was synthesized following our previously reported procedure [16]. The tested drugs, γ -hydroxybutyric acid (GHB), (–)-scopolamine hydrobromide trihydrate, ketamine, methcathinone (ephedrone) and diazepam were legally purchased from Sigma Aldrich with the previous authorization of the Spanish Agency of Medicines and Medical Devices (AEMPS). Blank cellulose paper discs for inhibition tests (6 mm diameter) were purchased from Liofilchem (Roseto degli Abruzzi, Italy). ^1H NMR and ^{13}C NMR spectra were registered with Bruker Avance 300 MHz or 500 MHz spectrometers, all of them referenced to residual solvent peak. High resolution mass spectra were carried out with a TripleTOFTM 5600 LC/MS/MS system, with 2 gas sources (both to 35 psi), 450 °C and ion gas voltage of 5500 V. All photophysical analysis was carried out in DMSO at 298 K, unless otherwise specified. UV–vis absorption spectra were recorded with a Shimadzu UV-2600 using quartz cells with path length of 1.0 cm. Luminescence spectra were recorded with a Shimadzu RF-6000 spectrofluorometer. Quantum yields were determined using fluorescein free acid as a standard ($\phi_{\text{fl}} = 0.91$ in aq. NaOH 0.1 M). Fluorescence emission spectra of the solid samples were collected with a Horiba-Jobin-Yvon Fluoromax-4[®] spectrofluorometer using an optic fiber connected to the equipment (provided by PROTEOMASS-BIOSCOPE facility at the NOVA FCT). All measurements ($\lambda_{\text{exc}} = 330$ nm, $\lambda_{\text{em}} = 528$ nm) were performed at 298 K.

2.2. Synthesis of probes 2a-b

0.214 mmol (1 equiv.) of the corresponding 2-aminophenol was mixed with 0.257 mmol (1.2 equiv.) of fluorescein-5-isothiocyanate in 10 mL of THF. After complete dissolution, 0.257 mmol (1.2 equiv.) of NEt_3 were added to the mixture and the stirring was kept overnight (the solution turned to orange). Next day, 0.428 mmol (2 equiv.) of H_2O_2 30 % and 0.021 mmol (0.01 equiv.) of tetrabutylammonium iodide were added, and the mixture was kept stirring for 4 h more at room temperature (immediately the solution turned to brown). The solvent was removed, and the crude was dissolved in AcOEt and washed several times with 0.1 M aq NaOH. The organic solvent was dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The products were isolated as a maroon powder without further purification in a 10 % of yield for compound **2a** and in a 45 % of yield for compound **2b**.

Compound 2a: ^1H NMR (300 MHz, DMSO- d_6) δ 11.17 (s, 1H), 10.11 (s, 2H), 8.52 (d, $J = 1.7$ Hz, 1H), 7.97 (dd, $J_1 = 8.3$ Hz, $J_2 = 1.8$ Hz, 1H),

7.59 (d, $J = 7.6$ Hz, 1H), 7.57 (d, $J = 7.6$ Hz, 1H), 7.29 (d, $J = 8.2$ Hz, 1H), 7.28 (t, $J = 7.6$ Hz, 1H), 7.20 (td, $J_1 = 8$ Hz, $J_2 = 1$ Hz, 1H), 6.69 (d, $J = 2.3$ Hz, 2H), 6.64 (d, $J = 8.8$ Hz, 2H), 6.57 (dd, $J_1 = 8.8$ Hz, $J_2 = 2.3$ Hz, 2H). ^{13}C (126 MHz, DMSO- d_6) δ 169.20, 159.94, 158.04, 152.40, 147.48, 146.23, 142.50, 140.92, 129.61, 127.83, 125.56, 125.16, 124.71, 122.70, 117.51, 113.06, 112.00, 110.25, 109.69, 102.68, 83.64. HRMS: m/z calculated for $\text{C}_{27}\text{H}_{17}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$: 465.1087; found: 465.1104.

Compound 2b: ^1H NMR (300 MHz, DMSO- d_6) δ 11.13 (s, 1H), 10.10 (s, 2H), 8.51 (d, $J = 1.9$ Hz, 1H), 7.96 (dd, $J_1 = 8.4$ Hz, $J_2 = 1.9$ Hz, 1H), 7.42 (d, $J = 7.9$ Hz, 1H), 7.39 (s, 1H), 7.28 (d, $J = 8.4$ Hz); 7.00 (d, $J = 8.3$ Hz, 1H), 6.68 (d, $J = 2.3$ Hz, 2H), 6.64 (d, $J = 8.8$ Hz, 2H), 6.56 (dd, $J_1 = 8.8$ Hz, $J_2 = 2.3$ Hz, 2H), 2.40 (s, 3H). ^{13}C (126 MHz, DMSO- d_6) δ 169.22, 159.94, 158.15, 152.40, 146.16, 145.64, 142.66, 140.96, 133.92, 129.63, 127.83, 125.51, 125.14, 123.29, 117.78, 113.06, 111.94, 110.27, 109.10, 102.68, 83.63, 21.56. HRMS: m/z calculated for $\text{C}_{28}\text{H}_{19}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$: 479.1243; found: 479.1261.

2.3. Fluorescence titration studies in solution with probes 1 and 2a-b and GHB

For probe **1**, in a 3 mL quartz cell (1 cm of path length), to 2800 μL of a 20 μM solution of the fluorophore in THF, increasing additions of 10 μL of a 600 μM solution of GHB in water were added. For each aliquot added, the solution was stirred for 3 s and then the fluorescence of the solution at the corresponding excitation wavelength was measured (Fig. S18 in the Supplementary Material).

For probes **2a-b**, in a 3 mL quartz cell (1 cm of path length), to 2475 μL of the corresponding fluorophore (10 μM in DMSO), increasing additions of GHB (1–4 μL , 2.5 mM in water) were added. For each aliquot added, the solution was stirred for 3 s and then the fluorescence of the solution at the corresponding excitation wavelengths was measured (Figs. S19–S20).

2.4. Preparation of the cellulose paper-based fluorescent sensors

In a 1.5 mL eppendorf, 500 μL of 1 mM solution of fluorescent chemosensor **1** in THF was prepared. Then, cellulose blank paper discs (Liofilchem) were impregnated with **1** by introducing them into the previous THF solution for 3 s. After drying in the air for 5 min, the cellulose system turned to orange giving rise to a ready portable and practical device for fast GHB detection. The high reproducibility of the method (five replicas) was demonstrated by UV–vis quantification of the amount of fluorophore in the final devices.

2.5. Fluorescence titration studies with the solid phase detection kit and GHB in water samples, soft drinks, and alcoholic beverages

15 μL of the GHB solution (in water, soft drinks, or alcoholic beverages) were added to the blank discs (Liofilchem) previously impregnated with probe **1**. Each single material was spiked with increasing GHB concentrations (from 0 to 180 mM). The fluorescence emission spectra of the solid samples ($\lambda_{\text{exc}} = 330$ nm, $\lambda_{\text{em}} = 528$ nm) were collected at 298 K after 1 h, although the fluorescence response was immediately observed.

2.6. Selectivity studies with the cellulose paper-based sensor in water

15 μL of a 15 mM solution of each drug in water were added to the blank discs (Liofilchem) previously impregnated with probe **1**. The fluorescence spectra of the solid samples were collected ($\lambda_{\text{exc}} = 330$ nm, $\lambda_{\text{em}} = 528$ nm) at 298 K after 1 h, although the fluorescence response was immediately observed.

2.7. Time stability studies of the cellulose paper-based sensor

15 μL of 90 mM GHB solution in water were added to the cellulose paper-based sensors, previously stored in the dark or under daylight, at different times after their preparation, from 15 min to 7 days. The corresponding fluorescence emission spectra of the solid samples in the presence of GHB were collected at 298 K ($\lambda_{\text{exc}} = 330 \text{ nm}$, $\lambda_{\text{em}} = 528 \text{ nm}$).

3. Results and discussion

3.1. Synthesis and spectroscopic properties of probes 1 and 2a-b

The chemical structures of the 2 aminonaphtoxazole- (1) and 2-aminobenzoxazole-based (2a-b) fluorescent chemosensors, for GHB detection, are shown in Chart 1. Compound 1 was synthesized in two steps (one pot), from 3-amino-2-naphtol and fluorescein isothiocyanate, as previously reported. [14] First, stirring in THF in the presence of Et_3N yielded the corresponding thiourea which was converted to 2-aminonaphtoxazole by oxidative cyclodesulfurization with hydrogen peroxide in the presence of tetrabutylammonium iodide (see Fig. 1).

We decided then to synthesize two new 2-aminobenzoxazoles 2a-b, also bearing the fluorescein moiety, and evaluate their ability to detect the presence of GHB by fluorescence enhancement, in the same way as observed for compound 1. Thus, the reaction of the corresponding 2-aminophenol with fluorescein 5-isothiocyanate in THF in the presence of Et_3N , followed by cyclodesulfurization of the resulting *o*-phenolic thioureas using TBAI and H_2O_2 , yielded the corresponding 2-aminobenzoxazoles 2a and 2b, which were fully characterized by ^1H and ^{13}C NMR, and HRMS.

Next, we studied the UV-vis and fluorescence properties of probes 2a and 2b in DMSO solution (Table 1). Both compounds (10^{-5} M in DMSO) show an intense absorption band around 300 nm with a shoulder at ca. 370 nm which is responsible of the pale-yellow color of their solutions. Regarding their emission properties, as previously observed for probe 1 [16], compounds 2a and 2b are very weakly fluorescent, with an emission band at wavelength around 450 nm (when irradiated at $\lambda_{\text{exc}} = 300 \text{ nm}$) (see Fig. S16).

3.2. GHB fluorescent sensing in solution

Once the spectroscopic properties of the new compounds 2a and 2b were assessed, we decided to evaluate their ability to act as fluorescent chemosensors towards GHB in DMSO solution.

Addition of excess GHB to a solution of compound 2a (10 μM in DMSO) resulted in the immediate appearance of a strong fluorescence emission band at $\lambda_{\text{em}} = 532 \text{ nm}$ ($\lambda_{\text{exc}} = 470 \text{ nm}$) which was clearly observed by the naked eye as bright green color, under a common UV lamp (see Fig. 2).

In order to evaluate the sensitivity of the probe, fluorescence titration experiments were performed by adding increasing amounts of GHB (600 μM in water) to a DMSO solution of compound 2a. This resulted in a progressive enhancement of the fluorescence emission at 532 nm. From the titration profile shown in Fig. 2 and using the equation: Limit of Detection (LOD) = $3\sigma_b/m$ (where σ_b is the standard deviation of the

blank and m is the slope of the calibration curve), a LOD of 0.06 μM for GHB was determined.

A fluorescence emission enhancement at $\lambda_{\text{em}} = 534 \text{ nm}$ ($\lambda_{\text{exc}} = 495 \text{ nm}$) was also observed for compound 2b (10 μM in DMSO) in the presence of increasing amounts of GHB, with a calculated LOD of 0.24 μM of GHB (Fig. S19). These results with 2-aminobenzoxazoles derivatives 2a-b were very similar to those previously reported for DMSO solutions of compound 1 and GHB. We believe that as for 1, the detection mechanism is based on a deprotonation of the probe by GHB sodium salt which leads to the observed fluorogenic response [16]. Finally, we also tested the fluorescence behaviour of THF solutions of chemosensor 1 in the presence of GHB. Again, a progressive increase in the fluorescence emission at $\lambda_{\text{em}} = 528 \text{ nm}$ ($\lambda_{\text{exc}} = 330 \text{ nm}$) of compound 1 (10 μM in THF) was observed upon increasing concentrations of GHB. From the calibration curve, a LOD of 0.45 μM was determined (Fig. S20).

The fluorescence quantum yields of 1, 2a and 2b in the presence of two equivalents of GHB were measured in DMSO, using fluorescein free acid ($\phi_{\text{fl}} = 0.91$ in aq NaOH 0.1 M) as a standard. All three compounds in the presence of GHB exhibit good quantum yields ($\phi = 0.71, 0.77$ and 0.78 for 1, 2a and 2b respectively).

3.3. Fabrication of the cellulose paper-based sensors and GHB sensing experiments

Compound 1 was initially chosen as a the GHB-sensitive fluorescent dye to prepare the cellulose paper-based sensing kits, and to evaluate the response and sensitivity of the kits towards GHB. It is important to remark that initial studies employing compounds 2a and 2b as fluorescent probes led to similar results as we will comment again later.

Our primary objective in this work was to obtain an eco-friendly solid phase sensor for the sensitive and *in situ* fluorescent detection of GHB in water, soft drinks, and alcoholic beverages. In pursuit of this objective, we evaluated the detection capabilities of cellulose-based materials impregnated with the fluorescent dyes, using THF as a volatile solvent. First, cellulose paper disks were immersed for 3 s into 500 μL of a solution of chemosensor 1 (10^{-4} M in THF). After drying in the air, solid-state fluorescence titration experiments with the cellulose paper-based sensors, in the presence of increasing amounts of GHB, were taken (see Fig. 3). In a typical experiment, a 15 μL aliquot of an aqueous solution of GHB was added to each cellulose disc (from 0 to 180 mM GHB concentration range), and after a certain time, the fluorescence emission spectra of the solid samples were collected ($\lambda_{\text{exc}} = 330 \text{ nm}$, $\lambda_{\text{em}} = 528 \text{ nm}$) at room temperature, using an optic fiber connected to a spectrofluorometer. The limit of detection (LOD) of the paper-based sensors was determined from the plot of the emission at 528 nm vs GHB concentration, using equation $\text{LOD} = 3\sigma_b/m$ (where σ_b is the standard deviation of the blank and m is the slope of the titration curve). A LOD of 7.3 mM for GHB could be determined, with a linear response towards GHB in the 0–125 mM range.

As can be seen in Fig. 3C, the fluorescence changes in the cellulose paper-based detection kits, upon addition of different amounts of aqueous GHB, could be directly observed by the naked eye under a common UV-lamp, with a visual LOD of ca. 10 mM of GHB which is below the concentration required for chemical submission purposes (ca. 96 mM) [20].

Finally, the recovery and accuracy of the method to detect GHB in aqueous samples were also calculated and are shown in Table S2.

3.4. Selectivity studies

Considering the positive response of the sensor kit in the presence of GHB, we also decided to test the selectivity of the kit in front of other drugs commonly employed for chemical submission, such as scopolamine, ketamine, ephedrone (methcathinone), diazepam and GBL [24]. As we expected, Fig. 4 reveals no discernible changes in the presence of the mentioned substances. Nevertheless, a pronounced enhancement of

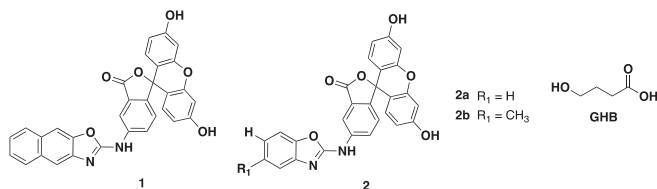


Chart 1. Chemical structures of 2 aminonaphtoxazole- (1) and benzoxazole- (2a-b) fluorophores used in the cellulose paper-based sensors for GHB detection.

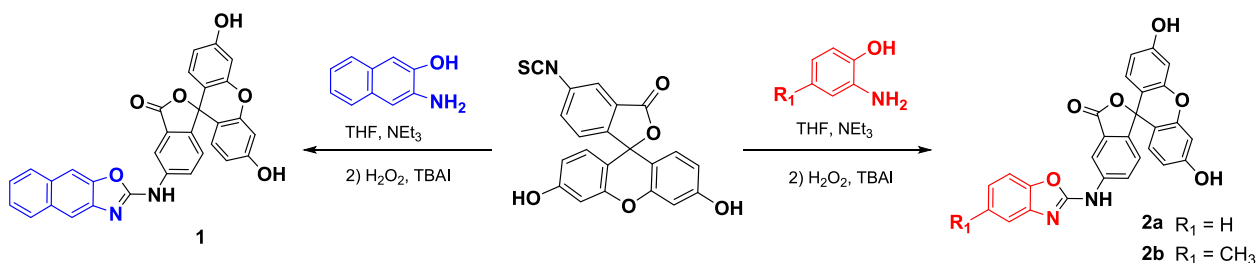


Fig. 1. Synthesis of compounds 1 and 2a-b.

Table 1

Optical properties of probes 1 and 2a-b in DMSO (10^{-5} M).

Compound	λ_{abs} (nm)	ϵ ($M^{-1} cm^{-1}$)	λ_{em} (nm)	λ_{exc} (nm)
1	336	14,900	425	330
2a	295	16,300	445	300
2b	297	29,000	460	300

the fluorescence emission intensity was observed when GHB was introduced in the presence of all these substances. It is important to remark that the concentration of the drugs employed in these selectivity studies were higher than those required for chemical submission. However, as we mentioned before, chemical submission through GHB ingestion requires, at least, 96 mM.

3.5. Response time studies and stability of the cellulose paper-based sensing devices

Next, time-stability and response time studies of the prepared cellulose paper-based sensors under specific conditions were also carried out. The prepared sensor kits were spiked with GHB and were stored either in the dark or under daylight for a certain time. Then, their fluorescence response towards GHB was evaluated. As can be observed in Fig. 5, the primary conclusion is that the GHB response remains stable over two days, irrespective of the storage conditions. With respect to the response time, the maximum response occurs after 1 h; however, fluorescence changes are readily distinguishable (< 1 min) when the cellulose disc impregnated with probe 1 is stored in dark. With respect to their stability with time, the kits were stable over months when they were kept in the darkness.

3.6. Fluorescent detection of GHB in soft drinks and alcoholic beverages

Finally, we decided to test our cellulose paper-based probes under real conditions, by spiking some soft drinks and alcoholic beverages with a known amount of GHB. These experiments were carried out at room temperature and the response could be observed almost immediately. Fig. 6 illustrates the fluorescence changes observed in the cellulose paper-based kits, upon addition of different beverages spiked with GHB (90 mM). It is also worth noting that no changes were observed when the beverages were spiked with other abuse drugs, such as GBL, scopolamine, diazepam, ketamine or ephedrone. Fluorescence calibration curves for each soft drink and alcoholic beverage, were also carried out by adding increasing amounts of GHB to the sensor kits (see Figs. S21-S29 in the Supplementary Material). The corresponding fluorescence changes visually observed on the paper-based sensors, upon addition of soft drinks and alcoholic beverages spiked with increasing concentrations of GHB (0, 10, 25, 50, 90 and 125 mM) are shown in Fig. S30.

Finally, compounds 2a and 2b were also tested as fluorescent chemosensors in the preparation of cellulose paper-based sensing kits. Preliminary detection experiments showed that, in the presence of water, soft drinks and alcoholic beverages spiked with GHB, the solid phase sensors led rapidly to similar fluorescence emission enhancements as those observed with chemosensor 1 (see Fig. S31).

4. Conclusions

In conclusion, our development of a cost-effective and portable solid-phase kit marks a significant advancement in the detection of GHB, a chemical submission drug, across various liquid media. Utilizing cellulose paper disks infused with a 2-aminonaphthoxazole fluorophore, this sensor kit offers a rapid, user-friendly, and reliable method for

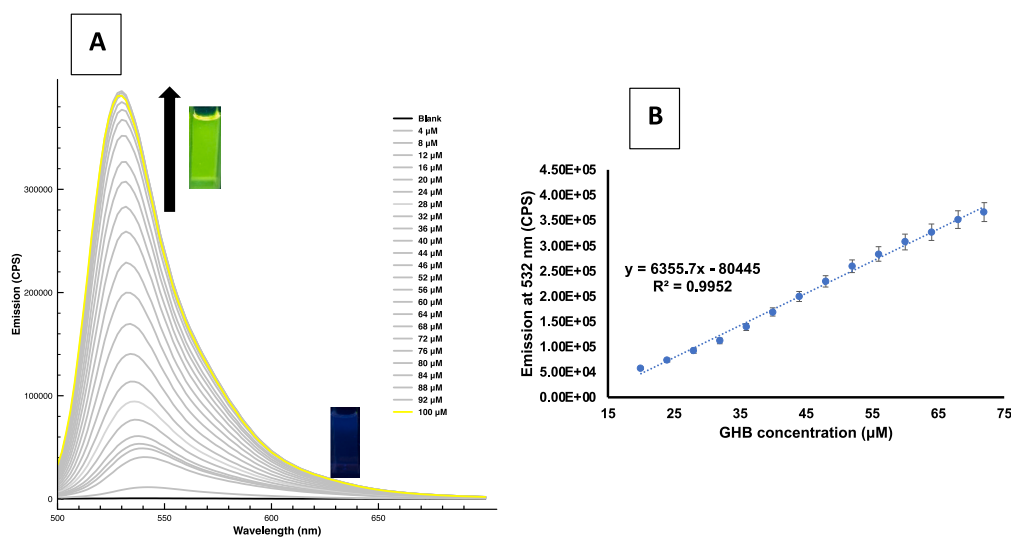


Fig. 2. (A) Emission spectra ($\lambda_{exc} = 470$ nm; $\lambda_{em} = 532$ nm) of compound 2a (10 μM in DMSO) in the presence of increasing amounts of GHB, until arriving to saturation point. (B) Calibration curve.

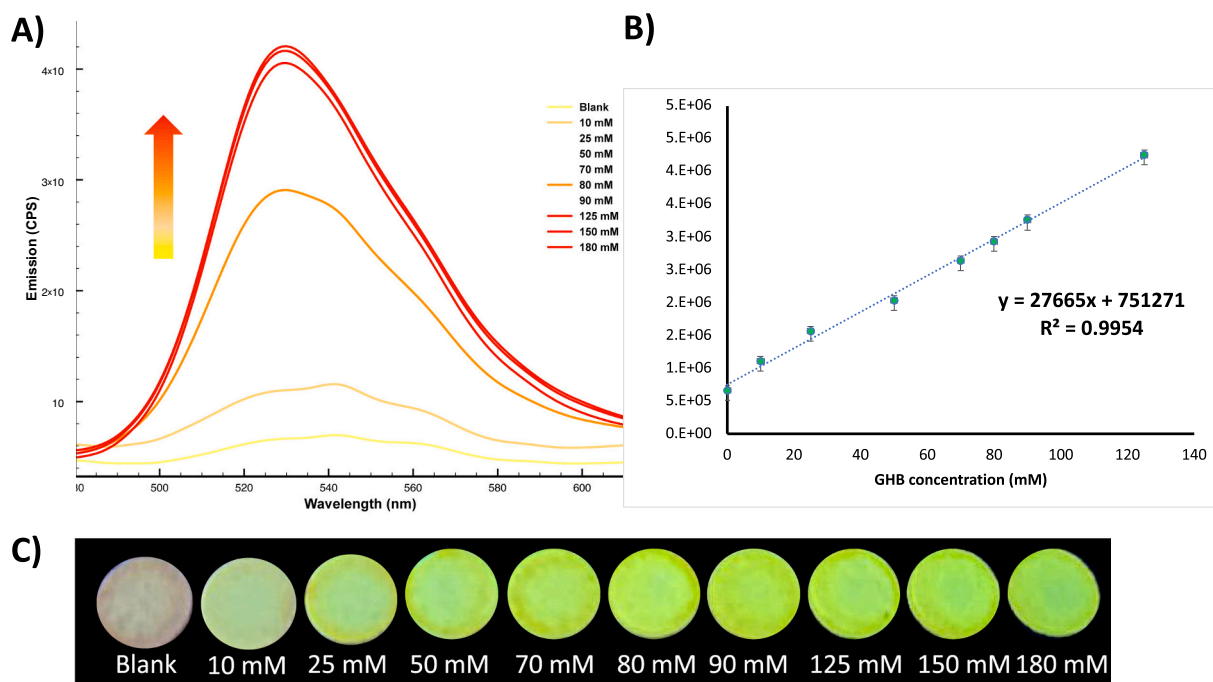


Fig. 3. (A) Solid-state fluorescence emission spectra ($\lambda_{exc} = 490$ nm; $\lambda_{em} = 528$ nm) of each blank disc impregnated with compound 1 and increasing amounts of GHB (from 0 to 180 mM). (B) Calibration curve representing the emission intensity at $\lambda_{em} = 528$ nm ($\lambda_{exc} = 490$ nm) vs the concentration of GHB. (C) Observed fluorescence changes in the cellulose paper-based sensors under a common UV lamp.

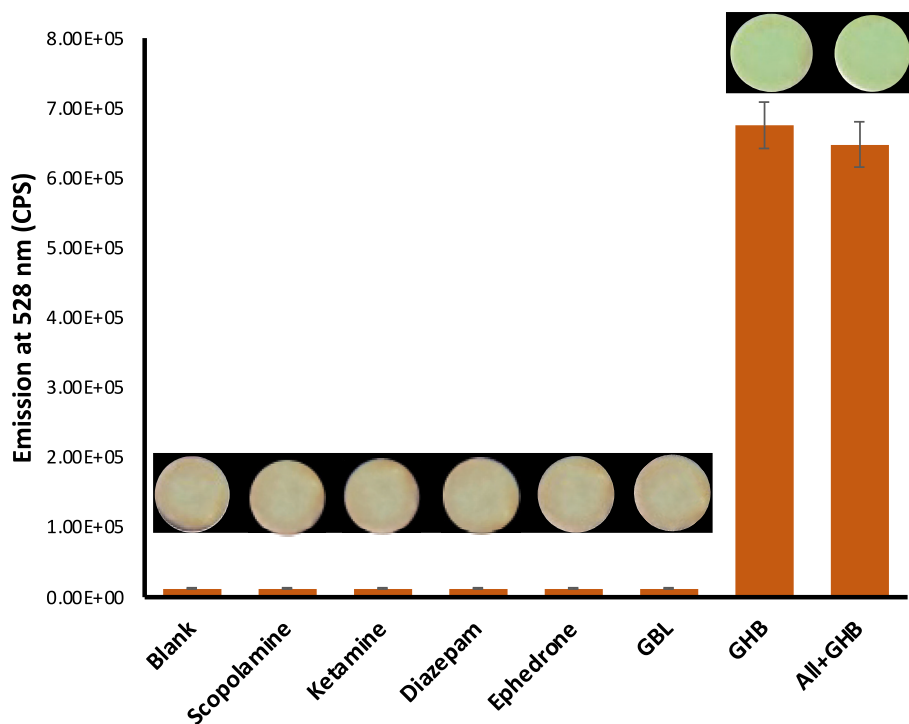


Fig. 4. Emission at 528 nm ($\lambda_{exc} = 490$ nm) of different cellulose paper discs impregnated with compound 1, in the absence (blank) and in the presence of some drugs of abuse (15 mM in water).

discerning the presence of GHB, even in diluted solutions found in water, soft drinks, and alcoholic beverages. The emergence of green fluorescence upon interaction with GHB, visible to the naked eye under a standard UV lamp, signifies a detection capability well below the threshold for chemical submission effects.

Moreover, the synthesis and characterization of two novel

fluorogenic probes, based on 2-aminobenzoxazol bearing a fluorescein derivative (2a and 2b), further expand our arsenal against GHB detection. Demonstrating proficiency in both solution and cellulose paper-supported environments, these chemosensors enrich the versatility and reliability of our detection methodology.

We firmly believe that the deployment of these paper-based probes

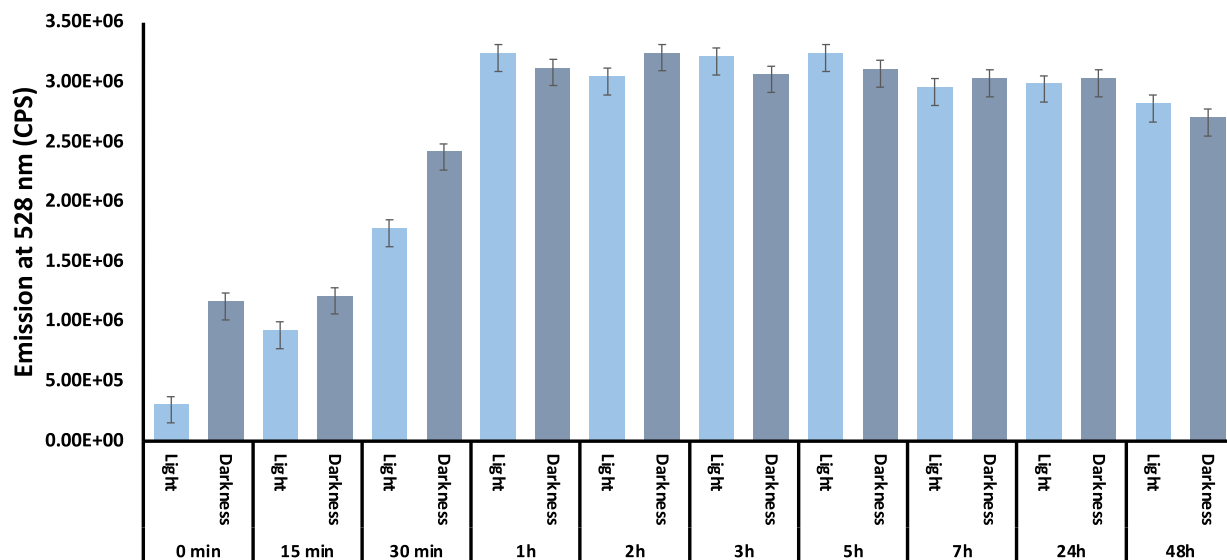


Fig. 5. Emission at 528 nm ($\lambda_{\text{exc}} = 490$ nm) of different cellulose paper discs impregnated with compound 1, in the presence of GHB (90 mM), in the dark or in daylight, overtime.

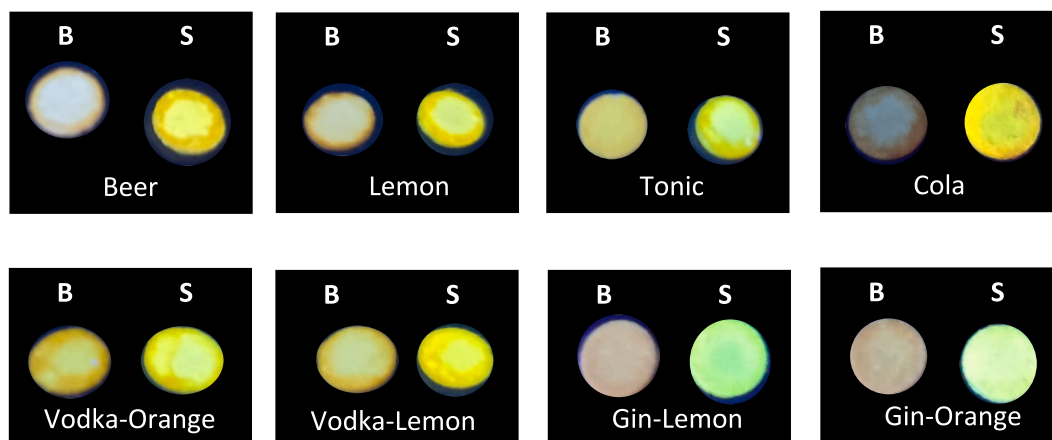


Fig. 6. Fluorescence changes immediately observed by naked eye, under a common UV lamp, in the presence of different soft drinks and alcoholic beverages, previously spiked with GHB, at the concentration required for chemical submission effects (90 mM). Left circle: the cellulose paper disc impregnated with compound 1 in the presence of the different soft drinks and alcoholic beverages (blank, B); right circle: the solid sensor in the presence of the drink spiked with GHB (90 mM) (spiked, S).

will significantly enhance surveillance efforts, not only in preempting instances of chemical submission but also in safeguarding public health and safety against such illicit activities. This innovation represents a critical step forward in the ongoing battle against clandestine threats, underscoring the pivotal role of scientific ingenuity in confronting emerging challenges.

Author statement

I the undersigned, as the Correspondin Author and in the name of all authors, declare that this manuscript SBSR-D-24-00116 entitled “Green and real-time detection of GHB in soft drinks and alcoholic beverages using an eco-friendly cellulose paper-based fluorescent probe”, by J. Hernández-Contreras, J. Roig-Rubio, M. Parra, S. Gil, P. Arroyo, J. A. Sáez, C. Lodeiro and P. Gaviña is original, has not been published before and is not currently being considered for publication elsewhere. I confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. I further confirm that the order of authors listed in the manuscript has been approved by all of us. We understand

that the Corresponding Author is the sole contact for the Editorial process. He is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

Dr. Pablo Gaviña.

CRediT authorship contribution statement

Jordi Hernández-Contreras: Writing – original draft, Methodology, Investigation, Data curation. **Jordi Roig-Rubio:** Investigation, Data curation. **Margarita Parra:** Writing – original draft, Supervision, Methodology, Data curation. **Salvador Gil:** Methodology, Data curation. **Pau Arroyo:** Writing – original draft, Validation, Formal analysis. **José A. Sáez:** Writing – original draft, Validation, Formal analysis. **Carlos Lodeiro:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Pablo Gaviña:** Writing – review & editing, Visualization, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

All data are included in the published article and its supplementary material.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.sbsr.2024.100691>.

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