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Disposable Stochastic Platform for the Simultaneous Determination of Calcipotriol and Betamethasone in Pharmaceutical and Surface Water Samples

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Abstract: A disposable stochastic platform based on calix [6]arene modified multi-walled carbon nanotubes-gold nanoparticles screen-printed electrode has been developed for the simultaneous determination of calcipotriol and betamethasone. For both analytes, very wide linear concentration ranges and extremely low limits of quantification (LOQ) were obtained: from 1.0×10^{-15} to 1.0×10^{-3} mol L^{-1} and with a 1.0×10^{-15} mol L^{-1} LOQ for calcipotriol, and from 1.0×10^{-16} to 1.0×10^{-2} mol L^{-1} with a 1.0×10^{-16} mol L^{-1} LOQ for betamethasone. The applicability of the sensing platform was successfully tested in commercially available topical pharmaceutical gel and surface water samples, obtaining recovery values ranging from 99.10 to 99.99% and relative standard deviation values under 0.05%. The obtained results render the proposed platform a viable, robust, selective, and sensitive tool that can be employed for the determination of the analytes in on-site routine quality control of pharmaceuticals and water quality monitoring.

Keywords: stochastic platform; disposable sensor; simultaneous determination; calcipotriol; betamethasone

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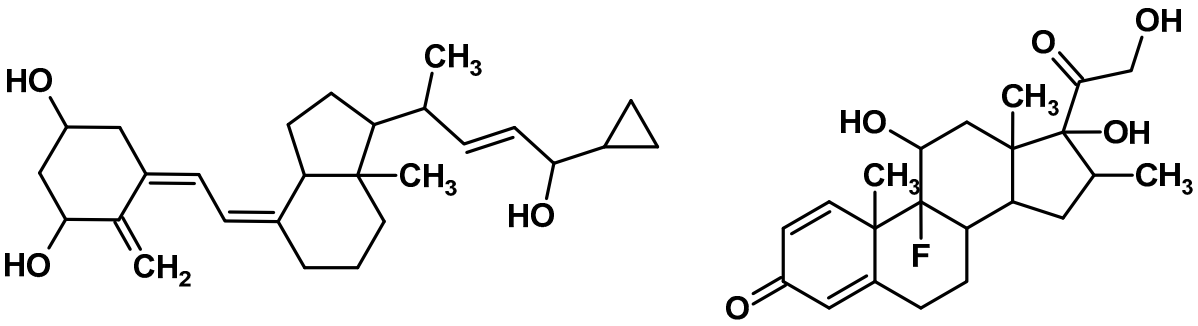
1. Introduction

Calcipotriol and betamethasone (Figure 1) are two active pharmaceutical ingredients used in combination in various formulations for the topical treatment of mild to moderate plaque psoriasis (psoriasis vulgaris). Psoriasis vulgaris is a chronic inflammatory immune-mediated cutaneous condition characterized by scaly, red, and itchy lesions on the limbs and trunk that are delimited from uninvolved skin by a distinct line of demarcation [1]. The lesions are caused by overactive T-helper lymphocytes which trigger an overgrowth of undifferentiated keratinocytes. The severity of psoriasis vulgaris can be intensified by various factors such as cutaneous injuries, sunburn, stress, and certain medications such as beta-blockers, ACE inhibitors, and lithium. The calcipotriol/betamethasone combination has proven effective due to the different mechanisms of action of the components. Betamethasone is a fluorinated corticosteroid that inhibits inflammation and epidermal hyperproliferation by acting on the glucocorticoid receptors while calcipotriol (or calcipotriene) is a vitamin D analog that has the effect of regulating cell proliferation and differentiation by acting via a vitamin D_3 receptor [2]. The combination of the two has proven to be more effective than calcipotriol and betamethasone in monotherapy [3]. Fur-

thermore, based on pharmacoeconomic evaluations, this combination is more financially beneficial than other topical treatments [4].



(**a**) (**b**)

Figure 1. Chemical structure of: (**a**) calcipotriol; (**b**) betamethasone.

The potential negative impacts of both calcipotriol and betamethasone necessitate careful management of their usage to prevent significant damage to human bodily functions. Prolonged utilization of topical corticosteroids has raised some concerns, as their administration may result in cutaneous side effects such as cutaneous atrophy, the formation of striae, and tachyphylaxis. Extended usage of large quantities may even result in hypothalamic-pituitary-adrenal axis suppression, although it occurs in very rare cases. Adverse reactions such as irritant contact dermatitis have also been reported with topical administration of vitamin D analogs more frequently than with corticosteroids [3].

Like other corticosteroids, betamethasone risks eliciting adverse reactions on the physiological functions and behavior of aquatic organisms once released into aquatic ecosystems. Corticosteroids have been observed to disrupt osmoregulation, metabolism, the immune system, and proper functioning of the musculoskeletal and cardiovascular systems, as well as reproductive functions [5]. For this reason, monitoring the betamethasone levels in water samples to identify sources of pollution and develop effective mitigation strategies could reduce the deleterious effects caused by their presence.

Whether calcipotriol or other vitamin D analogs pose environmental risks has not been identified.

The compendial method provided in the European Pharmacopoeia for the determination of calcipotriol is liquid chromatography whereas for the determination of betamethasone it is UV-Vis spectroscopy [6]. Numerous other methods have been reported for the quantification of calcipotriol and betamethasone up until the present times. These include HPLC with UV detection, TLC-densitometry, UPLC with UV detection, and UV spectrophotometry with two chemometrics methods: fuzzy interference system (FIS) and continuous wavelet transform (CWT) [7–10]. These methods have several drawbacks, such as pricey equipment that needs to be handled by qualified personnel, consumption of large quantities of expensive reagents, and complex and lengthy sample processing, even though they are reproducible, accurate, and sensitive. Electrochemical techniques possess desirable attributes such as sensitivity, selectivity, ease of use, affordability, and basic sample processing rendering them a viable substitute for the simultaneous determination of calcipotriol and betamethasone.

The cornerstone of a new generation of electrochemical sensors, called stochastic sensors, was laid out by Bayley and Cremer in 2001 when they presented membrane-bound channels or pores capable of distinguishing multiple molecules of interest. First, natural nanopores were used, for example, staphylococcal α-hemolysin [11]. Afterwards, the utilization of artificial nanopores embedded within solid membranes demonstrated significant versatility in the assay of individual molecules, as their integration in the design of stochastic sensors presents a compelling viewpoint regarding the identification and determination of molecular interactions. The interactions between the nanopores and individual molecules represent a random and reversible process that modulates the

electrical current passing through the nanopore. The current is measured as a function of time and is generated by applying a constant electrical potential. As the analyte molecule present in the solution flows through the nanopore, it generates a current blockade for a specific duration. Artificial nanopores represent advantageous tools as they are capable of interacting with multiple molecules but at distinct time intervals, hence they can be employed for the simultaneous analysis of multiple molecules. When analyzing a mixture of analytes, the signals of each analyte are distinguished based on the amount of time it takes to block the nanopore and the amount of time it takes to bind to the nanopore wall [12].

The utilization of the stochastic approach in electrochemistry enables qualitative and quantitative analysis. To date, numerous stochastic sensors have been developed for screening specific diseases, determining some pharmaceutically active compounds, evaluating water quality and food control, and successfully applying to many types of sample matrices [13–16]. Moreover, the stochastic method also allows for enantio-analysis [17].

Commercially available screen-printed electrodes (SPEs) are versatile tools with numerous applications in electrochemical analysis. This is mainly due to the variety of benefits they offer, such as cost-effectiveness, reproducibility, facile and convenient manufacturing and utilization processes, versatile design and customization options for diverse applications, compatibility with portable devices, and the ability to detect a wide range of compounds [18].

Carbon nanotubes exhibit exceptional mechanical, chemical, and thermal characteristics due to their nanostructure and aspect ratio. These include remarkable electrical conductivity, Young's modulus, tensile strength, flexibility, favorable chemical inertness, and elevated electrical conductivity. Their unique physical and catalytic features render them highly suitable for electrochemical sensors. There are two categories of carbon nanotubes, namely single-walled carbon nanotubes (SWCNTs) which exhibit sp2 hybridized carbon atoms displayed in a hexagonal honeycomb structure subsequently rolled into a tubular shape, and multi-walled carbon nanotubes (MWCNTs) which consist of multiple concentric tubes that encircle one another [19].

Gold nanoparticles (AuNPs) possess several advantageous properties in terms of surface area, conductivity, electro-catalytic characteristics, and stability. Consequently, they enhance the sensitivity and improve the limit of detection of the sensor by increasing the active area of the electrode [20–22].

Calixarenes are flexible macrocyclic compounds presenting hollow cavity-like structures with a conical shape. Calix [6]arene consists of six phenolic units linked by methylene groups. The selection of calix [6]arene as a constituent material for the design of the sensor was based on its 5.0 Å diameter cavity being suitable for stochastic detection [23].

The utilization of techniques that enable the simultaneous determination of multiple analytes offers the benefit of saving analysis time and diminishing the associated costs. Unlike classical methods, electrochemical methods used for simultaneous determination avoid the step of separating the analytes, thus simplifying the whole process.

This present study proposes a disposable stochastic platform based on a calix [6]arene modified multi-walled carbon nanotubes-gold nanoparticles screen printed electrode for the simultaneous determination of calcipotriol and betamethasone in topical pharmaceutical gel and surface water samples. To our knowledge, there have not yet been any electrochemical methods described for the simultaneous determination of calcipotriol and betamethasone. Only a limited number of electrochemical sensors have been proposed for the individual determination of betamethasone, while for calcipotriol there were no reports identified in the literature [24–26]. On site analysis is of high request in pharmaceutical industry (where the quality of the samples must be analyzed in order to produce high quality pharmaceutical formulations), as well as in water analysis, because the quality of water is a very important issue for the health of population. Developing such robust platforms for on site analysis, connected by wireless to mobile instrumentation (e.g., laptop/tablet/smart phone) and further to databases and agencies for the quality of environment facilitate the

real-time monitoring of calcipotriol and betamethasone concentrations in different samples. Therefore, the novelty of this paper is given by the simultaneous assay of calcipotriol and betamethasone in pharmaceutical and water samples using newly designed screen-printed electrodes integrated into a platform able to connect to a mobile device which is performing data acquisition, data processing, and data transmission to a central point that requires monitorization of, e.g., the water quality. Compared with the standard HPLC methods recommended by national and international pharmacopoeias, who largely recommend the determination of one of the active compounds (either calcipotriol, either betamethasone), methods which are not cost-effective, given the costs of gas, column, and sample-processing for each of the active compounds, the proposed platform is cost effective as it can be used for more than 100 measurements, no sample preparation is needed, and the cost of the platform is far lower than the cost of one-run chromatographic method used singly for either calcipotriol or betamethasone determination.

2. Materials and Methods

2.1. Materials and Reagents

Calcipotriol, betamethasone, calix [6]arene, monosodium phosphate, disodium phosphate, ethanol, and dimethyl sulfoxide were procured from Sigma Aldrich (Milwaukee, Brookfield, WI, USA). The multi-walled carbon nanotubes-gold nanoparticles modified screen-printed carbon electrodes (ref. DRP-110CNT-GNP) were procured from Metrohm. The electrode has the following measurements: 33.0 mm length, 10.0 mm width, and 0.5 mm height, with the diameter of the working electrode being 4.0 mm. The reference electrode is silver based and the auxiliary electrode is carbon based. The electrode is constructed on a ceramic substrate.

Phosphate buffer solution (PBS, 0.1 mol L^{-1}) was obtained by mixing aqueous monosodium phosphate and disodium phosphate. Then, the pH was adjusted to the desired 5.0 pH using a 0.1 mol L^{-1} HCl solution.

Calcipotriol and betamethasone were dissolved in dimethyl sulfoxide to prepare the stock solutions (1.0×10^{-3} mol L^{-1} calcipotriol and 1.0×10^{-2} mol L^{-1} betamethasone). The solutions used for platform calibration were prepared using the successive dilution method by buffering with PBS pH 5.0.

2.2. Apparatus and Methods

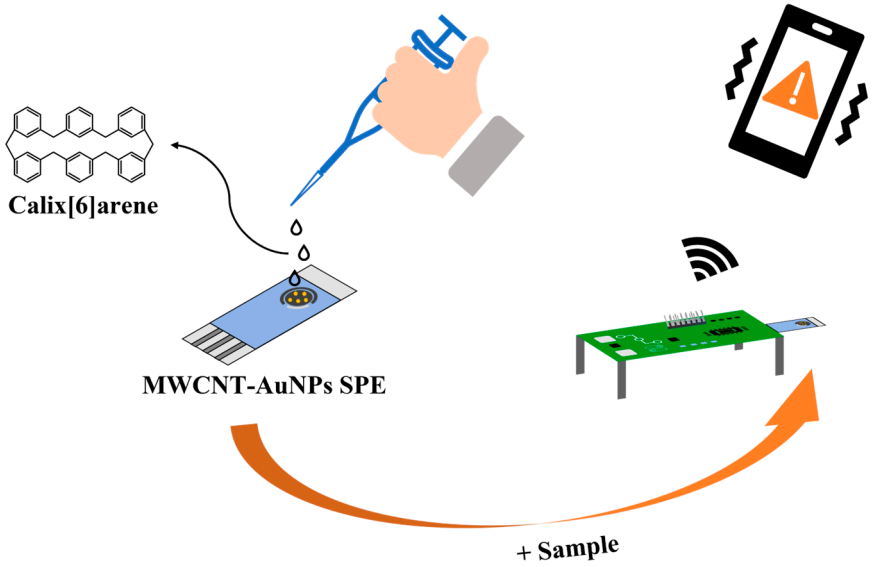
All the stochastic measurements were conducted on an EmStat Pico mini potentiostat linked to a smartphone running the version 2.7 PStouch mobile application (PalmSens BV, Houten, The Netherlands). The pH adjustments were done employing a Mettler Toledo pH meter. Deionized water was acquired using a Direct-Q 3 Water Purification System (Molsheim, France) to prepare the solutions.

The experiments were carried out at ambient temperature.

2.3. Design of the C6A/MWCNT-GNP SCPE Disposable Platform

The disposable sensing platform was constructed by chemical immobilization of calix [6]arene (C6A) on multi-walled carbon nanotubes-gold nanoparticles (MWCNT-AuNPs) substrate by drop casting technique. Firstly, 3.18 mg of C6A was mixed with ethanol to create a dispersion. Then, 1.0 µL of C6A dispersion was drop-casted on the surface of MWCNT-AuNPs SPE, obtaining the disposable stochastic platform denoted C6A/MWCNT-AuNPs SPE. The platform (Scheme 1) was rapidly prepared for use within a matter of seconds due to the utilization of ethanol as a dispersion medium, which exhibits a rapid evaporation rate at room temperature.

The modified platforms were stored in a dry place, at room temperature, and away from direct sunlight.



Scheme 1. Design of the platform used for the assay of calcipotriol and betamethasone.

2.4. Stochastic Mode

The measurements were carried out in stochastic mode using the chronoamperometry technique. The current was recorded at a constant potential of 200.0 mV vs. Ag/AgCl. This potential value was optimized by screening from 10 to 10 mV starting with a potential of 10 mV, so that the value of t_{off} could be read reliably using both automatic and manual reading of the diagrams (values lower than 1 ms are not reliably read manually, and values higher than 10 s will enlarge the analysis time while quantitative parameters (sensitivity LOQ_ remain the same. Two parameters, t_{on} and t_{off}, are identified in the obtained diagrams. The t_{on} parameter is used for quantitative analysis, as it describes the frequency of analyte-channel interactions, while the t_{off} parameter represents the signature of the analyte and is used for qualitative analysis, providing information about the duration and amplitude of these interactions. For the calibration of the proposed disposable platform, standard solutions with varying concentrations of calcipotriol and betamethasone, respectively, were utilized. The following calibration equations were established based on the linear regression approach:

$$1/t_{on} = a + b \times C_{calcipotriol} \quad (1)$$

$$1/t_{on} = a + b \times C_{betamethasone} \quad (2)$$

where a—intercept, and b—slope/sensitivity.

Based on these equations, the unknown concentrations of calcipotriol and betamethasone contained in the samples were calculated.

2.5. Samples

The proposed disposable platform was applied for the simultaneous determination of calcipotriol and betamethasone from real samples, namely pharmaceutical gel and surface water samples.

The pharmaceutical gel was acquired from a local drugstore. It contained 50.0 µg per gram of calcipotriol and 0.5 mg per gram of betamethasone as active pharmaceutical ingredients. The other components of the gel are liquid paraffine, polyoxypropylene stearyl ether, hydrogenated castor oil, butylhydroxytoluene (E321), and racemic α-tocopherol. The pharmaceutical sample was not subjected to any preliminary processing.

The samples of surface water were collected from a nearby river and stored in the refrigerator before the analysis. The samples were buffered in a 1:1 (*v*/*v*) ratio with pH 5.0 PBS. The absence of calcipotriol and betamethasone signatures in the water samples

indicated the non-existence of these particular molecules in the samples. Subsequently, the water samples were spiked with various concentrations of calcipotriol and betamethasone.

3. Results

3.1. Response Characteristics of the C6A/MWCNT-AuNPs SPE Disposable Platform in the Stochastic Mode

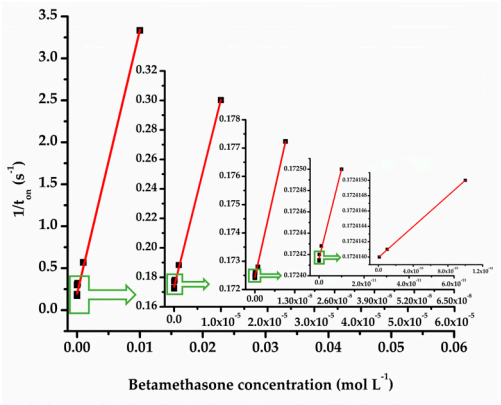
The stochastic mode is an approach that relies on the interactions of the target analyte with a conductive channel. The process of stochastic sensing involves two distinct steps. During the initial stage, a constant potential is applied, resulting in a current flowing through the channel. Then, the analyte is extracted from the solution at the membrane-solution interface. The current subsequently drops to 0 when the analyte enters the channel and blocks the current flow. This process, known as the pattern recognition phase, is useful in qualitative analysis because the time duration in which it takes place is specific to each analyte. Because the t_{off} parameter is closely related to the size and shape of the analyte molecule, it is often referred to as the analyte signature. The second phase occurs when the analyte flows through the pore, where it binds to its wall, and redox processes occur. The time in which this step takes place is the t_{on} parameter used in the quantitative analysis. This stage is called the binding phase and is defined by the following equilibrium reactions:·

$$Ch_{(i)} + \text{calcipotriol}_{(i)} \Leftrightarrow Ch \bullet \text{calcipotriol}_{(i)} \quad (3)$$

$$Ch_{(i)} + \text{betamethasone}_{(i)} \Leftrightarrow Ch \bullet \text{betamethasone}_{(i)} \quad (4)$$

where Ch is the channel and i is the interface.

Calibration graphs obtained using the stochastic mode are shown in Figure 2.



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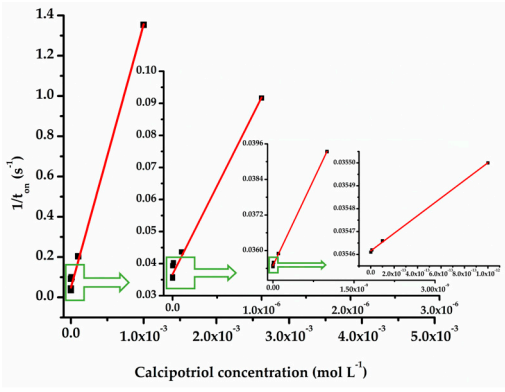


(**b**)

Figure 2. Calibration graphs obtained using the C6A/MWCNT-AuNPs SPE stochastic disposable platform for the assay of (**a**) betamethasone (**b**) calcipotriol.

Table 1 displays the response characteristics of the C6A/MWCNT-AuNPs SPE stochastic disposable platform, as determined from the t_{on} parameter values. The obtained results suggest that the proposed platform represents an accurate and reliable approach for determining calcipotriol and betamethasone simultaneously in real samples with minimal to no pre-treatment. This conclusion is based on the correlation between the very wide linear concentration range, remarkably low limit of quantification (LOQ), and significant sensitivity achieved. Thus, the proposed platform has the potential to be employed for quality control in the manufacturing of topical dosage forms but also in water quality monitoring.

Table 1. Response characteristics of the C6A/MWCNT-AuNPs SPE disposable stochastic platform.

Calibration Equation; Correlation Coefficient (r)	Linear Concentration Range (mol L^{-1})	t_{off} (s)	Sensitivity (mol L^{-1} s^{-1})	LOQ (mol L^{-1})
Calcipotriol				
$1/t_{on} = 0.04\ (\pm0.01) + 5.86\ (\pm0.03) \times 10^8 \times C_{calcipotriol}$ r = 0.9999	1.0×10^{-15}–1.0×10^{-3}	2.2 ± 0.1	$5.86\ (\pm0.03) \times 10^8$	1.0×10^{-15}
Betamethasone				
$1/t_{on} = 0.07\ (\pm0.01) + 3.25\ (\pm0.02) \times 10^9 \times C_{betamethasone}$ r = 0.9992	1.0×10^{-16}–1.0×10^{-2}	0.7 ± 0.1	$3.25\ (\pm0.02) \times 10^9$	1.0×10^{-16}

The proposed stochastic platform exhibited a significantly low LOQ (of fg mL^{-1} order of magnitude) for both calcipotriol and betamethasone, as well as a broader linear concentration range in comparison to previously described methods developed for the simultaneous determination of calcipotriol and betamethasone. The LOQ is given by the lowest concentration found in the linear concentration range according to the new IUPAC recommendation (paragraph 3.36, Note 3) [27]. The comparison is depicted in Table 2.

Table 2. Comparison of various proposed methods used for the simultaneous determination of calcipotriol and betamethasone.

Method	Analyte	Linear Concentration Range (mol L^{-1})	LOQ (mol L^{-1})	Ref.
HPLC with UV detection	Calcipotriol Betamethasone	2.42×10^{-6}–4.85×10^{-5} 9.91×10^{-7}–3.96×10^{-4}	2.9×10^{-7} 7.96×10^{-7}	[7]
UPLC with UV detection	Calcipotriol Betamethasone	3.03×10^{-5}–1.82×10^{-4} 3.15×10^{-4}–1.91×10^{-3}	2.37×10^{-5} 9.64×10^{-5}	[9]
UV spectrophotometry with FIS and CWT	Calcipotriol Betamethasone	2.42×10^{-6}–2.42×10^{-5} 1.98×10^{-6}–1.98×10^{-5}	5.45×10^{-8} 5.49×10^{-8}	[10]
Stochastic using C6A/MWCNT-AuNPs SPE disposable platform	Calcipotriol Betamethasone	1.0×10^{-15}–1.0×10^{-3} 1.0×10^{-16}–1.0×10^{-2}	1.0×10^{-15} 1.0×10^{-16}	This work

The results obtained using the proposed stochastic platform were compared in terms of betamethasone determination with other proposed electrochemical sensors in Table 3.

For the assay of both calcipotriol and betamethasone, far lower limits of quantification were obtained when the proposed platform was used; furthermore, wider linear concentration ranges were obtained compared to previously developed methods (Tables 2 and 3). Additionally, the proposed platform and method is able to determine simultaneously, in the same run the two active compounds, both calcipotriol, and betamethasone, making it faster compared to the other methods, as well as also cost-effective. The wide linear concentration range also facilitates the determination of calcipotriol and betamethasone in water samples, where there is a need for fast, reliable, cost-effective, on-site determination, in order to avoid accumulation of calcipotriol and betamethasone reaching values that are dangerous for the health of the population.

Table 3. Comparison of various proposed electrochemical sensors used for the determination of betamethasone.

Electrochemical Method	Sensor	Linear Concentration Range (mol L^{-1})	LOQ (mol L^{-1})	Ref.
SWV	SWNT/EPPGE	1.0×10^{-9}–2.5×10^{-8}	1.0×10^{-9}	[24]
SWV	SWNTs–CTAB/EPPGE	0.5×10^{-9}–1.0×10^{-7}	0.86×10^{-9}	[25]
DPV	Hg(Ag)FE	5.0×10^{-9}–0.8×10^{-6}	5.0×10^{-9}	[26]
Stochastic	C6A/MWCNT-AuNPs SPE disposable platform	1.0×10^{-16}–1.0×10^{-2}	1.0×10^{-16}	This work

SWV = square wave voltammetry; DPV = differential pulse voltammetry; SWNT/EPPGE = single wall carbon nanotube modified edge plane pyrolytic graphite electrode; SWNTs–CTAB/EPPGE = single wall carbon nanotubes–cetyltrimethylammonium bromide nanocomposite film modified edge plane pyrolytic graphite electrode; Hg(Ag)FE = silver-based amalgam film electrode.

The possibility of simultaneous determination of calcipotriol and betamethasone in one run facilitates the on-site uniformity content test of the pharmaceutical formulations containing both active compounds (calcipotriol, and betamethasone). This is a valuable advantage for pharmaceutical industry because the quantitative determinations of calcipotriol, and betamethasone can be performed in real time, with low cost, also facilitating the adjustment of the quantities of calcipotriol and betamethasone if the on-site analyses show that they are not in accordance with the recommendation of national or international pharmacopoeias.

3.2. Selectivity of C6A/MWCNT-AuNPs SPE Disposable Stochastic Platform

The selectivity of stochastic sensors relies on the distinct signature associated with each analyzed molecule. In the case of calcipotriol and betamethasone, the experimental results demonstrate that different values of the t_{off} parameter were obtained, suggesting that the proposed platform is selective towards the two analytes. The selectivity was also checked versus other components of the pharmaceutical formulation: polyoxypropylene stearyl ether, butylhydroxytoluene, and α-tocopherol wherein t_{off} values higher than 2.7 s were recorded: 3.5 s for polyoxypropylene stearyl ether, 3.1 s for α-tocopherol, and 2.8 s for butylhydroxytoluene. Accordingly, the proposed platform is selective versus the tested compounds.

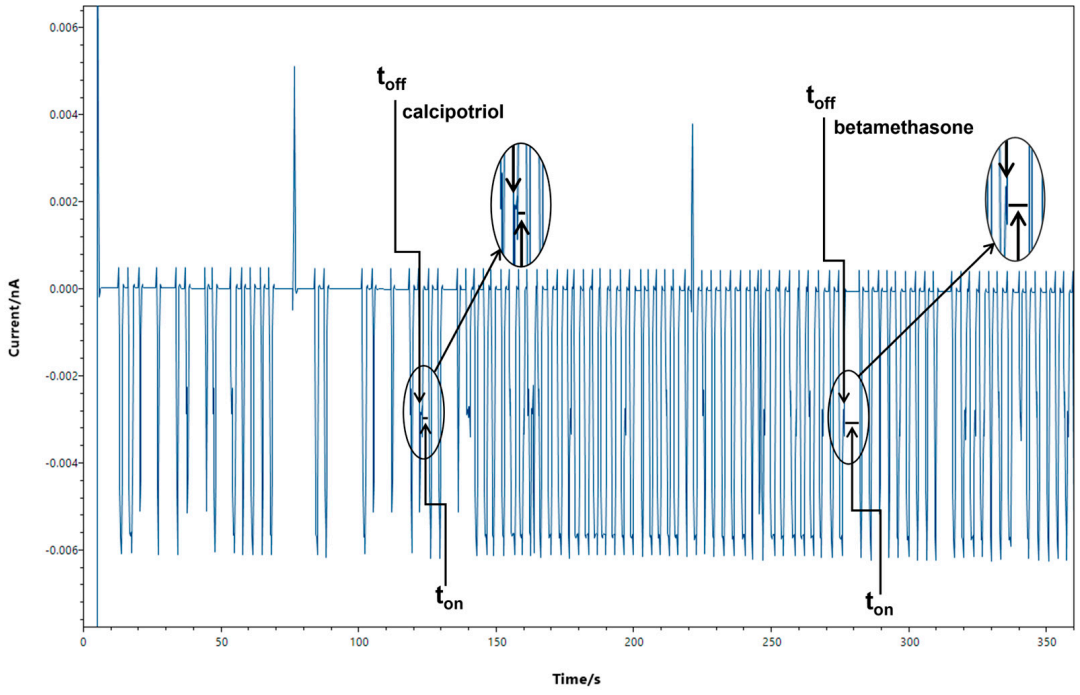
3.3. Reproducibility and Stability of C6A/MWCNT-AuNPs SPE Disposable Stochastic Platform

The reproducibility and stability of the proposed stochastic platform were tested by preparing 10 identical platforms. For the reproducibility studies, the sensitivity of each platform was determined and then the relative standard deviation (RSD%) value was calculated based on the variation of the sensitivities, obtaining a value of 0.09%. For the stability studies, the 10 platforms were stored for 2 months prior to being utilized for the simultaneous determination of the two analytes. The obtained results exhibited consistency over the duration of the study, with no significant variations observed in the sensitivity values of the platforms. These variations were found to be less than 0.15%. These findings indicate that the proposed platform exhibits high reproducibility and long-term stability.

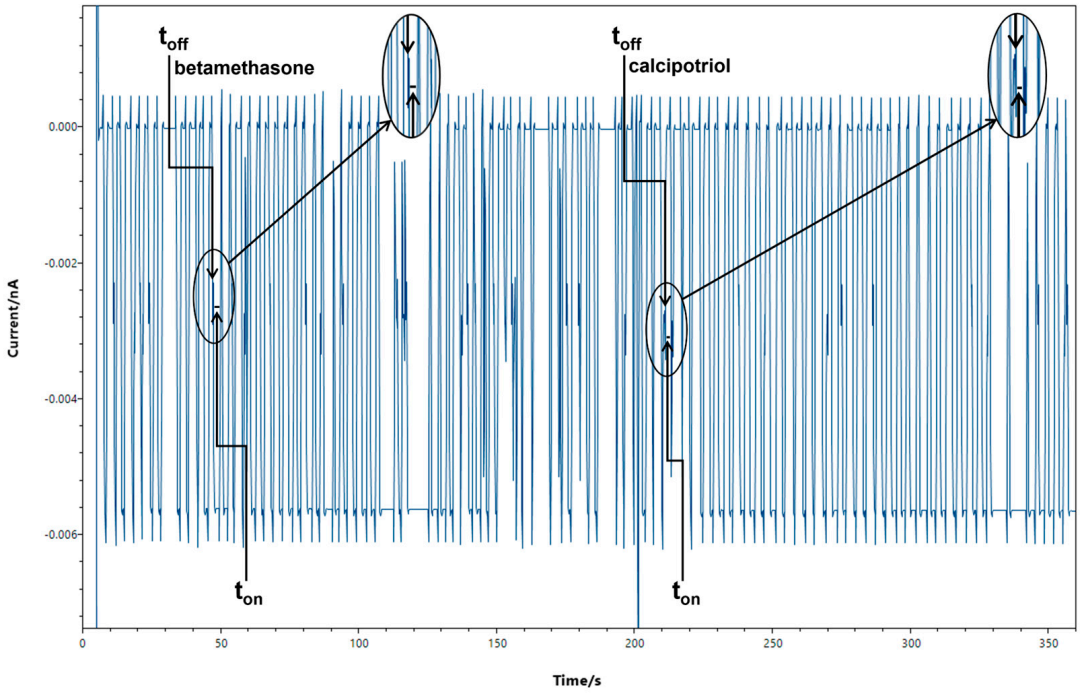
3.4. Simultaneous Determination of Calcipotriol and Betamethasone from Real Samples Using C6A/MWCNT-AuNPs SPE Disposable Stochastic Platform

The applicability of the proposed stochastic disposable platform for the simultaneous determination of calcipotriol and betamethasone was tested on real samples (pharmaceutical gel and surface water). The recorded diagrams were analyzed and the t_{off} and t_{on} parameters were determined for both the analytes, as illustrated in Figure 3a,b. Based on the values of t_{off} (signatures) recorded, the active components: calcipotriol and betamethasone were determined, and the t_{on} value read just after the signature (in between two t_{off} values) was used to create the calibration curves reported in Table 1 to determine the

concentrations of calcipotriol and betamethasone in the samples (see also the paragraph related to the stochastic mode). Table 4 shows the computed recovery and relative standard deviation (RSD) values.



(**a**)



(**b**)

Figure 3. Stochastic diagrams obtained employing the C6A/MWCNT-AuNPs SPE disposable stochastic platform for the simultaneous determination of calcipotriol and betamethasone in: (**a**) pharmaceutical gel sample; (**b**) spiked surface water samples.

Table 4. Simultaneous determination of calcipotriol and betamethasone in a pharmaceutical gel and spiked surface water samples using the proposed C6A/MWCNT-AuNPs SPE disposable stochastic platform (N = 10).

Sample	Calcipotriol and Betamethasone, Added Amount (mol L^{-1})	Recovery (%)	
		Calcipotriol	Betamethasone
Topical pharmaceutical gel	–	99.15 ± 0.03	99.93 ± 0.02
Surface water samples	1.0×10^{-4}	99.21 ± 0.03	99.47 ± 0.04
	1.0×10^{-6}	99.50 ± 0.05	99.30 ± 0.02
	1.0×10^{-8}	99.21 ± 0.03	99.47 ± 0.03
	1.0×10^{-10}	99.10 ± 0.02	99.99 ± 0.02
	1.0×10^{-12}	99.12 ± 0.04	99.97 ± 0.03

The results indicate that the proposed platform exhibits a high degree of reliability for qualitative and quantitative analysis of calcipotriol and betamethasone from pharmaceutical and water samples, as shown by the recorded values for the recoveries and the relative standard deviations. Moreover, the other components present in the sample matrix did not influence the platform's response. Since the platform is connected to a portable device, this could enable on-site analysis. Additionally, cross-contamination of the samples is avoided by using disposable detection platforms. The combination of these features and the fact that the stochastic method requires minimal sample processing makes the proposed approach a convenient alternative for the quality control of pharmaceuticals and for the screening of surface water quality.

4. Conclusions

A disposable stochastic platform based on calix [6]arene and a commercially available screen-printed electrode was proposed for the simultaneous recognition and determination of calcipotriol and betamethasone in two types of samples: a pharmaceutical formulation, and water samples. When employing the proposed platform, it was possible to achieve a very low limit of quantification, an extensive linear concentration range, and very good sensitivity values. All these characteristics facilitated the assay of calcipotriol, and betamethasone in both the pharmaceutical formulation and water samples with high reliability. The response of the platform was not influenced by the complex sample matrices in which the analysis was performed. For these reasons, the proposed disposable stochastic platform represents a promising versatile candidate as a tool for both the pharmaceutical industry (where it can be reliably used for on-site analysis of the pharmaceutical formulations containing calcipotriol and betamethasone as active compounds), as well as the on-site analysis of water, especially that coming out from hospitals and clinics where gel containing calcipotriol and betamethasone is used. The cost-effectiveness (the cost of 100 analyses of simultaneous assay of calcipotriol and betamethasone in either pharmaceutical or water samples is far less than the cost for HPLC analysis of just one of the active compounds) as well as the high reliability of the developed platform make it an excellent candidate for the on-site analysis of pharmaceutical and water samples.

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