# ANALYTICAL STUDY OF SULFONAMIDE COMPOUNDS BASED ON THE DIRECT QUENCHING EFFECT

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## ABSTRACT

*Antimicrobial sulfonamide medicines are widely used in human and veterinary medicine. Sulfonamide pharmaceuticals Medical and veterinary professionals still rely on this group of antibacterial medicines. Although a number of analytical approaches have been offered, many of them are not appropriate for routine quality control due to lengthy procedures or expensive gear. Drugs with sulfonamide functional group chemistry (SN) are a major part of the pharmaceutical industry. Sufonamides are capable of treating a wide range of conditions, including diuresis, hypoglycemia, thyroiditis, inflammation, and glaucoma, in vivo. This is because they have anti-carbonic anhydrase and anti-t dihydropteroate synthase actions in the human body. Sulfonamide chemicals (sulfasalazine, sulfanilamide, and sulfamethoxazole) have a direct quenching impact on terbium (III) luminescence, as we demonstrate in this study. From Sigma we acquired the SSZ and Tb (III)-nitrate pentahydrate, as well as SNM, SMX, and SNMX (Madrid, Spain). It was received from Panreac that sodium hydroxide, di-sodium hydrogen phosphate 2-hydrate, sodium hydrogen phosphate 2-hydrate, and methanol were available (Barcelona, Spain). Analytical-grade reagents were used in this study. Using the automated approach multicommutation to construct the flow assembly, the suggested method was able to determine up to 50 samples per hour.*

**Keywords:** Automation; Lanthanide luminescence; Multicommutation; Quenching; Sulfonamides

## 1. INTRODUCTION

They were the first antimicrobial medications, commonly known as Sulfa drugs, and cleared the way for the antibiotic revolution in medicine. Sulfonamide pharmaceuticals Medical and veterinary professionals still rely on this group of antibacterial medicines. Sulfonamide formulations are widely available in the pharmaceutical business due to the importance and time-consuming nature of routinely monitoring them. In addition, there are rising concerns about the quality of medications and an increasing number of fakes in the market. For sulfonamides, the approved USP (United States Pharmacopoeia) approach is titrimetric, necessitating temperature control and end-point detection by biamperometry or starch-iodide paper. Both approaches take a long time and require a lot of effort.

Sulfonamide medicines may be detected using a wide range of analytical techniques, the most common of which being spectrophotometry luminescence, electroanalysis, and high-performance liquid chromatography (HPLC). Pretreatment and costly instruments are required for HPLC, which can give excellent sensitivity and accuracy. Sulfonamides can also be analysed using immunochemical methods or Fourier-transform Raman spectroscopy. For this category of chemicals, lanthanide luminescence has not before been documented. The cornerstone of this identification method for many organic compounds is the fluorescence spectra of lanthanide ions, especially when they are chelated with ligands. These chelates exhibit substantial Stokes shifts, narrow emission bands, and extended luminescence lives. In order to enhance the luminescence signal, it is possible to transfer energy from an organic component to ion. The lanthanide ion's background luminescence can only be quenched in rare circumstances when the organic molecule has a triplet-state level lower than the excited-state level of the lanthanide ion.

## LITERATURE REVIEW

**Lucía Molina García(2010)**Antimicrobial sulfonamide medicines are widely used in human and veterinary medicine. Although a number of analytical approaches have been offered, many of them are not appropriate for routine quality control due to lengthy procedures or expensive gear. Sulfonamide chemicals (sulfasalazine, sulfanilamide, and sulfamethoxazole)

have a direct quenching impact on terbium (III) luminescence, as we demonstrate in this study. Using the automated approach multicommutation to construct the flow assembly, the suggested method was able to determine up to 50 samples per hour.

**Leonenko (2011)** Terbium (III) complexes of 4-carboxybenzo-15-crown-5 (L1) and 4-carboxybenzo-18-crown-6 (L2) are examined for their spectrum luminous characteristics. Lanthanide luminescence is quenched by alkali metal ions, which is known as the creation of Tb (III)-L1-Na+ and Tb (III)-L2-K+ complexes. They may be used as molecular sensors for the detection of Na+ and K+ luminescence with detection limits of 1.5 and 25.0 g/mL, respectively. In the presence of a 1000-fold excess of potassium, sodium may be measured using the Tb (III)-L1 combination. For the measurement of KCl in the Kalipoz tablet form and the total sodium salts (NaCl, NaHCO3) in the Trisol solution for intravenous infusions, the established methodologies are used.

**María José Ruedas Rama (2006)** Raman spectroscopy (FT) is used as a detection method in a flow-through sensor system. The suggested approach is very selective due to the chemical and structural information found in Raman spectra and the retention of just the species of interest on the sorbent. It was possible to measure sulfathiazole and sulfamethoxazole directly in the presence of other species that are commonly found with these analytes thanks to the flow-through sensor. In the flow-through cell, Sephadex QAE A-25 resin was utilised as the packing material. Sulfonamides were briefly held there. In this experiment, the samples were transported in NaOH 10(-2) mol l (-1), and the eluent was prepared from 2 ml of a solution of [NaCl (0.10 mol l(-1))/NaOH (10(-2) mol l(-1)). In the range of sulfamethoxazole (0.5-10 g l(-1)) and sulfathiazole (0.7-10 g l(-1)), the analytical signal was linear for a volume of 1 ml sample. Both analytes had RSDs (percentage) lower than 4%. The sensor worked well with a variety of commercially available pharmacological formulations for humans and animals, including capsules, syrup, tablets, powders, injectables, and suspensions.

**ElhamAnwerTaha(2007)**Somesulfur-containing substances such as acetylcysteine, carbocisteine (Cc), and thioic acid (Th) may be determined utilising two simple, sensitive, and selective fluorimetric procedures that use uranium U+3 as a fluorescence probe. A ternary complex with Tb+3 in the presence of Tris-buffer (I) and a binary complex with aqueous Uranyl Acetate solution (II) are two of the proposed approaches (II). Tb+3 fluorescence quenching was detected quantitatively for Ac, Cc and Th at 510, 488 and 540 nm (lambda(ex) 250, 241 and 268 nm) and for uranyl acetate at 512 nm (lambda(ex) 240 nm) as a result of complex formation. The complexes' reaction conditions and fluorescence spectrum characteristics have been studied. Using the methods described in this paper, the three cited drugs were able to be analysed at concentrations between 0.2 and 2.5 microg ml (-1), 1-4 microg ml (-1), and (0.5 to 3.5 microg ml (-1), respectively, with mean percentage recoveries of 99.74+/-0.36, 99.70+/-0.52 and 99.43+/-0.23 for method (I), and between 0.56 and 0.6 microg ml (-1).

**Yongnian Ni (2006)**Many anti-bacterial medications, such as sulfonamides and trimethoprim, are found in both human and veterinary medicine. Sulfadiazine, sulfadimidine, sulfamethoxazole, sulfanilamide, and trimethoprim are all often included in the pills. This led to the development of an easy, quick, and low-cost technique for the simultaneous determination of various medications, using chemometrics methods that compare classical least squares (CLS), principle component regression (PCR), and partial least square models.. An orthogonal array design was used to gather UV-spectra from aqueous ethanolic solutions (pH = 9.9) containing drug combinations produced from the aforesaid chemicals. According to preliminary research into the UV spectra of the individual compounds, satisfactory linear regression calibration models could be constructed for all compounds with LOD values in the range of ca. 0.2–1.0 mg l 1 for each of the five drugs in the concentration range of approximately 1.0–24.0 mg l 1. There was substantial spectrum overlap between the UV spectra of the various medications, indicating the necessity of chemometrics modelling for the examination of mixtures at the same time, according to these studies.

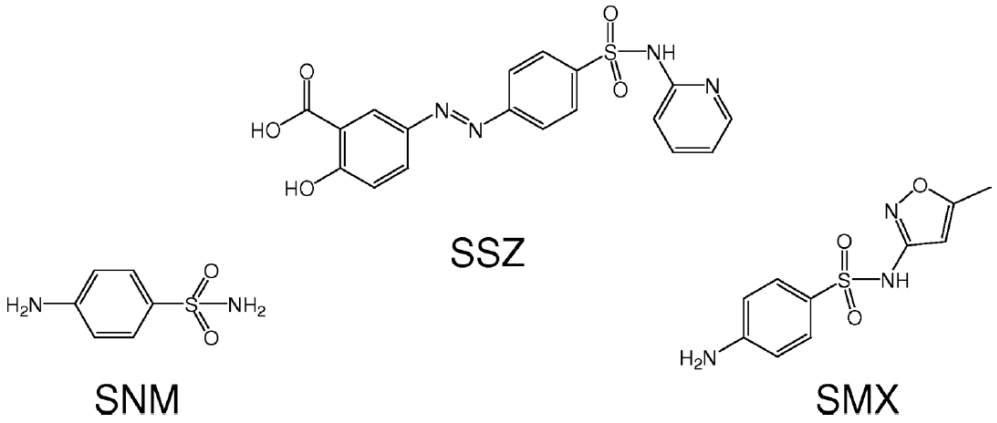


**Figure 1. Molecular structures of the analytes.**

## 2. MATERIALS AND METHODS

### 2.1 Reagents and Solutions

From Sigma we acquired the SSZ and Tb(III)-nitrate pentahydrate, as well as SNM, SMX, and SNMX (Madrid, Spain). It was received from Panreac that sodium hydroxide, di-sodium hydrogen phosphate 2-hydrate, sodium hydrogen phosphate 2-hydrate, and methanol were available (Barcelona, Spain). Analytical-grade reagents were used in this study. In order to make the SSZ stock solution of 200 mg L-1, we dissolved the needed weight in the minimal amount of NaOH 1M and diluted it to 100 mL with water. By dissolving the appropriate weight in a 10 percent MeOH:H2O solution, 200 mg L-1 stock solutions of SNM and SMX were created (v:v). At 4-C, all stock solutions were steady for at least three months. Deionized water was used to create the 0.1M terbium (III) stock solution. Daily, appropriate dilutions of stock solutions in deionized water were used to create the required working solutions of analytes and terbium (III).

### 2.2 Instrumentation

A Cary-Eclipse Luminescence Spectrometer was used to measure the luminescence (Varian Inc., Mulgrave, Australia). Cary-Eclipse (Varian) software was used to gather and process data from the spectrometer. All analytical measurements were carried out in phosphorescence mode. The delay and gate timings were 0.1 ms and 3 ms, respectively, for this experiment. For this experiment, 20 nm was chosen for both the instrument's excitation and emission slits. The voltage of the detector was 725 volts. In order to create the multicommutation manifold depicted in Figure 2, a four-channel Gilson Minipuls-3 peristaltic pump (Villiers le Bel, France) was fitted with a rate selector and pump tubing type Solvflex (Elkay Products, Shrewsbury, MA, USA), four 161T031 NResearch three-way solenoid valves, a Hellma flow cell 176.752-QS (25 mL of inner volume and a light path length of 1.5 mm), and an electronic interface, based on ULN 2803 integrate circuits, to control the flow cell and the pump were used. In addition, PTFE tubing (0.8 mm inside diameter) and methacrylate connectors were utilised. Visual Basic was used to create the system control software.

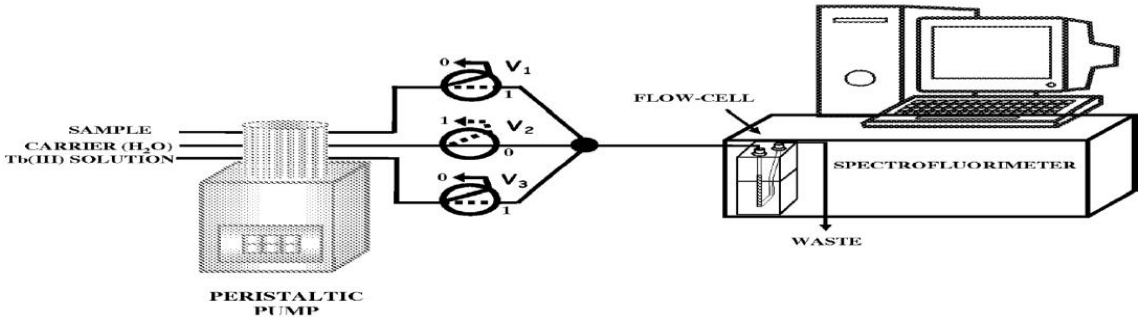


**Figure 2. Manifold: For each solenoid valve, 0 and 1 mean that the valve is OFF and ON, respectively.**

### 2.3 Preparation of Pharmaceuticals

Six different medications from the Spanish Pharmacopoeia were examined. SNM was detected in one of the SSZ samples, whereas SMX was present in three of the three. After dissolving each commercial sample in the proper solvent and filtering it through a 0.45-mm pore size filter to eliminate any insoluble materials, each commercial sample was tested for purity. NaOH 1M and deionized water were used to dissolve and dilute SSZ-containing pharmaceuticals in a 250mL volumetric flask. A 10 percent MeOH (v:v) solution was used as the solvent for medications containing SMX or SNM, resulting in a total volumetric flask volume of 250 millilitres. Simply diluting pharmaceutical solutions with deionized water to get the correct concentration for analytes was all that was required for the sample pre-treatment.

## 3. RESULTS AND DISCUSSION

We used SSZ (25 mg L-1) as a model analyte for this system's optimization and then checked the findings for the other sulfonamides. As the flow rate was 1.2mLmin-1 and the insertion duration was 40 s, we began using terbium (4x10-3 M) and sample solutions made in deionized water for this work (Ph 5.5). Afterwards, the results of each variable were locked in for future studies.

### 3.1 Quenching Mechanism

As long as the experimental findings demonstrate a linear variation, the prior equation holds. For each analyte, the plots produced are shown in Figure 3, with linearity seen in all cases, following a collisional quenching. Table 1 lists the Stern-Volmer constants.

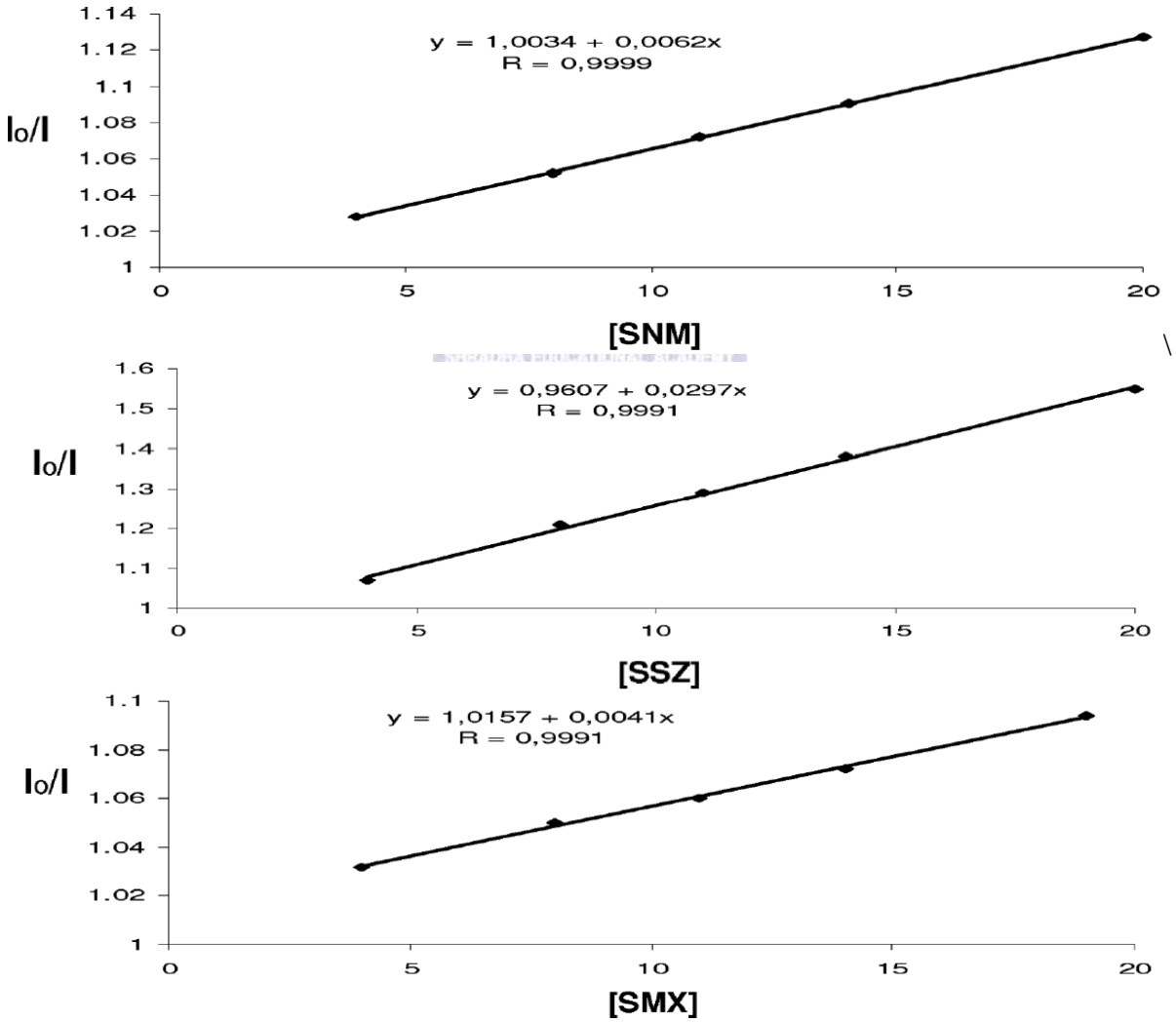


**Figure 3. Stern-Volmer plots of I0=I against [Q] for each Tb(III)-analyte system.**

**Table 1. Analytical parameters**

| Parameter | SSZ | SNM | SMX |
|---|---|---|---|
| Lineardynamicrange=mgmL$^{-1}$ | 3–22 | 4–25 | 4–20 |
| Calibrationgraph | | | |
| Intercept | 4.35 | 5.73 | 1.49 |
| Slope(mLmg$^{-1}$) | 16.95 | 6.55 | 5.82 |
| Correlationcoefficient | 0.9946 | 0.9975 | 0.9999 |
| Detectionlimit=mgmL$^{-1}$ | 0.9 | 1.2 | 1.2 |
| Quantitationlimit=mgmL$^{-1}$ | 3 | 4 | 4 |
| IntradayRSD$^{a}$(%) | 3.1 | 3.5 | 2.9 |
| InterdayRSD$^{a}$(%) | 5.3 | 5.4 | 5.9 |
| $^{b}$Ksv=Lmg$^{-1}$ | 0.0297 | 0.0062 | 0.0041 |
| Samplingfrequency=h$^{-1}$ | 50 | 50 | 50 |

**3.2 Interference Study**

Compounds that are often present in medicines with SSZ, SNM, and SMX were subjected to tolerance studies to investigate the influence of probable interfering species. Twelve milligrammes per litre of each analyte were used in the experiment. A chemical was regarded to interfere if the analytical signal showed a fluctuation of more than -2r, which was the standard deviation of the signal.

**Table 2. Analytical applications**

| | | Analyte | |
|---|---|---|---|
| | Amount | Amount | Recovery |
| Pharmaceutical | added(mg) | found (mg) | R.S.D.(%) |
| Salazopyrin[1](PfizerLtd.) | – | 527 | 105 3 |
| | 100 | 97 | 97 2 |
| | 300 | 302 | 101 3 |
| | 500 | 526 | 105 2 |
| Azol[2](KernPharmaLtd.) | – | 5078 | 102 3 |
| | 1000 | 988 | 99 1 |
| | 2000 | 2042 | 102 2 |
| | 3000 | 2925 | 97 2 |
| Cilinafosal[3](MedicalLtd.) | – | 4.9 | 99 3 |
| | 5 | 5.2 | 104 3 |
| | 10 | 10.4 | 104 2 |
| | 15 | 14.9 | 99 3 |
| Balsoprim[4](JusteLtd.) | – | 395 | 99 2 |
| | 150 | 154 | 103 3 |
| | 300 | 289 | 96 2 |
| | 500 | 496 | 99 3 |
| Momentol[5](Bristol-MyersSquibbLtd.) | – | 418 | 104 3 |
| | 200 | 197 | 98 3 |
| | 400 | 398 | 99 4 |
| | 600 | 617 | 103 3 |
| Septrin[6](CelltechLtd.) | – | 407 | 102 2 |
| | 200 | 207 | 104 3 |
| | 500 | 486 | 97 3 |
| | 750 | 744 | 99 2 |

In the event that any interference was noticed, the ratio interfering species: analyte (w:w) was gradually lowered until this interference was eliminated completely.. An analyte-interferent ratio of more than 500-fold for lactose, saccharose, glucose, and starch is presented in the suggested approach. A 5:1 ratio of ephedrine to SNM was tested for interference potential

and found to be completely devoid of interference. Ephedrine is commonly present in medicines containing SNM at a ratio of 1:1 (EPD:SNM). Finally, a tolerance ratio of more than 10:1 was achieved in the instance of trimethoprim, which is present in pharmaceuticals in a 1:5 ratio (TMP:SMX) with the suggested approach.

## 4. CONCLUSION

The quenching effect of sulfonamides on the luminescence of terbium (III) ions has been used successfully for the first time in the identification of these organic compounds in solution. New, easy, and accurate methods for the detection of Sulfonamides are the goal of this research, which focuses on the quenching effect of terbium (III) luminescence on sulfonamides. Automated multicommutation (Catala'-Icardo, Garca-Mateo, and Mart'nez-Calatayud2002) was introduced in the suggested arrangement, where a number of separate solenoid valves were used for flow network setup. Allowing for binary sampling, multicommutation can be used to introduce sample, carrier, and reagent into the flow route. There are certain advantages to this technology, such as great flexibility and minimal investment costs because solenoid valves are affordable. The first spectroscopic approach for determining SSZ has been proposed to date. The approach proposed here is fully automated thanks to the use of multicommutated assembly. It's also worth noting that samples don't need to be pre-treated. Because to its simplicity and speed (50 samples per hour), the technology is well-suited for regular quality control of sulfonamides in the pharmaceutical industry.

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