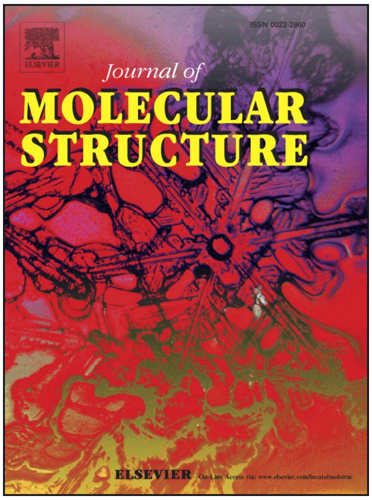


Combination of sensor potential and antimicrobial activity of a new 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide

Desislava Staneva, Evgenia Vasileva-Tonkova, Mohamad S.I. Makki, Abdullah M. Asiri, Ivo Grabchev

PII: S0022-2860(14)00437-2
DOI: http://dx.doi.org/10.1016/j.molstruc.2014.04.070
Reference: MOLSTR 20577

To appear in: *Journal of Molecular Structure*

Received Date: 3 April 2014
Revised Date: 23 April 2014
Accepted Date: 23 April 2014

Please cite this article as: D. Staneva, E. Vasileva-Tonkova, M.S.I. Makki, A.M. Asiri, I. Grabchev, Combination of sensor potential and antimicrobial activity of a new 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide, *Journal of Molecular Structure* (2014), doi: http://dx.doi.org/10.1016/j.molstruc.2014.04.070

Combination of sensor potential and antimicrobial activity of a new 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide

Desislava Staneva[1], Evgenia Vasileva-Tonkova[2], Mohamad S. I. Makki[3],
Abdullah M. Asiri[3,4], Ivo Grabchev[3,5,*]

[1]University of Chemical Technology and Metallurgy, 1756 Sofia, Bulgaria
[2]Institute of Microbiology, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria
[3]Chemistry Department, Faculty of Science, King Abdulaziz University, Jeddah 21589, Saudi Arabia
[4]Center of Excellence for Advanced Materials Research (CEAMR), King Abdulaziz University, Jeddah 21589, Saudi Arabia
[5]Sofia University "St. Kliment Ohridski", Faculty of Medicine, 1407 Sofia, Bulgaria

ABSTRACT

A blue emitting 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide bearing a dimethylaminoethyloxy group as a receptor fragment for metal ions and protons has been designed and synthesized. The basic photophysical properties of the compound have been investigated in organic solvents of different polarity. The detection of different metal cations (Pb^{2+} Cu^{2+}, Cd^{2+}, Co^{2+}, $Zn^{2+}$and Mn^{2+}) has been studied by fluorescence spectroscopy. Depending on pH, the new compound shows "off-on" switching from alkaline to acid media. A new complexe of Cu(II) with the 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide has been synthesized and characterized. The antibiotic activity of the complex was evaluated against some bacterial and yeast cultures.

Keywords: 1,8-naphthalimide, fluorescence, sensor, metal ions, metal complex, antibiotic activity

Corresponding author: Ivo Grabchev; i.grabchev@chem.uni-sofia.bg
Tel: 359 2 8161319

Introduction

Metal ions are important part of the development of medical chemistry from many years. Some of them have been used in the drugs and diagnostic agents to treat a variety of diseases [1,2]. Biological important metal ions as Zn(II), Cu(II), Co(II), Fe(II) and Fe(III), play key roles in the structural organization and activation of enzymes and biologically important compounds [3] . The antibacterial activity of the metal complexes is highly dependent on the nature of the metal ions and the ligands because different ligands exhibit different biological properties. Currently there is a real need for the discovery of new compounds with antimicrobial activities. These compounds must be more effective and possibly to act through a distinct mechanism from those of well-known classes of antimicrobial agents to which many clinically relevant pathogens are now resistant. Several biologically active compounds used as antimicrobial agents possess high antibacterial activity when administered in the form of metal complexes [4-9].

1,8-Naphthalimides and their 4-substituted derivatives are well known as typical intramolecular charge transfer chromophore which have been investigated in a large variety of areas due to their strong absorption and emission in the visible region, high photostability and large Stokes shift [10-19]. Recently, special attention was devoted to the photoinduced electron transfer (PET) occurring in tailored 1,8-naphthalimide systems and the potential use of these fluorophores as sensors for metal cations and protons [20-22]. The design of the multi-component PET fluorescence sensors has been chosen so that the electron transfer between the fluorophore signaling unit and the receptor results into a “switching off” of the fluorescence intensity. Due to the presence of guests in the system (protons or alkaline, alkaline-earth, transition or heavy metal ions capable to form a bond with the lone pair electrons of the receptor) leads to cutting-off PET interaction and to “switching on” the fluorescence of the system [20]. On the other hand, some 1,8-naphthalimides derivatives exhibit very interesting biological and antibacterial activity [23-29]. To our knowledge 1,8-naphthalimide metal complexes have not investigated as antimicrobial agents.

In this paper we present the synthesis and functional properties of a new 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide (NI) designed to act as a fluorescent PET sensor. The influence of some transition metal cations on the fluorescence intensity in *N,N*-

dimethylformamide solution has been discussed. The antibiotic activity of its complex with cuprum cations has been also investigated.

Experimental part

Material and methods

UV-Vis spectrophotometric investigations were performed using “Thermo Spectronic Unicam UV 500” spectrophotometer. Emission spectra were taken on a “Cary Eclipse” spectrofluorometer. All spectra were recorded using 1 cm path length synthetic quartz glass cells (Hellma, Germany). Fluorescence quantum yield was determined on the basis of the absorption and fluorescence spectra. All absorption and fluorescence measurements of the NI were carried out at 10^{-5} mol l^{-1} concentration. Anthracene was used as a reference ($\Phi_{st} = 0.26$) [30]. The effect of the metal cations and protons upon the fluorescence intensity was examined by adding a few μl of stock solution (c = 10^{-2} mol l^{-1}) of the metal cations to a known volume of the ligand solution (3 ml). The addition was limited to 0.08 ml, so that dilution remained insignificant [31]. $CuCl_2 \cdot 2H_2O$, $Pb(NO_3)_2 \cdot 6H_2O$, $Co(NO_3)_2 \cdot 6H_2O$ and $Zn(NO_3)_2 \cdot 4H_2O$, $Cd(NO_3)_2 \cdot 4H_2O$ $Mn(NO_3)_2 \cdot 4H_2O$ were investigated as sources for metal cations. The NMR spectra were obtained on an Oxford AS400 operating at 400 MHz and 100 MHz, for ^1H and ^{13}C, respectively. The measurements were carried out in a $CDCl_3$ solution at ambient temperature. The chemical shifts were referenced to a tetramethylsilane (TMS) standard. Thin layer chromatographic (TLC) analysis of the dyes was followed on silica gel (Fluka F_{60} 254 20x20; 0.2 mm) using the solvent system n-heptane/acetone (1:1) as an eluent.

In vitro antimicrobial activity assay

The synthesized complex was investigated for antibiotic activity *in vitro* against nine pathogenic indicator cultures using conventional well/disc diffusion assay. The following indicator microorganisms were used: Gram-positive bacteria *Bacillus subtilis*, *Bacillus cereus*, *Sarcina lutea* and *Micrococcus luteus*, Gram-negative bacteria *Pseudomonas aeruginosa*, *Escherichia coli*, *Acinetobacter johnsonii* and *Xanthomonas oryzae*, and yeast strain *Candida lipolytica*. Tetracycline (30 µg/disc, 6 mm in diameter) was used as positive control for comparison. The synthesized complex was dissolved in 5% DMSO to obtain a 0.5% stock solution. Exponentially grown cultures were smeared onto sterile nutrient agar medium in each

Petri plate. Wells (6 mm in diameter) were punched in the agar medium, to which 10, 30 and 50 µl of the stock solution were added. Three replicates were maintained for each treatment. The plates were incubated 24 h at 28 ± 2°C, and the size of the resulting zone of inhibition, if any, was determined.

Synthesis of 4-bromo-N-buthyl-1,8-naphthalimide

A ethanol solution (10 ml) of buthylamine (0.8 ml, 0.01 mol) was added drop wise over 3 hours to 4-bromo-naphthalic anhydride ethanol solution at vigorously stirring (50 ml solution of 2.88 g, 0.01 mol) at 75 ºC. After cooling the precipitate was filtered, washed with water, and then dried in vacuum at 40^0C. Yield: 89 %

FT-IR, cm^{-1}: 2951, 2823, 2770, 1692, 1651, 1595, 1350, 1261, 1232, 1085, 1029, 781.

^{1}H NMR ($CDCl_3$, δ, ppm): 8.63 (d, J=7.07 Hz, 1H-Ar), 8.53 (d, J=8.47 Hz, 1H-Ar), 8.39 (d, J=7.55 Hz, 1H-Ar), 8.01 (d, J=7.36, 6.1 Hz, 1H-Ar), 7.82 (t, J=7.18 Hz, 1H-Ar), 4.15 (t, J=7.18 Hz, 2H), 1.69 (m, 2H) 1.43 (q, 2H), 0.98 (t, J=6.48, Hz, 3H)

^{13}C NMR ($CDCl_3$, δ, ppm):164.3, 133.9, 132.7, 131.9, 131.7, 130.8, 129.6, 128.7, 123.7, 123.0, 41.0, 30.8, 21.0, 14.5.

Analysis: $C_{16}H_{14}NO_2Br$ (332.1 g mol^{-1}) Calculated (%): C 57.83, H 4.21, N 4.21; Found (%): C 57.79, H 4.27, N 4.18

Synthesis of 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide (NI)

A solution of (3.32 g, 0.01 mol) of 4-bromo-*N*-buthyl-1,8-naphthalimide and 2-(*N,N'*-dimethylamino)ethanol (1.0, 0.01 mol) in 20 ml *N,N*-dimethylformamide was stirred at 50^0C in the presence of 0.01 mol KOH for 3 hours. The process was controlled by thin-layer chromatography and the final product was filtered off with very high yield and purity after pouring the liquor into water. The resulting precipitate was washed with water, and then dried in vacuum at 40^0C. Yield: 82 %

FT-IR, cm^{-1}: 3071, 2958, 1692, 1650, 1595, 1457, 1350, 1159, 1030, 781.

^{1}H NMR ($CDCl_3$, δ, ppm): 8.53 (m, 3H-Ar), 7.61 (dd, J=7.5, 6.1 Hz, 1H-Ar), 6.94 (d, J=7.99 Hz, 1H-Ar), 4.34 (t, 2H,), 4.16 (t, J=6.8 Hz, 2H), 2.93 (t, 2H), 2.43 (s, 6H), 1.71 (m, 2H) 1.45 (q, 2H), 0.99 (t, J=6.83 Hz, 3H).

^{13}C NMR ($CDCl_3$, δ, ppm): 164.8, 164.2, 160.3, 133.6, 131.8, 129.6, 129.,126.2, 113.8, 122.7, 115.4, 106.2, 68.0,58.5, 46.6, 40.5, 30.7, 20.9, 14.4.

Analysis: $C_{20}H_{24}N_2O_3$ (340.05 g mol^{-1}) Calculated (%): C 70.58, H 7.06, N 8.23; Found (%): C 70.39, H 7.10, N 8.16

Scheme 1. Chemical structure of 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide (NI)

Synthesis of [Cu(NI)(Cl)$_2$] complex

Coper complexes of NI were prepared by mixing of NI and CuCl2•2H2O in a molar ratio of 1:2 in ethanol solution and the reaction mixture was refluxed for 3h.The completion of the reaction was monitored by thin layer chromatography. After cooling to room temperature the solid complexes formed were filtered, washed with ethanol (10 ml, 3 times) and finally dried under vacuum.

FT-IR, cm^{-1}: 3076, 2957, 1695, 1649, 1593, 1352, 1155, 1234, 777, 752,

^{1}H NMR ($CDCl_3$, δ, ppm): 8.71 (brs, 1H-Ar), 8.46 (bs, 2H-Ar), 7.81 (brs, 1H-Ar), 7.40 (brs, 1H-Ar), 4.64 (bs, 2H,), 4.00 (t, J=7.1 Hz, 2H), 2.93 (t, J=7.6 2H), 2.50 (s, 6H), 1.57 (t, 2H) 1.31 (q, 2H), 0.89 (t, J=6.9 Hz, 3H).

^{13}C NMR ($CDCl_3$, δ, ppm): 164.0, 163.3, 146.3, 133.6, 131.6, 129.4, 129.0,126.5, 123.3, 122.3, 115.0, 107.8, 63.5, 58.3, 46.8, 40.3, 30.2, 20.7, 14.4.

Analysis: $C_{20}H_{24}N_2O_3CuCl_2$ (469.08 g mol^{-1}) Calculated (%): C 51.17, H 5.12, N 5.97; Found (%): C 51.26, H 5.04, N 5.89

Results and discussion

Photophysical characteristics of NI

Table 1 presents the spectral characteristics of 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide (NI) under study in DMF, ethanol and acetonitrile solution: absorption (λ_A) and fluorescence (λ_F) maxima, the extinction coefficient (ε), Stokes shift (ν_A - ν_F), and quantum fluorescence yield (Φ_F).

Table 1

As seen from the data in Table 1, the NI absorb in the near UV region with maxima at λ_A=365-367 nm. The respective fluorescence maxima are at 427-433 nm. The molar extinction coefficient (ε) is at 14900-16200 l mol^{-1} cm^{-1}, corresponding to a $S_0 \rightarrow S_1$ transition.

The polarity of the organic solvents is of great importance for the photophysical properties of NI under study and especially for the quantum fluorescence yield and Stokes shift. The Stokes shift is a parameter, which indicates the difference in the properties and structure of the fluorophore between the ground state S_0, and the first exited state S_1. The Stokes shift has been calculated by the equation 1.

$$(\nu_A - \nu_F) = (1/\lambda_A - 1/\lambda_F) \times 10^7 \text{ cm}^{-1}, \qquad (1)$$

The obtained Stokes shift values are in the 4155-4439 cm^{-1} region. It is seen that the polarity of the environment do not influence on the Stokes shift values (Table 1) which is in a good accordance with other our investigations on 1,8-naphthalimide derivatives [32,33]. The ability of the NI molecules to emit absorbed light energy is characterized quantitatively by the quantum yield of fluorescence Φ_F. The fluorescence quantum yield has been calculated on the basis of the absorption and fluorescence spectra using antracene as reference (Φ_{st} = 0.26) according to equation 2.

$$\Phi_F = \Phi_{st} \frac{S_u}{S_{st}} \frac{A_{st}}{A_u} \frac{n_{Du}^2}{n_{Dst}^2} \qquad (2)$$

where the Φ_F is the emission quantum yield of the sample, Φ_{st} is the emission quantum yield of the standard, A_{st} and A_u represent the absorbance of the standard and sample at the excited wavelength, respectively, while S_{st} and S_u are the integrated emission band areas of the standard and sample, respectively, and n_{st} and n_u is the solvent refractive index of the standard and sample, subscripts *u* and *s* refer to the unknown and standard, respectively. As seen from Table 1, in acetonitrile and DMF solutions the quantum yield is low, $\Phi_F = 0.007\text{-}0.009$, while in ethanol solutions the respective quantum yield is two times higher, but retains the low value. This fact can be explained by the photoinduced electron transfer (PET) process which is favored in polar solvents and the fluorescence emission is lower [34].

Influence of metal cations on the fluorescence intensity of NI

The fluorescent intensity of NI as a ligand in the presence of different metal cations (Pb^{2+} Cu^{2+} , Cd^{2+}, Co^{2+}, $Zn^{2+}$and Mn^{2+}) has been investigated in acetonitrile solution. This particular solvent has been chosen for all the spectral measurements since it has a low quantum florescent yield and favours the PET fluorescence switch. On the other hand, acetonitrile guaranties a good solubility of the used metal salts, ligand and the respective complexes.

The presence of metal cations in the solution the NI acts as a ligand during the interaction between the components which is signalled by the changes in the fluorescence intensity. These changes depend on the electronic configuration of the metal cation used.

The influence of the metal cations on the fluorescence enhancement (*FE*) as a qualitative parameter is presented in Figure 1. The $FE = I/Io$ has been determined from the ratio of maximum fluorescence intensity *I* (after addition of metal cations) and minimum fluorescence intensity *Io* (before metal cations addition).

Some of the metal cations (Cd^{2+}, $Co^{3+}$and Mn^{2+}) induce a negligible enhancement of the fluorescence intensity. Probably in the case the complex formed is instable. On the other hand, metal cations as Pb^{2+}, $Cu^{3+}$and Zn^{2+} enhance the fluorescence intensity. The highest values have been observed in the presence of Cu^{2+} cations ($FE = 51.5$).

Figure 1

Figure 2 plots as an example the changes in the fluorescent intensity of the NI ($c = 1x10^{-5}$mol l^{-1}) in acetonitrile solutions as a function of the concentration of Cu^{2+} cations. Free of metal cations NI has a very weak fluorescence emission. A pronounced increase in the fluorescence intensity has been observed by increasing the concentration of Cu^{2+} cations up to $2.0x10^{-4}$ mol l^{-1} (Figure 2). Above this concentration the change in the fluorescence intensity is negligible. The fluorescence titration profile shows that a linear curve appears (R=0.99865) in the $0.5x10^{-5}$ – $10x10^{-5}$ mol l^{-1} concentration range of Cu^{2+} cations (Inset to Figure 2). A detection limit of 0.05 $x10^{-5}$ mol l^{-1} for Cu^{2+} has been determined. Such a linear curve and a detection limit are sufficient enough to sense and determined Cu^{2+} ions.

Figure 2.

The fluorescence characteristics obtained for NI in acetonitrile solution in the presence of metal cations under study are collected in Table 2. It is seen that during the complexation the position of the fluorescence maximum does not change significantly. The Pb^{2+}, $Cu^{3+}$and Zn^{2+} metal cations induce a small hypsochromic shift in the fluorescence maxima ($\Delta\lambda_F$ = 3-4) indicating a possible interaction between NI and the metal cations [32,33]. On the other hand, the fluorescence quantum yield is improved from $\cdot_F = 0.007$ to $\cdot_F = 0.347$ when Cu^{2+} cations are added. The respective increase in the fluorescence depends on the nature of the metal cations used. We suppose the higher quantum yield in the case to be on account of the better coordination ability of Cu^{2+} cations as well as because of the stabilized coplanar system of the complex formed.

Table 2.

Effect of protons on the NI fluorescence intensity

Figure 3 presents the pH dependence of NI fluorescence intensity in an ethanol/water solution (1:4). As seen, the fluorescence intensity depends strongly on pH values in the 3.5-11.0 pH region. The results show that the protonation of the tertiary amino group from 2-dimethylaminoethyloxy substituent at C-4 position increases the florescence intensity, which demonstrates the high sensitivity to proton concentration. As Figure 3 reveals, the constant value of the fluorescence intensity which is observed up to pH = 7.5 decreases strongly and at values higher than pH 9.6 the curve forms again a plateau of a weak fluorescence. A 15 fold fluorescence quenching is observed from the acidic and neutral medium to the basic pH = 10.2.

The pH dependence of the fluorescence intensity has been analyzed using equation (3).

$$pH\text{-}pKa = \log(I_{Fmax}\text{-}I_F)/(I_F\text{-}I_{Fmin}) \quad (3)$$

The calculated value pKa = 8.32. This value is similar to that of the other 1,8-naphthalimide with the same receptor fragment in the fluorophores structure (pKa = 8.40) [32]. Both values are higher, if compared to those of the bis-4-(2-dimethylaminoethyl oxy)-1,8-naphthalimide whose pKa = 7.61 [35].

Figure 3.

The change in the fluorescent spectra of NI in the pH range of 5 ÷ 10.2 is shown in Figure 4. Enhancement of the fluorescence emission was observed in an acidic environment when compared with that at pH = 10.2. It is also seen a slightly hypochromic shift of the fluorescence maximum with 6 nm during the transition from an alkaline to an acidic media.

Figure 4.

Preparation of [Cu(NI)(Cl)$_2$] complex

A copper complex of NI is obtained by mixing with copper chloride in an ethanol solution and the reaction system was refluxed for 3 hours. Thus obtained copper complex was studied by NMR, FTIR, UV-Vis and fluorescent spectroscopy and elemental analysis. The results of elemental analysis showed that the complex was prepared in a 1:1 stoichiometry. FTIR spectral characteristics of NI as a ligand and its cuprum complex are presented in Table 3 and Figure 5. The FT-IR stretching frequencies of free ligand were compared with that of [Cu(NI)Cl$_2$].

Table 3.

Symmetrical and asymmetrical oscillations of C = O band are at 1649-1650 cm^{-1} and at 1692-1695 cm^{-1}, respectively, which values are common for other 1,8-naphtjhalimide derivatives with an alkoxy substituent at C-4 position of the 1,8-naphthalimide structure [36]. The comparison of those data with the data obtained for [Cu(NI)Cl$_2$] show a slight change in the positions of the characteristic bands though there is only a change in the intensity of the bands in this region, indicating non-participation of the coordination of C=O with cuprum ions (Figure 5A). The results show that the polarity of both 1,8-naphthalimide chromophoric systems are different. The absorption bands in the 1350-1352 cm^{-1} region are characteristic for the imide (C-N-C) bonds in the 1,8-naphthalimide structure. The infrared frequencies at 1159-1232cm^{-1} are assigned to C-N bonds. The characteristic vibrations of C-O-C bond for the free NI are at 1030 cm^{-1} and 1233 cm^{-1}. In the spectrum of the [Cu(NI)Cl$_2$], a decrease of the band intensity at 1233 has been observed as well as a disappearance of the band at 1030 cm^{-1} (Figure 5B). This result indicates that the ether oxygen atom participates in the formation of a complex with the copper ions. The suggested structure of [Cu(NI)Cl$_2$] complex is presented in Scheme 2.

Figure 5.

Scheme 2.

Absorption and fluorescence spectra of NI and its [Cu(NI)Cl$_2$] complex was recorded in acetonitrile solution with concentration c = 10^{-5} mol l^{-1} at room temperature. As seen from Figure 6A plotting both spectra, the absorption maximum of the cuprum complex is shifted hypsochromicaly with 8 nm. But more interesting fact has been observed in the visible spectral region, where it occurs with a small peak with maximum at 464 nm. Probably this insignificant absorption in the visible region is due to the complex formed and the change the polarization of the 1,8-naphthalimide chromophoric system. The formation of the complex causes the enhancement of the fluorescence intensity, without any change of the position of fluorescence peak (Figure 6B).

Figure 6.

Antibiotic activity

The synthesized [Cu(NI)Cl$_2$] complex has been investigated *in vitro* for its antibiotic activity against eight bacterial and one yeast culture. The complex inhibited the growth of all tested indicator cultures; applied in 30 and 50 µl, it showed good or better zones of inhibition against most indicator cultures compared with standard (Figure 7). The highest inhibition activity was observed against *X. oryzae* and *A. johnsonii* (zones 40 and 38 mm in diameter, respectively), followed by *P. aeruginosa*, *B. subtilis*, *B. cereus* and *S. lutea* (zones in the range 29 - 30 mm) (Figure 8). The lowest inhibitory activity of the compound has been observed against *E. coli* (inhibition zone 17 mm). The complex showed good inhibition zone against yeasts *C. lipolytica* (inhibition zone 25 mm). Therefore, the newly synthesized complex could be used in designing new effective antimicrobial preparations. The antibiotic activity of the complex against phytopathogenic *X. oryzae* opens a perspective for future application in the agriculture for plant protection.

Figure 7.

Figure 8.

Conclusions

In this paper we described the synthesis and characterization of a new 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide. Its photophysical properties have been investigated in three organic solvents. The dependence of the fluorescence intensity on the presence of different metal cations (Pb^{2+}, Cu^{2+}, Cd^{2+}, Co^{2+}, $Zn^{2+}$and Mn^{2+}) and protons has been investigated in an acetonitrile solution. The results showed that the new 1,8-naphthahlimide can detect metal cations in the concentration range from $0.5x10^{-5}$ – $10x10^{-5}$ mol l^{-1}. The detection is realized via the quenching of photoinduced electron transfer processes occurring in the chromiphore system. A cuprum complex of 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide has been synthesized and characterized. The synthesized [Cu(NI)Cl_2] complex has been investigated *in vitro* for antibiotic activity against eight bacterial and one yeast cultures. The complex demonstrated inhibitory activity against all indicator cultures producing the best effect against *X. oryzae* and *A. johnsonii*.

Acknowledgement

This paper was funded by the Deanship of Scientific Research (DSR), King Abdulaziz University, under grant No. 17-130-35-HiCi. The authors, therefore, acknowledge with thanks DSR technical and financial support.

References

1. Metal Ions in Biological Systems: Volume 41: Metal Ions and Their Complexes in Medication, 2004, 600, Eds. A Sigel, H. Sigel. Marcel Dekker INC, ISBN: 0-8247-5351-8
2. J. Anastassopoulou, T. Theophanides, Bioinorganic chemistry, 459 (1995) 209-218.
3. J.P. Glusker, A.K. Katz, Ch.W. Mock, The Rigaku Journal, 16 (1999) 8-18.
4. T.A. Yousef, G.M. Abu El-Reash, O.A. El-Gammal, R.A. Bedier, Journal of Molecular Structure, 1029(2012) 149-160
5. R. Johari, G. Kumar, D. Kumar, S. Singh, J. Ind. Council Chem. 26 (2009) 23-27
6. N. Shashidhar Reddy, B. S. Shankara, P. Murali Krishana, C. Basavaraj, B. Mahesh, International Journal of Inorganic Chemistry ,2013 (2013), Article ID 614628, 10 pages
7. M. Shakir, S. Khanam, F. Firdaus, A. Latif, M. Aatif, S.I. Al-Resayes, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 93 (2012) 354–362
8. A.-N. M.A. Alaghaz, Journal of Molecular Structure, 1068, (2014) 27-42
9. M. B. Halli, R.B. Sumathi, Journal of Molecular Structure, Volume 1022 (2012) 130-138
10. K.-I. Nakaya, K. Funabiki, H. Muramatsu, K. Shabata, M. Matsui, M. Dyes Pigm. 43 (1999) 235−239.
11. K. Kawai, K. Kawabata, S. Tojo, T. Majima, Bioorg. Med. Chem. Lett. 12 (2002) 2363−2366.
12. B. Ramachandram, G. Saroja, N.B. Sankaran, A. Samanta, J. Phys. Chem. B 104 (2000) 11824−11832.
13. S. K. Das, P.K. Sahu, U.P. Kar, A. Rahaman, M. Sarkar, M. Soni J. Phys. Chem. C 117 (2013) 14338−1434.
14. X. Huang, Y. Fang, X. Li, Y. Xie, W. Zhu, Dyes Pigm. 90 (2011) 297−303.
15. V. Mohan, A. Nijamudheen, S.K. Das, P.K. Sahu, U.P. Kar, A. Rahaman, M. Sarkar, ChemPhysChem 13 (2012) 3882− 3892.
16. J. Wang, L. Yang, C. Hou, H. Cao, Org. Biomol. Chem. 10 (2012) 6271−6274.
17. P. Alaei, S. Rouhani, K. Gharanjig, J. Ghasemi, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 90 (2012) 85−92.
18. T. Gunnlaugsson, P. Kruger, P. Jensen, F. Pfeffer, G. Hussey, Tetrahedron Letters 44 (2003) 8909−8913.
19. S. Stoyanov, P. Petrov, M. Stoyanova, M. Dangalov, B. Shivachev, R. Nikolova, I. Petkov, J. Photochem. Photobiol. A: Chem. 250 (2012) 92−98.
20. K. Rurack, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 57 (2001) 2161−2195.
21. V. Bojinov, N. Georgiev, Journal of the University of Chemical Technology and Metallurgy 46 (2011) 3−26.
22. A.P. de Silva, N.Q.N. Gunaratne, Y. Gunnlaugsson, A.J.M. Huxley, C.P. McCoy, J.T. Radmancher, T.E. Rice, Chem. Rev. 97, (1997) 1515−1566.
23. L. Yin, C. He, C. Huang, W. Zhu, X. Wang, Y. Xu, X. Qian, Chem. Commun. 48 (2012) 4486–4488.
24. T.C. Chanh, B.J. Archer, R.E. Utecht, D.E. Lewis, M.M. Judy, J.L. Matthews, Biomed. Chem. Lett. 3 (1993) 555−558.

25. T.C. Chanh, D.E. Lewis, M.M. Judy, B.F. Sogandares, G.R. Michalek, R.E. Utecht, H. Skiles, S.C. Chanh, J.L. Matthews, Anti Viral Res. 25 (1994) 133−146.
26. R.C. de Souza, V. Chechinel Filho, I. Grabchev, V. Bojinov, Pharmazie 56 (2002) 430−431.
27. M. Verma, V. Luxami, K. Paul, European Journal of Medicinal Chemistry 68 (2013) 352−360.
28. S. Banerjee, J. A. Kitchen, T. Gunnlaugsson, J. M. Kelly, Org. Biomol. Chem. 10 (2012) 3033–3043.
29. S. Tan, H. Yin, Zhuo Chen, X. Qian, Y. Xu, European Journal of Medicinal Chemistry 62 (2013) 130−138.
30. D.E. Eaton, Pure Appl. Chem. 60 (1988) 1107−1114.
31. B. Ramachamdram, N.B. Sankaran, R. Karmakar, S. Saha, A. Samanta, Tetrahedron 56 (2000) 7041−7044.
32. S. Sali, S. Guittonneau, I. Grabchev, Polymers for Advanced Technology 17 (2006) 180−185.
33. I. Grabchev, J.-M. Chovelon, Dyes and Pigments 77 (2008) 1−6.
34. X. Poteau, A.I. Brown, R.G. Brown, C. Holmes, D. Matthew, Dyes and Pigments 47 (2000) 91−105.
35. S. Yordanova, S. Stoyanov, I. Grabchev, I. Petkov, Hindawi Pub. Corp., 2013, Article ID 628946,
36. I. Grabchev, Ch. Petkov, V. Bojinov, Chem. Engin. 287 (2002) 904−908.

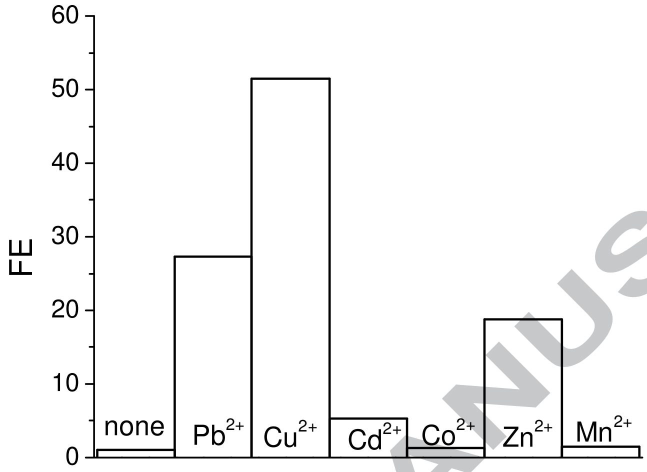


Figure 1. Fluorescence enhancement factor (*FE*) of NI (c = $1x10^{-5}$ mol l^{-1}) in the presence of different metal cations (c = 1 x 10^{-4} mol l^{-1}) in acetonitrile solutions.

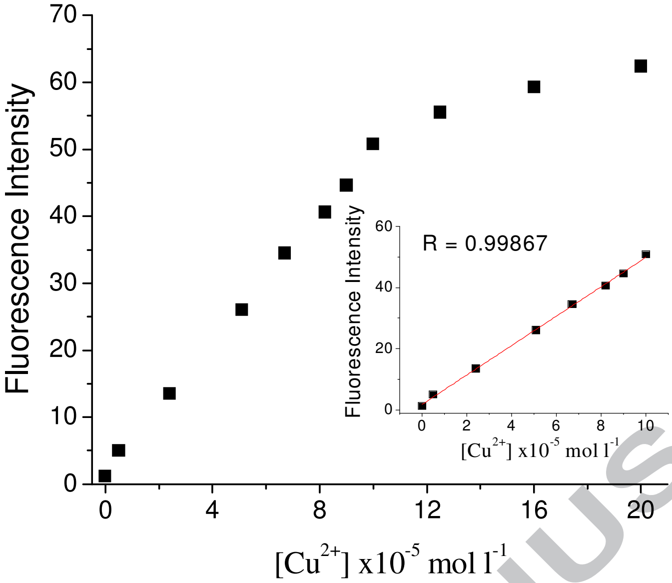


Figure 2. Variation of the fluorescence intensity of NI (c = 1x10^{-5} mol l^{-1}) as a function of cuprum cation concentrations. The insert shows the linear curve fluorescence intensity and Cu^{2+} cation concentrations.

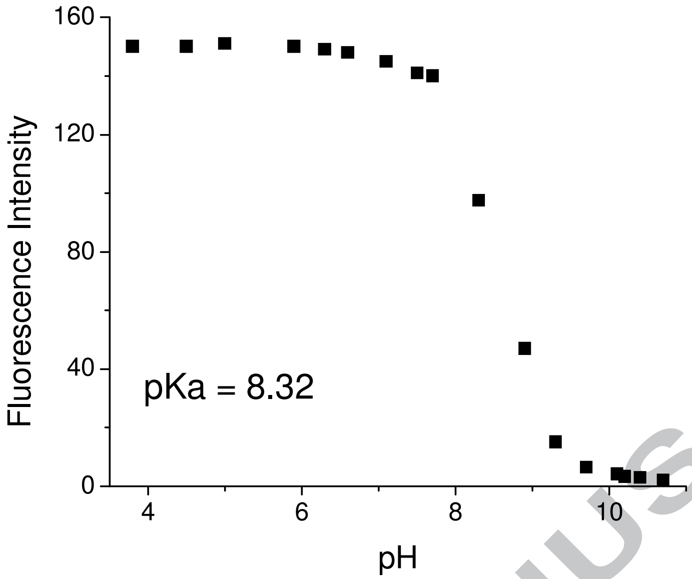


Figure 3. The influence of pH upon the fluorescence intensity of NI in ethanol-water solution (1:4, v/v)

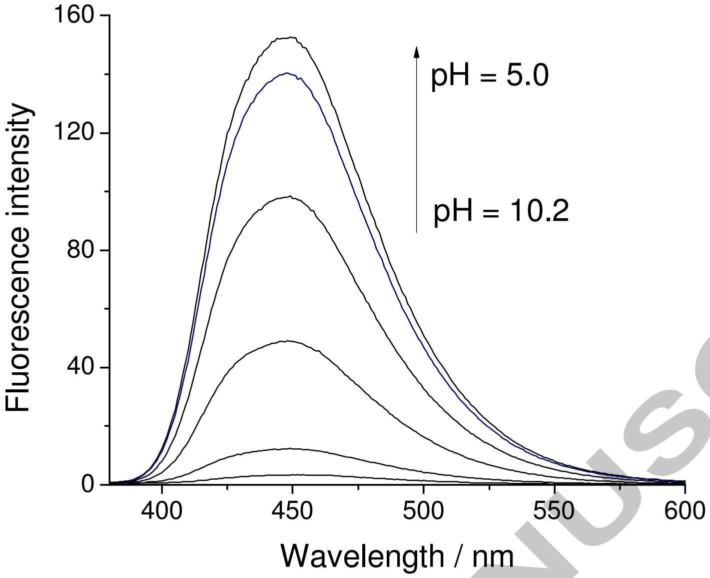


Figure 4. Fluorescence spectra of NI in ethanol-water solution (1:4, v/v) at different pH values

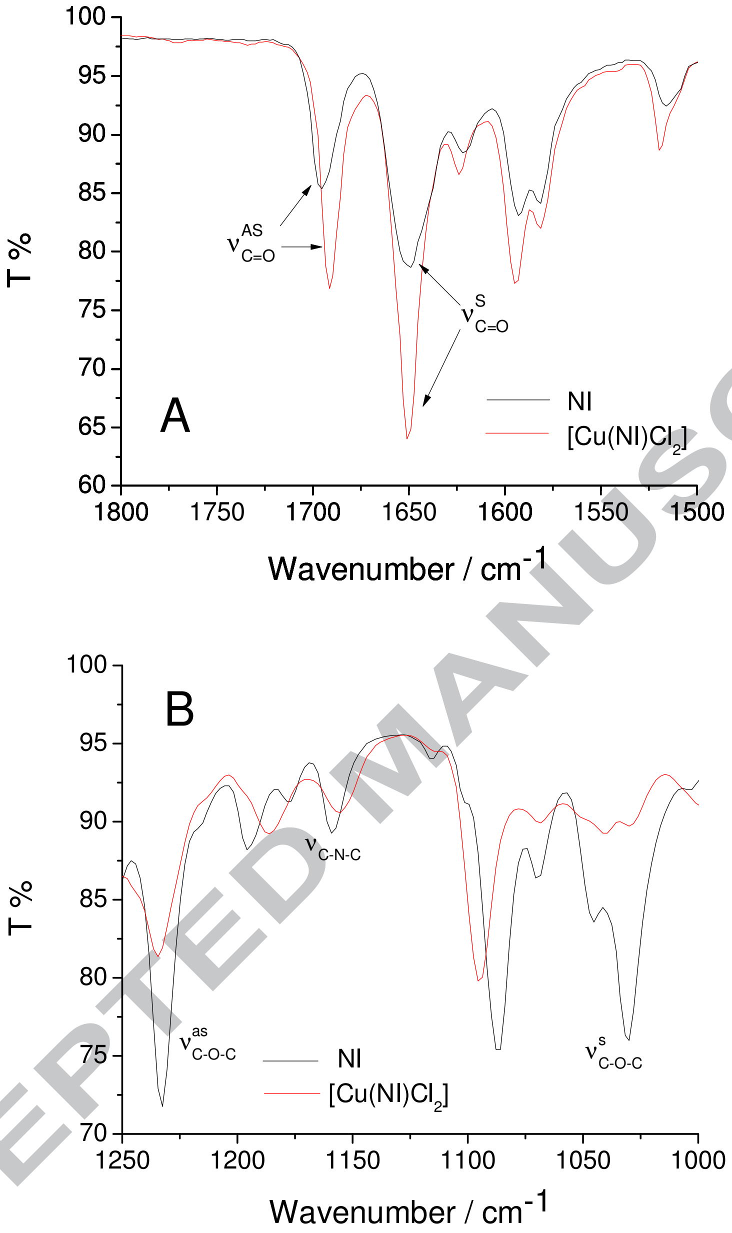


Figure 5. Infrared spectra of solid NI and $[Cu(NI)Cl_2]$

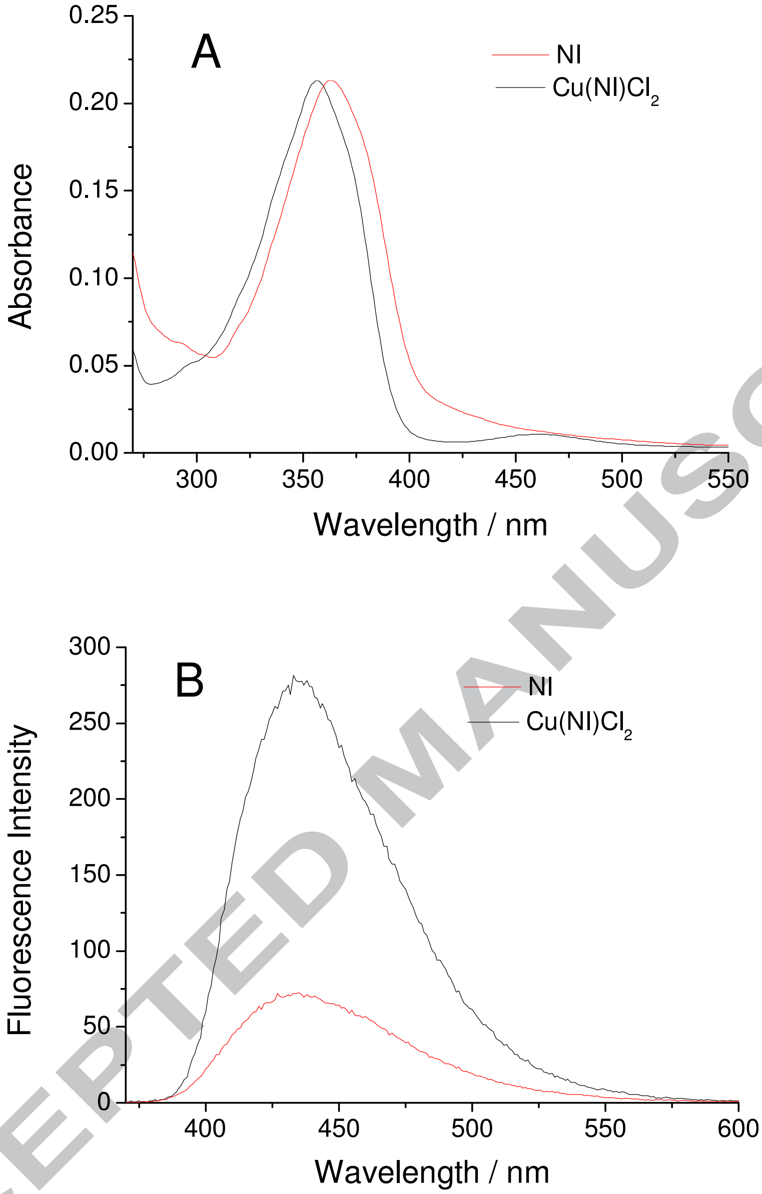


Figure 6. Absorption (A) and Fluorescence (B) spectra of NI and [Cu(NI)Cl$_2$] in acetonitrile solution.

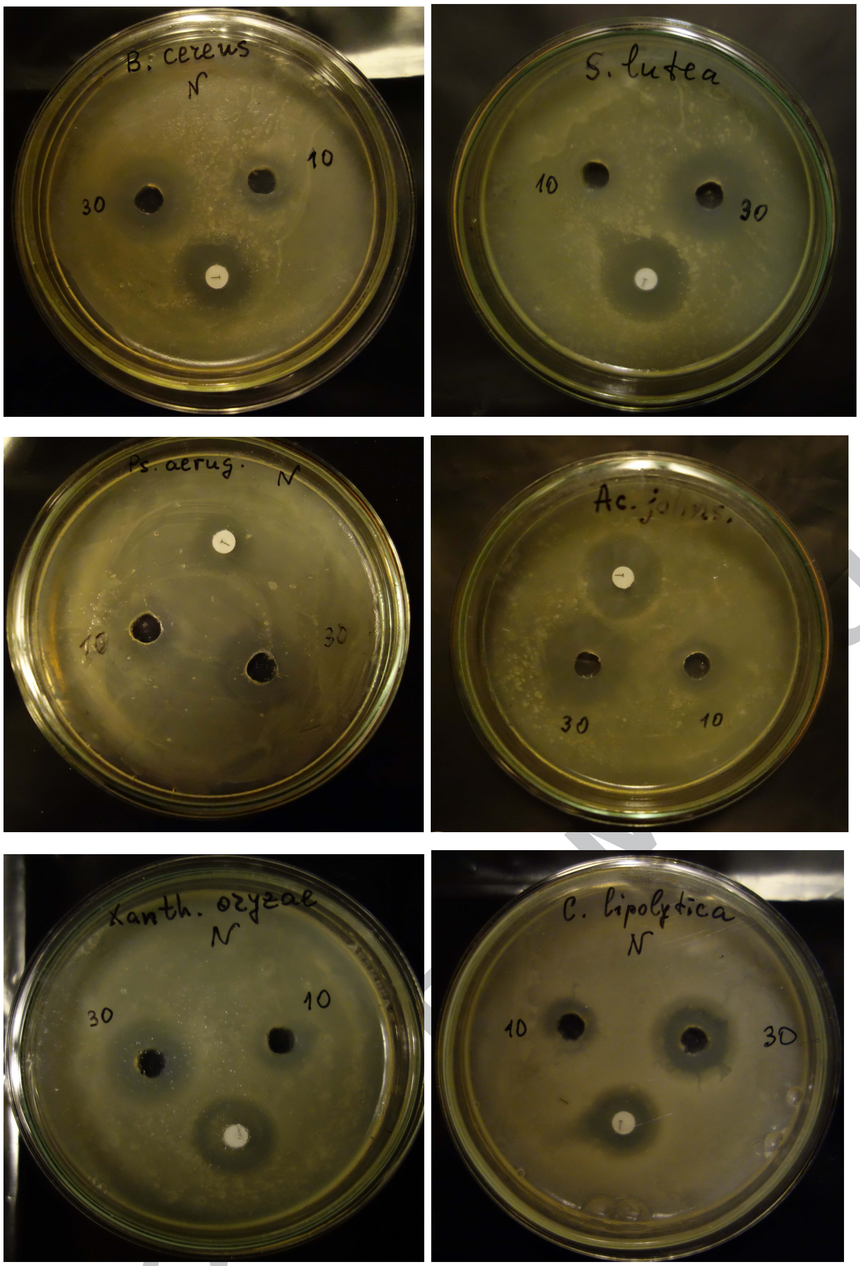


Figure 7. Growth inhibition of some of the tested indicator cultures by the synthesized complex (10 and 30 µL). T, Tetracycline (30 µg/disc)

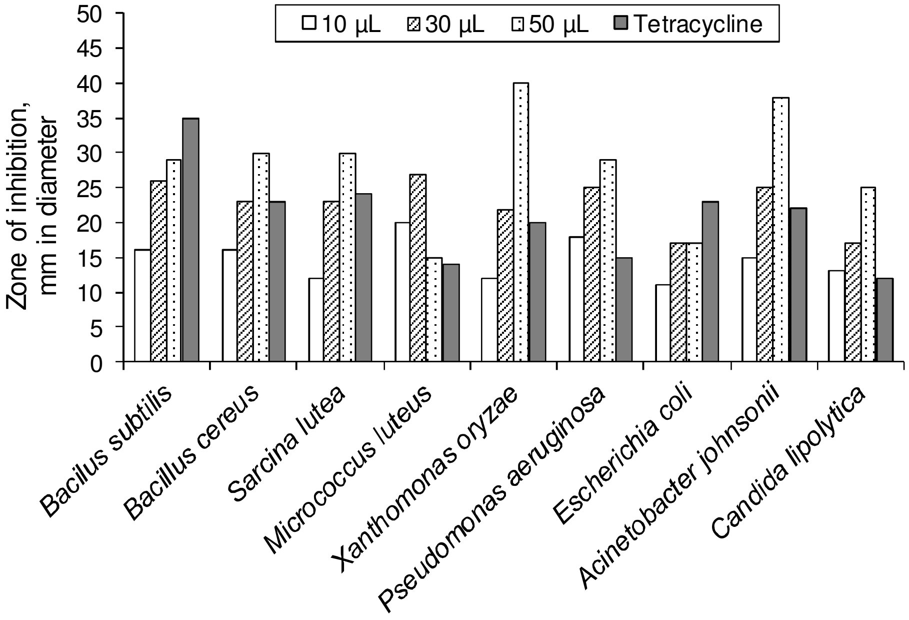
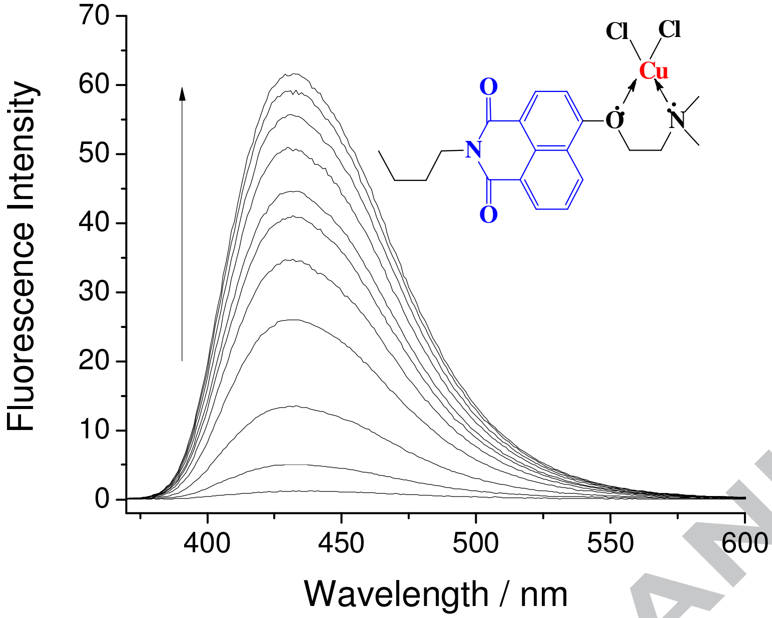


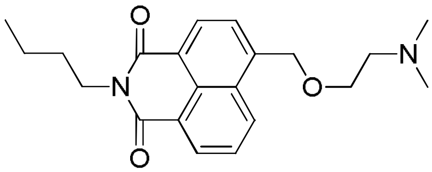
Figure 8. Zones of inhibition of the tested indicator cultures caused by the [Cu(NI)Cl_2] complex

Graphical abstract

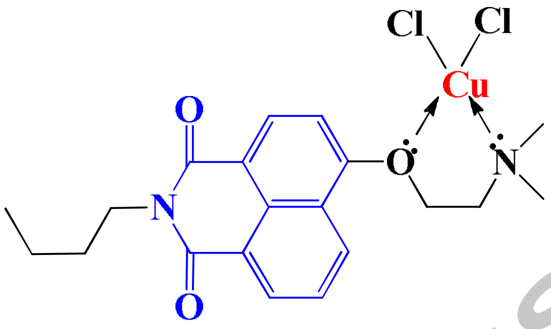


Highlights

- The synthesis and functional properties of a blue fluorescent 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide as sensor for metal ions and protons have been described.
- A cuprum complex of 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide has been synthesized and characterized.
- The antibacterial activity of [Cu(NI)Cl_2] complex demonstrated inhibitory activity against all indicator cultures producing the best effect against *X. oryzae* and *A. johnsonii*.



Scheme 1. Chemical structure of 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide (NI)



Scheme 2. Suggested structure of [Cu(NI)Cl_2] complex

Table 1. Photophysical characteristics of NI in organic solvents with different polarity

Organic solution	λ_A nm	ε l mol $^{-1}$ cm^{-1}	λ_F nm	ν_A - ν_F cm^{-1}	Φ_F
Acetonitrile	364	15300	434	4355	0.007
DMF	367	16200	433	4153	0.009
Ethanol	366	14900	437	4439	0.018

Table 2. Fluorescence characteristics of NI in acetonitrile in the presence of metal cations

Metal cations	λ_F / nm	$\Delta\lambda_F$ / nm	Φ_F
free	434	-	0.007
Zn^{2+}	432	2	0.133
Pb^{2+}	431	3	0.189
Cu^{2+}	430	4	0.347
Mn^{3+}	433	3	0.035
Ni^{2}	434	0	0.008
Co^{2+}	434	0	0.008
Cd^{2+}	432	2	0.035

Table 3. Infrared spectra of 4-(2-dimethylaminoethyloxy)-N-buthyl-1,8-naphthalimide and its complex [Cu(NI)Cl_2]

	NI	[Cu(NI)Cl_2]
$\nu_{C\text{-}H}$ arom	3071	3076
ν_{CH2} aliph	2958 2874	2957 2733
$\nu^{AS}_{C=O}$	1692	1695
$\nu^{S}_{C=O}$	1650	1649
$\nu_{C=C}$ arom	1624 1595	1593
ν_{CH2} aliph	1457	1458
ν_{COC}	1233 1030	1234 1029
ν_{CNC}	1350 1159	1352 1155
$\delta_{C\text{-}H}$ arom	874 781	840 777 752