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Synthesis, spectroscopic characterization and structural investigation of a new charge transfer complex of 2,6-diaminopyridine with 4-nitrophenylacetic acid: Antimicrobial, DNA binding/cleavage and antioxidant studies

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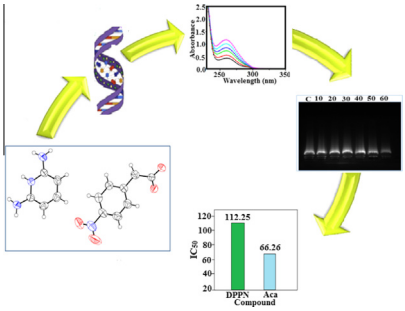
HIGHLIGHTS

- Molecular structure of the complex was confirmed by single crystal X-ray diffraction technique.
- The complex possesses a significant antimicrobial activity against a panel of microbes.
- The complex interacts with CT-DNA, *via* intercalatively.
- The complex can efficiently cleave CT-DNA *via* oxidative cleavage.
- The complex possesses valuable antioxidant property against DPPH radical.

GRAPHICAL ABSTRACT

The organic charge transfer complex was synthesised and characterized by UV–Vis, FT-IR, NMR spectroscopic techniques and thermal analysis. The CT complex was screened for its antibacterial and antifungal activity against various bacterial and fungal species, which shows good antimicrobial activity. The DNA binding results indicated that the compound could interact with DNA through intercalation. It should have weak to moderate capacity of scavenging with DPPH.



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ABSTRACT

A new hydrogen-bonded charge-transfer complex (CT) formed by the reaction between donor, 2,6-diaminopyridine and acceptor, 4-nitrophenylacetic acid in methanol at room temperature. The crystal was characterized by elemental analysis, IR, NMR spectroscopic studies and thermal studies. The elemental analysis of CT complex, obtained data revealed that the formation of 1:1 ratio CT complex was proposed. Infrared and NMR studies confirm the chemical constituents and molecular structure of the synthesized complex crystal. The high thermal stability is due to the molecular frame work through H-bonding interactions. Structural investigation indicates that cation and anion are linked through strong N^{+}–H···O^{-} type of hydrogen bond. The hydrogen bonded charge transfer crystal was screened for its pharmacology, such as antimicrobial, DNA binding/cleavage and antioxidant studies. The CT complex was screened for its antibacterial and antifungal activity against various bacterial and fungal species, which shows good antimicrobial activity. The DNA binding results indicated that the compound could interact with DNA through intercalation. It should have weak to moderate capacity of scavenging with DPPH.

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Introduction

There is a great interest in the synthesize of new organic charge transfer crystal with effective biological activity, due to their potential applications in biological systems, such as antimicrobial activity and DNA binding as well as in laser technology, optoelectronics, optical communications, photo catalysis and optical signal processing [1–8]. The charge transfer reactions of certain π acceptor have been successfully utilized in pharmaceutical analysis [9–12]. Hence CT complexes promoted extensive studies on them [13–15]. The charge transfer complexes formed in the reaction of electron acceptors with donors containing nitrogen, sulfur, oxygen atoms have attracted considerable attention and growing importance in recent years [16–20]. The charge transfer complexes lead a versatile role in the quantitative estimation of drugs. Charge-transfer complexes of organic species are intensively studied because of their special type of interaction, which is accompanied by transfer of an electron from the donor to acceptor. Some researchers have studied the CT interactions between the drugs and various acceptors to throw light on the role of weak interactions in understanding drug–receptor mechanism. Moreover, DNA is one of the most important aspects in biological investigations and aimed for discovering and developing new type of antiproliferative agents [21] because DNA is one of the main molecular targets in the design of anticancer compounds [22].

Aminopyridines are bioactive N-heterocyclic amines, which increase the strength of the nerve signal by blocking of the voltagedependent K^+ channel [23,24]. Also, aminopyridines have been proposed as drugs for the treatment of many diseases such as myocardial infarction as antithrombus agents and diarrhea as antimicrobial agents [25–27]. Moreover, aminopyridines are commonly present in synthetic and natural products [28]. They form repeated moiety in many large molecules with interesting photophysical, electrochemical and catalytic applications [29].

Nowadays, it is important to engage with pharmaceutical development scientists when identifying new solid forms of a particular drug. Early detection of alternative solid forms such as polymorphs, hydrates, solvates, salts, co-crystals and amorphs can lead to significant benefits throughout the various stages of drug development. The compactibility of a final drug form is also important to consider for tableting purposes. Ideally, an improvement in these physical properties would assist potential new drug candidates in reaching the market sooner.

Researchers have worked on proton transfer complex of 2,6-diaminopyridine with series of nitro substituted aromatic carboxylic acids and 2,4,6-trinitrobenzoic acid were also reported and studied their crystal structures. On the background of these findings, we describe in the present article, we report the formation of newly hydrogen bonded charge transfer (CT) complex due to the proton-transfer interaction between 2,6-diaminopyridine and 4-nitrophenylacetic acid. DNA-binding studies of complex is one of the most important aspects in biological investigations were researched by electronic absorption spectroscopy and cleavage properties of the complex performed by gel electrophoresis with CT-DNA. Finally, we have studied their antioxidative property against DPPH radical. The complex has been synthesized and characterized by elemental analysis, IR, ^{1}H and ^{13}C NMR and its crystal structure has been deduced by Single-crystal X-ray studies.

Experimental details

Materials and instrumentation

All chemicals were purchased from Sigma–Aldrich in the highest purity available. Solvents were purified and dried according to the standard procedure [30]. Elemental analysis (C, H and N) were performed on a Perkin Elmer 240C elemental analyser at University of Hyderabad, Hyderabad, India. The electronic absorption spectrum was measured in methanol using SHIMADZU 1601 UV–Vis spectrophotometer in the range of 200–800 nm. In order to confirm the functional groups, the crystal was subjected to FT-IR spectral analysis by Perkin Elmer FT-IR 8000 spectrophotometer in the range of 400–4000 cm^{-1} using the KBr pellets method. ^{1}H and ^{13}C NMR spectra were recorded using Bruker AV III 500 MHz spectrometer instrument using TMS as an internal standard and DMSO was used as solvent. The emission spectrum was recorded by exciting the sample at 280 nm with Xenon lamp and the emission was fed into a monochromator where the emission intensity was recorded as a function of the wavelength. DNA cleavage study was carried out using Gelstan–Gel documentation system. An antioxidant study was carried out at the Kovai Medical Centre and Hospital Pharmacy College, Coimbatore, Tamil Nadu, India.

Single crystal X-ray diffraction studies

Single crystal X-ray diffraction data of DPPN compound was collected at room temperature on a Bruker Diffractometer equipped with a fine focused sealed tube. The unit cell parameters were determined and the data collections of DPPN was performed using a graphite-mono chromate Mo Kα (λ = 0.71073 Å) radiation by φ and ω scans. The structure of the compound was solved by direct method [31] using SHELXS-97, which revealed the position of all non-hydrogen atoms and refined by full-matrix least squares on F^2 (SHELXL-97) [32]. All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were placed in calculated positions and refined as riding atoms.

Material synthesis and Growth of single crystal

Equimolar ratio of 2,6-diaminopyridine and 4-nitrophenylacetic acid in methanol were prepared at room temperature and stirred well for about 2 h to get clear solution. This solution was filtered using Whatmann 41 filter paper and kept aside unperturbed in a dust-free room for the growth of single crystals. Well-defined, transparent crystals were collected at the end of 10th day. The collected crystals were recrystallised using dry methanol to get good quality crystals. The reaction scheme and the chemical structures were illustrated in Scheme 1.

Biological evaluation

DNA binding – titration experiments

The binding affinities with CT-DNA of the compound was carried out in doubly distilled water with tris(hydroxymethyl)-aminomethane (Tris, 5 mM) and sodium chloride (50 mM) and adjusted to pH 7.2 with hydrochloric acid. A solution of CT-DNA in the buffer gave a ratio of UV absorbance of about 1.8–1.9 at 260 and 280 nm, indicating that the DNA was sufficiently free of protein. The DNA concentration per nucleotide was determined by absorption spectroscopy using the molar extinction coefficient value of 6600 $dm^3 \cdot mol^{-1} cm^{-1}$ at 260 nm. The compound was dissolved in a mixed solvent of 5% DMSO and 95% Tris–HCl buffer for all the experiments. Stock solutions were stored at 4 °C and used within 4 days. Adsorption titration experiments were performed with fixed concentration of the compound (25 μM) with varying concentrations of DNA (0–50 μM). While measuring the absorption spectra, an equal amount of DNA was added to the all test solutions and the reference solution to eliminate the absorbance of DNA itself.