

Accepted Manuscript

A 4:1 stoichiometric binding and stabilization of mitoxantrone-parallel stranded G-quadruplex complex established by spectroscopy techniques

Tarikere Palakashan Pradeep, Ritu Barthwal

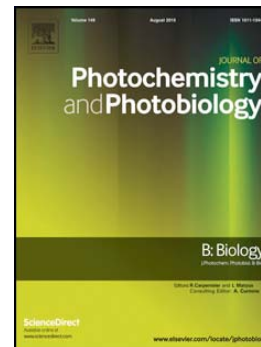
PII: S1011-1344(15)30212-8
DOI: doi: [10.1016/j.jphotobiol.2016.06.019](https://doi.org/10.1016/j.jphotobiol.2016.06.019)
Reference: JPB 10425

To appear in:

Received date: 12 December 2015
Revised date: 10 June 2016
Accepted date: 11 June 2016

Please cite this article as: Tarikere Palakashan Pradeep, Ritu Barthwal, A 4:1 stoichiometric binding and stabilization of mitoxantrone-parallel stranded G-quadruplex complex established by spectroscopy techniques, (2016), doi: [10.1016/j.jphotobiol.2016.06.019](https://doi.org/10.1016/j.jphotobiol.2016.06.019)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



A 4:1 stoichiometric binding and stabilization of mitoxantrone-parallel stranded G-quadruplex complex established by spectroscopy techniques

Tarikere Palakashan Pradeep and Ritu Barthwal*

Department of Biotechnology, Indian Institute of Technology Roorkee, Roorkee 247667, India,

E-Mail: ritubfbs@iitr.ac.in; Fax: +91-1332-273560

Highlights

- Absorbance of mitoxantrone shows hypo- and hyper-chromism with 15 nm red shift on binding.
- Fluorescence of mitoxantrone decreases and then increases with 8 nm red shift.
- Binding induces positive CD band at 645 nm and two exciton bands at 619 and 664 nm.
- Fluorescence lifetimes, 0.17 ns (91%) and 0.44 ns (9%), indicate dual binding mode.
- G-quadruplex Melting saturates on 4 mole equivalent addition of mitoxantrone by 25 °C.

Abstract

Small molecule ligands which specifically bind and stabilize G-quadruplex structures in telomeric ends inhibit the activity of telomerase enzyme, an important marker for cancer. Understanding of the binding mode of ligand-G quadruplex complex is important for evaluating relative efficacy of anti-tumor drugs. The present study is focused on interaction of anti-tumor drug mitoxantrone (MTX) with tetra-molecular parallel stranded G-quadruplex sequence d-TTGGGGT using absorbance, fluorescence and circular dichroism spectroscopy techniques. Absorbance of mitoxantrone shows hypochromism up to MTX (D)/DNA quadruplex (N) ratio ~5, followed by hyperchromism up to D/N=0.21 accompanied by a red shift of 15 nm. The fluorescence emission of MTX shows decrease up to D/N ~5 and then increases with red shift of 8 nm. The two observed fluorescent lifetimes, 0.17 ns (91%) and 0.44 ns (9%), indicate dual binding mode. Absence of isobestic and isoemissive point indicates presence of multiple complexes. Circular Dichroism spectra showing positive induced band at 645 nm and two exciton bands centered at 619 and 664 nm suggest binding of mitoxantrone as a dimer. Proton NMR studies show intermolecular MTX-MTX short contacts confirming existence of stacked dimer of MTX. Thermal melting transitions of DNA saturate at D/N=4 with $\Delta T_m=25$ °C. The

Download English Version:

<https://daneshyari.com/en/article/6493504>

Download Persian Version:

<https://daneshyari.com/article/6493504>

[Daneshyari.com](https://daneshyari.com)