# FT- SERS Study of Adriamycin - DNA Intraction

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**ABSTRACT:** *FT-SERS (Fourier Transform Surface Enhanced Raman Scattering) of adriamycin and its complex with DNA is reported. It is shown that in agreement with previous Raman studies the interaction of adriamycin with DNA takes place through an intercalation mechanism. The presence of a new band at 731 $cm^{-1}$ suggests that ring D of adriamycin is not involved in the intercalation process.*

**KEY WORDS:** *FT-SERS, Adriamycin, DNA, Medical Research, Antitumor activity.*

## INTRODUCTION

Molecular biology and medical research have now established that DNA mutation and the oncogenes are cancer- causing agents. They encode the growth factors and as a result a tumor is formed. Activation of oncogenes may originate from two kinds of changes; a structural change of the gene or a change in the regulation of gene expression[1].

Several drugs of anthracycline antibiotics such as adriamycin**,** aclacinomycin and daunomycin have been widely used as chemotheraputic agents in the treatment of cancer[2]. Adriamycin is the most powerful drug in this respect and its antitumor activity and mechanism of action with DNA has been the subject of extensive research work[3-8]. These include FTIR spectroscopy[3], fluorescence spectroscopy[4], circular dichroism[5]. NMR [6], resonance Raman spectroscopy[7] and surface–enhanced resonance Raman spectroscopy[8].

However, the antitumor activity of adriamycin is not yet fully understood[9], and the question of the different clinical activity of this drug remains unanswered. It is belived that the biological activity of adriamycin is mostly due to the formation of an intercalation complex between the chromophore framework of adriamycin and base pairs of DNA which inhibits DNA replication [10,11]. It has also been proposed that adriamycin may exert its cytotoxic action through intraction at the surface of the cell membrane [12] or through the generation of active oxygen species which may damage DNA [9].

In view of this situation, we have attempted an FT-SERS study of the adriamycin-DNA interaction, since this new technique enables the effective Raman cross-section to be increased by a factor of about $10^8$ and hence the Raman scattered intensity of the adsorbed species will be enhanced. This will give rise to structural information not always obtained with other methods. Moreover previous Raman studies (even SERS) have all concentrated on resonance Raman with laser excitation in visible or ultra–violet regions. At present work, excitation at 1064 nm is quite far–off resonance and this may result in new information.

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## EXPERIMENTAL

### *Materials*

Adriamycin was obtained form Aldrich (Milwaukee, Wisconsin, USA) and was used without purification. Stock solutions of adriamycin were prepared in Tris/HCl buffer at concentration of $10^{-3}$ M and diluted to the desired concentrations before each experiment. DNA solution with concentration of about 5 mg/ml was kindly supplied by Dr. T. Walsh (Biochemistry Department, QUT, Australia). The adriamycin–DNA complex was prepared by mixing the DNA and adriamycin solutions at room temperature.

The final concentration of DNA in this mixture is estimated to be of the order of about 2 mg/ml .

### *Instrumentation*

FT-SERS spectra were recorded using a perkin–Elmer FT-Raman Spectrometer Model 2000 equipped with an indium-gallium–arsenide detector. The excitation wavelength of 1064 nm was obtained from a Nd/YAG laser(I.E.Optomech, Model 385). SERS was carried out on a specially designed silver surface which was roughened by an electrochemical oxidation-reduction procedure.

## RESULTS AND DISCUSSION

Fig. 1 shows the molecular structure of the adriamycin molecule. FT-SERS spectra of the adriamycin (a) and its complex with DNA (b) in the wave number shift range 400-1600cm $^{-1}$ are shown in Fig.2. The comparison of these two spectra reveals that the DNA bands are hidden under the strong SERS signals of adriamycin. In the SERS Spectrum of adriamycin there is a very strong band at 731 $cm^{-1}$ which is observed for the first time. This band has not been reported either in resonance Raman spectra [13], or in SERS spectra [14] of adriamycin. Moreover the intensity of this band does not chang upon complexation of adriamycin with DNA. The C-H out–of–plane vibration of aromatic rings is a possible assignment for this band [15]. Thus the 731$cm^{-1}$ band can be assigned to the ring D in adriamycin molecule. Since the intensity of this band remaines unchanged in both spectra (a and b ), it shows that in the adriamycin–DNA complex the ring D is free and does not contribute to intercalation. This conclusion is in exact agreement with the UV-RRS study of the adriamycin–DNA interaction[16].

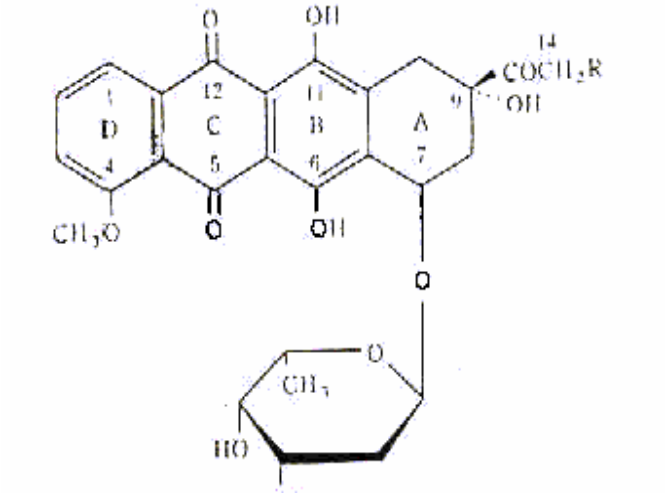


***Fig.1: Molecular structure of adriamycin.***

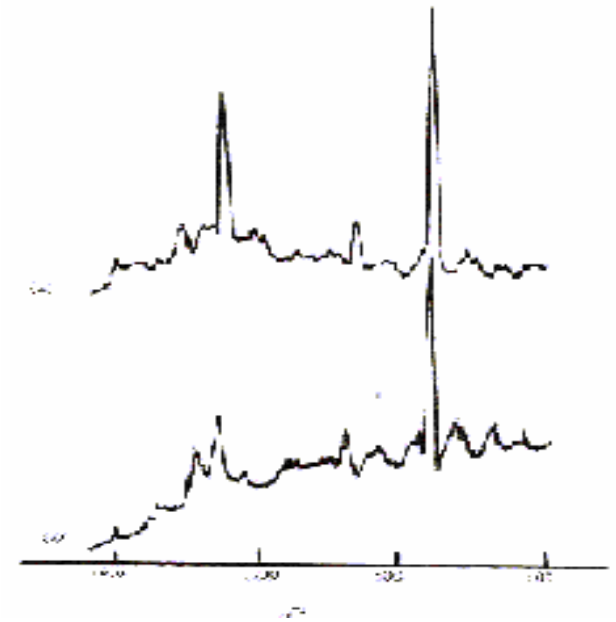

***Fig.2 Raman spectra of adriamycin (a) and adriamycin– DNA complex (b) in the wavenumber shift range 400-1600 $cm^{-1}$***

On the other hand as can be seen from Fig.2, the intensity of Raman band at 1330 $cm^{-1}$ is decreased relative to other Raman bands of adriamycin upon complexation with DNA.

This band has been assigned to aromatic ring skeletalstretching [14]. It may belong to ring B, confirming its intercalation with DNA. No more significant changes are observed in the FT -SERS spectrum of adriamycin upon complexation with DNA.

## CONCLUSIONS

We may conclude that in agreement with previous Raman spectroscopic studies, our FT-SERS data supports the intercalation of adriamycin with DNA. However, the presence of the new bond at 731 $cm^{-1}$ which has not been reported before indicates that ring D does not contribute to intercalation process.

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