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## RESEARCH ARTICLE

# INTERACTION STUDY OF CURCUMIN WITH $\beta$ -CYCLODEXTRIN

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### INTRODUCTION

Curcumin (1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-Dione) is the main constituent of the Indian spice turmeric [1–7]. It is a fluorescent molecule, with emission properties highly dependent on the polarity of its environment [8–10]. However, the most intriguing aspect of this compound is that it shows a wide array of pharmaceutical activity, including potent antioxidant, anti-inflammatory, and anti-carcinogenic properties [1–7]. Unfortunately curcumin has an extremely low aqueous solubility, limiting its pharmaceutical use. One possible way to increase its aqueous solubility is to form inclusion complexes, i.e. to encapsulate curcumin as a guest within the internal cavity of a water-soluble host.

Tang *et al.* [11] used absorption spectrophotometry to study the supramolecular host-guest inclusion of curcumin into  $\beta$ -cyclodextrin, and reported a strong 2:1 host: guest complex with an apparent formation constant of  $5.53 \times 10^5 \text{M}^{-2}$ . Tønnesen *et al.* [12] investigated the inclusion of curcumin into the three common cyclodextrins,  $\alpha$ -,  $\beta$ - and  $\gamma$ -, as well as their hydroxypropylated derivatives, using relative hydrolysis rates. In addition, they measured the solubility enhancement of the modified CDs on curcumin in aqueous solution.

However, they assumed 1:1 host: guest inclusion (which is not an obvious stoichiometry given the two identical phenyl groups at either end of the curcumin molecule which are available for

### ABSTRACT

Curcumin, a hydrophobic polyphenolic compound derived from the rhizome of the herb *curcuma longa*, possesses a wide range of biological applications including cancer therapy. It is a low molecular weight polyphenol yellow compound. It has been widely used in traditional Ayurvedic and Chinese medicine since the second millennium BC. Curcumin is a well studied natural compound due to its putative cancer prevention and anti-cancer activities which are mediated influencing multiple signalling path ways. One possible way to increase its aqueous solubility is to form inclusion complexes, i.e., to encapsulate curcumin as a guest within the internal cavity of a water-soluble host. The photo physical properties in curcumin vary significantly depending on the medium and there act as suitable tools for following the inclusion behaviour to different systems. Here, an attempt has been made to estimate the binding constant of 1:1 curcumin and  $\beta$ -cyclodextrin (  $\beta$ -CD) complex by following the emission and absorption properties. The formation of inclusion complex of curcumin with  $\beta$ -cyclodextrin has been characterized by fluorescence and absorption spectroscopy.

binding), and only determined minimum and/or estimated formation constants. Here, an attempt has been made to estimate the binding constant of 1:1 curcumin and  $\beta$ -cyclodextrin (  $\beta$ -CD) complex by following the fluorescence and absorption properties.

### MATERIALS AND METHOD

#### Materials

Curcumin (1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-Dione) and  $\beta$ -cyclodextrin were purchased from Sigma Aldrich Company Bangalore. The chemicals were used without further purification.

#### Method

All fluorescence measurements were performed on solutions in 1 cm<sup>2</sup> quartz cuvettes. Fluorescence spectra were measured on a **RF – 5301 PC Shimadzu, Spectrofluorophotometer**, with excitation and emission monochromator, band passes set at 5 nm and an excitation wavelength of 421 nm.

The absorption spectra were recorded on a **1650 PC Shimadzu, UV- Visible spectrophotometer**.

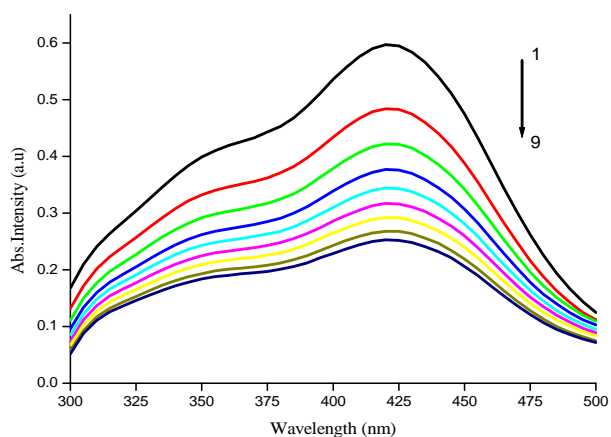
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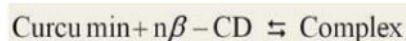
## RESULTS AND DISCUSSION

### Absorption spectral studies

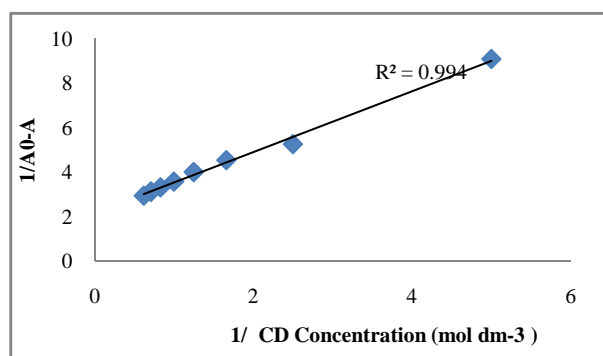
Curcumin in the absence of  $\beta$ -CD shows absorption maximum at 421 nm and  $\beta$ -CD does not absorb appreciably in the wavelength region. On addition of  $\beta$ -CD, the absorbance at 421 nm was nearly half of its value on addition of  $1 \times 10^{-4} \text{ mol dm}^{-3}$   $\beta$ -CD. The absorption spectra of curcumin with different concentrations of  $\beta$ -CD are shown in [Fig.1]. This spectral change is attributed to a complex formation between curcumin and  $\beta$ -CD [15], represented by equation (1):



**Fig. 1** Absorption spectra of Curcumin with different concentrations of  $\beta$ -CD ( $\text{mol dm}^{-3}$ ) (1)0, (2)0.2 (3)0.4,(4)0.6,(5)0.8, (6)1.0,(7)1.2,(8)1.4,(9) 1.6



For the equilibrium, assuming 1:1 complex formation, binding constant was estimated by employing the double reciprocal plot known as Benesi-Hildebrand equation. Thus linear fit of the double reciprocal plot of absorption changes ( $\Delta A$ ) at 421 nm as a function of  $\beta$ -CD concentration ( $0\text{-}1.6 \text{ mol dm}^{-3}$ ) gave binding constant (K) to be  $3.311 \times 10^{-3} \text{ M}^{-1}$  [Fig 2]

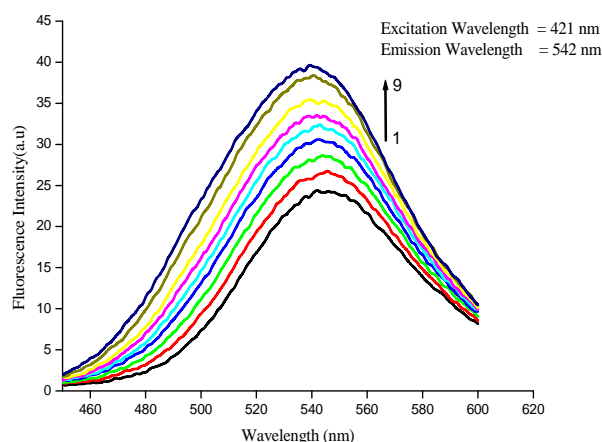


**Fig.2** Plot of  $1/A_0 - A$  and  $1/CD$

### Fluorescence enhancement

$\beta$ -cyclodextrin studies had significant effects on the fluorescence spectrum of curcumin, both in terms of peak position and intensity. For example, the effect of various

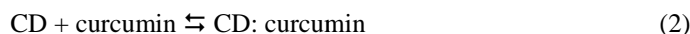
concentrations of  $\beta$ -CD on the curcumin fluorescence spectrum is shown in [Fig. 3]. In this figure, a significant blue shift and very large enhancement of the curcumin fluorescence with increasing  $\beta$ -CD concentration can clearly be observed. Table.1 lists the observed wavelength of maximum emission of the spectrum,  $\lambda_{\text{flu}}$ .



**Fig.3** Fluorescence spectra of Curcumin in different concentrations of  $\beta$ -CD ( $\text{mol dm}^{-3}$ ) (1)0, (2)0.2 (3)0.4,(4)0.6,(5)0.8, (6)1.0,(7)1.2,(8)1.4,(9) 1.6

### Formation constants

The fluorescence enhancement  $I/I_0$  measured as a function of host concentration can be used to obtain the formation constant(s) for the host-guest inclusion process. In the case of 1:1 host: guest inclusion, a single equilibrium is involved, with formation constant K:

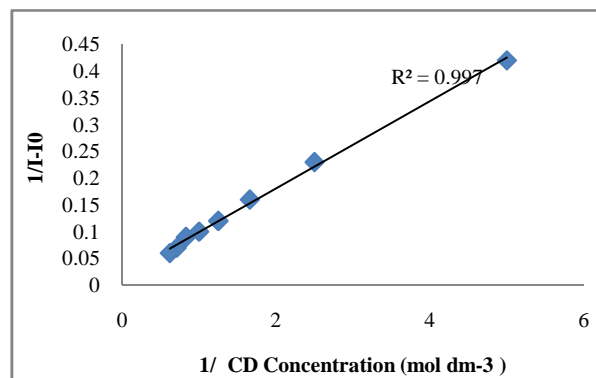


$$K = [\text{CD:curcumin}] / ([\text{CD}][\text{curcumin}]) \quad (3)$$

In this case, the dependence of  $I/I_0$  on added host concentration,  $[\text{CD}]_0$ , is given by the following equation [13,14]:

$$\frac{I}{I_0} = 1 + \left( \frac{I_{\infty}}{I_0} - 1 \right) \frac{[\text{CD}]_0 K}{1 + [\text{CD}]_0 K} \quad (4)$$

Where  $I/I_0$  is the maximum enhancement, when all guests are completed within a host. If only 1:1 complexes are formed, then the double-reciprocal plot of  $(1/I - I_0)$  versus  $(1/CD)$  will be linear; a non-linear double-reciprocal plot indicates the presence of higher-order inclusion complexes.



**Fig.4** Plot of  $1/I - I_0$  and  $1/CD$

The plot is shown in [Fig .4] and the data's are shown in Table.1.Binding constants and free energies for the ground and excited states were given in Table 1 along with absorption and emission maxima, molar extinction coefficient and Stokes shift values.

**Table.1** Absorption log ( $\text{m}^{-1}\text{cm}^{-1}$ ), fluorescence spectral data (nm) and Stokes's Shift ( $\text{cm}^{-1}$ ) of curcumin.

| $\lambda_{\text{abs}}$<br>(nm) | Log<br>( $\text{m}^{-1}\text{cm}^{-1}$ ) | $\lambda_{\text{fla}}$<br>(nm) | $K_g$<br>( $\text{M}^{-1}$ ) | $K_e$<br>( $\text{M}^{-1}$ ) | $G_g$<br>( $\text{KJ mol}^{-1}$ ) | $G_e$<br>( $\text{KJ mol}^{-1}$ ) | Stokes shift<br>( $\text{cm}^{-1}$ ) |
|--------------------------------|--|--------------------------------|------------------------------|------------------------------|-----------------------------------|-----------------------------------|--------------------------------------|
| 421                            | 6.62                                     | 542                            | 0.85                         | 0.05                         | 409.40                            | 7546.67                           | 5437.9                               |

## CONCLUSIONS

A phenolic and lipid soluble antioxidant has been examined for its complexing ability with  $\beta$ -CD. The binding constant of the complex was determined by following absorption, spectral changes. Curcumin forms strong 1:1 host: guest inclusion complexes with  $\beta$ -cyclodextrin. Formation constants of curcumin with  $\beta$ -CD have been calculated, and the calculated value is  $3.31 \times 10^{-3} \text{LM}^{-1}$ .

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