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Preparation and Characterization of Umbelliferone and Hydroxy Propyl α-Cyclodextrin Inclusion Complex.

KEYWORDS: Umbelliferone, HP-α-CD and Inclusion complex.

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ABSTRACT *Umbelliferone (7-hydroxy Coumarin) is an antioxidant. But Umbelliferone is insoluble in water. This study aimed to prepare the inclusion complex of Umbelliferone and to investigate the effects of solubility and increases the dissolution rate of the inclusion complex of Umbelliferone with Hydroxy propyl-α-cyclodextrine (HP-α-CD). The physico-chemical characterization of Umbelliferone HP-α-CD inclusion complex was performed using Absorption, Emission, Phase solubility studies, FT-IR, 1H-NMR, and SEM.*

Introduction
Umbelliferone (7-hydrony coumarin) is a natural product of the Coumarin family and it has antioxidant properties[1]. It is used as a sunscreen agent[2], optical brightener in textiles[3] fluorescence indicator for metal ions. Umbelliferone is less soluble in water this will decrease functions of the Umbelliferone and create problems. The objective of the present study was to investigate the physio-chemical properties of inclusion complex of umbelliferone and the possibility of improving the solubility and dissolution rate of Umbelliferone with HPα-CD.

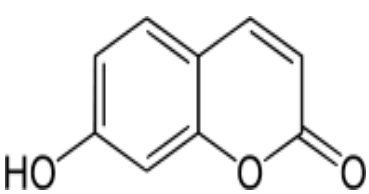

Fig1: Structure of Umbelliferone

Experimental Studies
Materials and Methods
Umbelliferone, HPα-CD were purchased from Sigma Alrich company, Mumbai.

UV-Spectroscopic and Fluorescence studies
Umbelliferone solution was added to the different concentrations of HPα-CD solution and the absorption and emission spectral measurements were carried out, with systronic double beam spectrophotometer 2203 SMART and ELICO SL 170 Spectrofluorometer.

Phase Solubility study
According to Higuchi and corners[4] 32 mg of Umbelliferone added to various concentrations of HPα-CD and shaken for 48hrs, then the samples were filtered and analysed with UV-deflection wave length at 328 nm. The apparent stability constant K_{st} was calculated K_{st} = slope/intercept (1-slope).

Preparation of Solid inclusion Complex
Umbelliferone and HP-α-CD solution are mixed and stirred for 48hrs in a magnetic stirrer[5].The complex was obtained as a yellow powder used for the following characterization studies.

(i) The FT-IR Spectra of Umbelliferone, HPα-CD and inclusion complex were taken using 7600 FT-IR Spectrophotometer (shimadzu corporation)

(ii) ^{1}H NMR spectras were recorded on AV 500 NMR Spectrometer (Bruker) at 500 MH_Z in NIIST, Trivandrum

(iii) Umbelliferone, HPα–CD and inclusion complex were morphologically analyzed with JEOL– JSM– 6390 LV Scanning Electron Microscope. STIC, Cochin.

Results and discussion
UV-Visible Spectrophotometry and Fluoresence Study

The fig 2 & 3 shows the absorption and emission Spectrum of the inclusion complex. As the Concentration of HP-α-CD increases the absorbance (or) intensity as well as the wavelength increases. For UV-visible study the wavelength changes from 318.8nm to 328.4nm with 1.526 to 1.978 absorbance respectively. Similarly for Fluoresence study, the wavelength changes from 457nm to 458nm with the change in the intensity values of 5688.98 to 6629.94. In both absorption and emission bathochromic shift is observed.Clevage of the hydrogen bond occurs due to complexation[6].This proves that Umbelliferone dissolves in HP α-CD and included in the HPα-CD cavity.

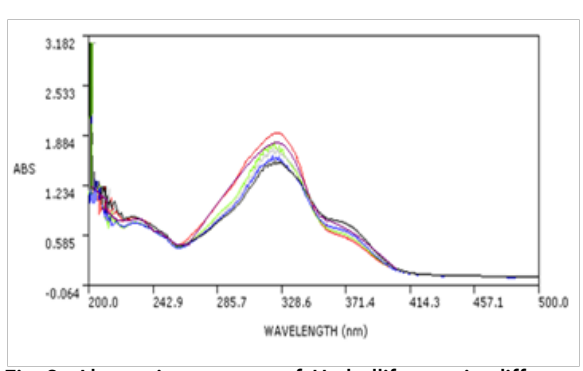

Fig 2: Absorption spectra of Umbelliferone in different HPα-CD concentration

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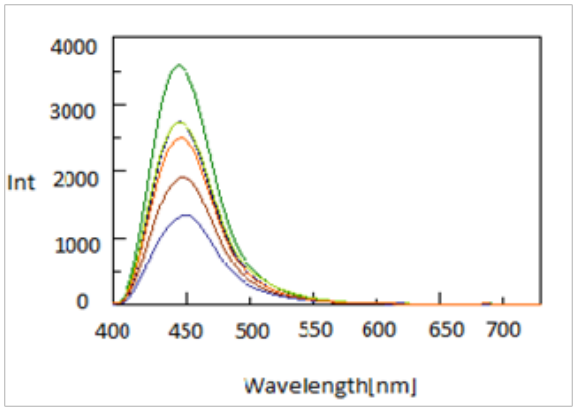


Fig 3: Fluorescence Spectra of Umbelliferone in different HPα-CD concentration

Phase Solubility Study

The aqueous solubility of Umbelliferone increases as a function of HPα-CD concentration. The phase solubility diagram of Umbelliferone in HPα-CD can be classified as A_L type. Umbelliferone with phenyl moiety have higher affinity for the hydroxypropyl-α- cyclodextrin.The apparent stability constant K_{st} value was 34 which indicates that Umbelliferone and HPα-CD forms a soluble complex at 1:1 ratio.

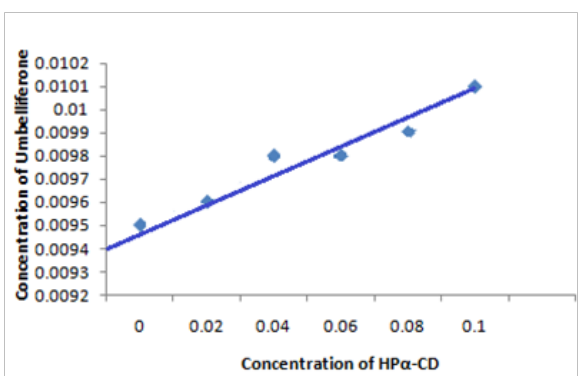


Fig 4: Phase Solubility diagram for Umbelliferone HPα – CD Complex

FT-IR Spectroscopy

The broad single OH peak in Umbelliferone is shifted from 3175.22cm^{-1} to 3430.74cm^{-1}. The CH bending vibration at 985.447cm^{-1} is changed to 890.952cm^{-1}. The C=C stretching mode moved from 1109.83cm^{-1} to1027.87cm^{-1}. The C= O peaks observed at 1623.77cm^{-1}, 1614.48cm^{-1} and 1609.99cm^{-1} are shifted to 1616.06cm^{-1} and 1705.73cm^{-1}. The above results confirms that there is a strong interaction between Umbelliferone and HPα-CD.

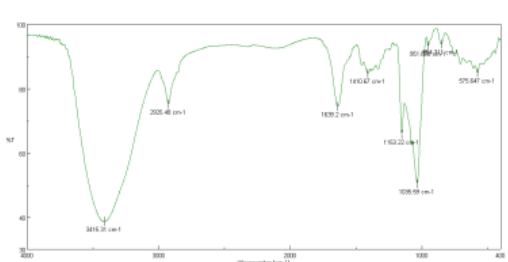


Fig 5:FT-IR Spectrum of HP α-CD

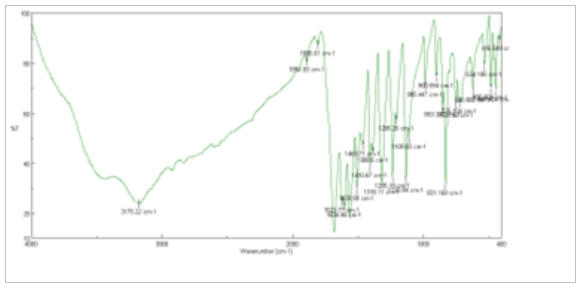
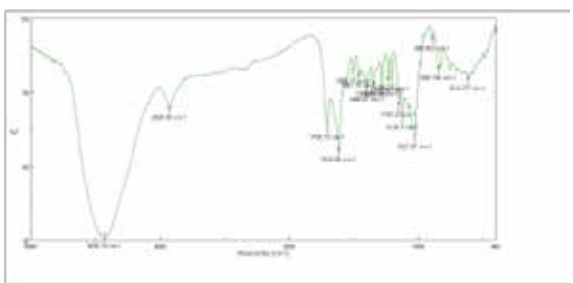


Fig 6: FT-IR Spectrum of Umbelliferone



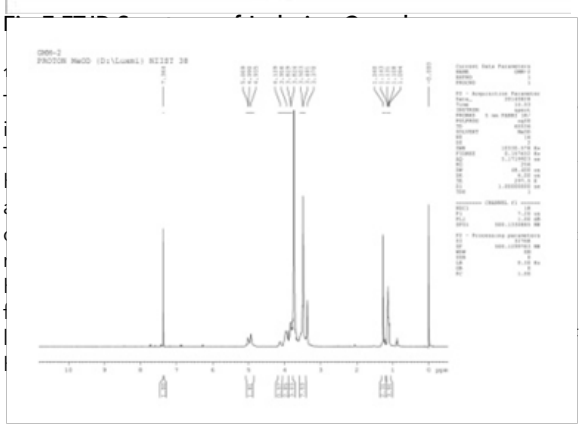


Fig 8: NMR Spectrum of HP α-CD

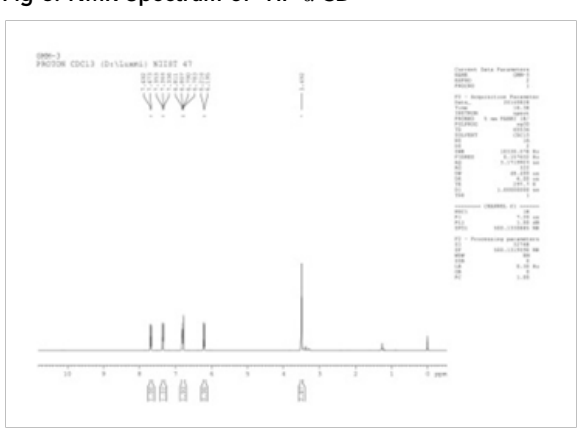


Fig 9: NMR Spectrum of Umbelliferone

Volume : 5 | Issue : 5 | May 2015 | ISSN - 2249-555X

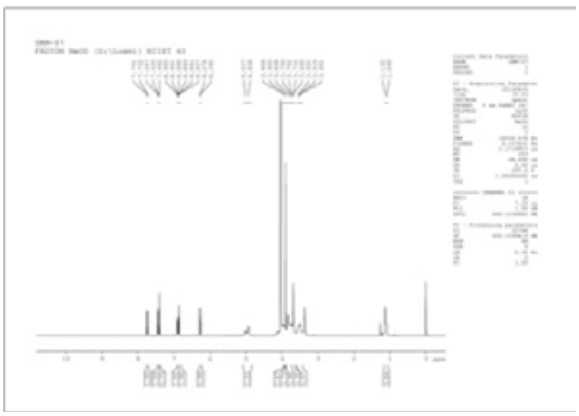


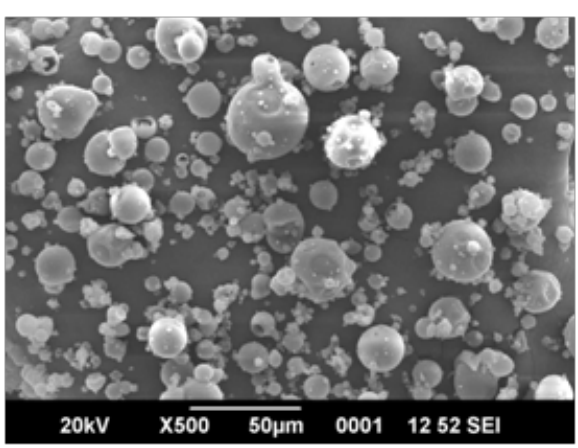
Fig 10: NMR Spectrum of Inclusion complex

Table 1 : Chemical shifts (ppm) for the Protons of HPα-CD and inclusion on complex

	H_1	H_2	H_3	H_4	H_5
HPα-CD	4.990	3.481	3.956	3.370	3.824
Inclusion Complex	5.017	3.515	4.170	3.501	3.959
Δδ	0.027	0.034	0.214	0.131	0.135

Microscopic Morphological Observation (SEM):
Powdered form of Umbelliferone ,hydroxypropyl α-cyclodextrin and the inclusion complex are shown in Fig 11-13, pictures clearly elucidated the difference of powder of each other . HP α-CD consisted of spherical particales,whereas Umbelliferone consisted of shrunken cylindrical particales.The inclusion complex structure is different from HP α-CD and Umbelliferone.A drastic change in the crystalline nature was observed. Modification of crystals and powder can be assumed as a proof of the formation of new interaction.

Fig 11: SEM image of HPα-CD



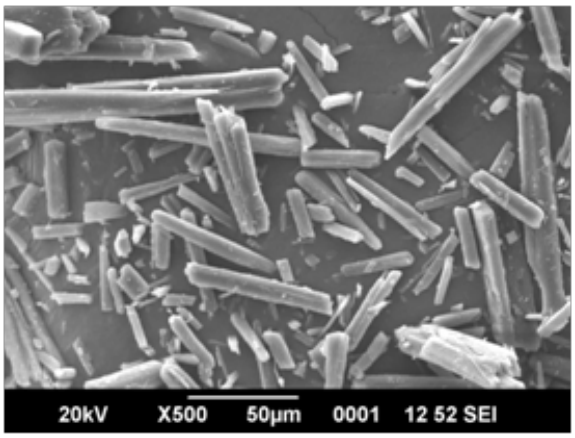


Fig 12: SEM image of Umbelliferone

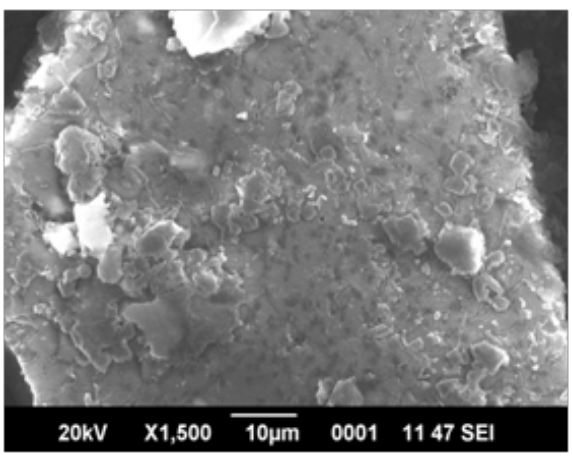


Fig 13: SEM image of Inclusion Complex

Conclusion
Umbelliferone -HPα-CD complex prepared by inclusion method showed increasing the solubility and dissolution rate in comparision with the plain Umbelliferone.The change in chemical shift value proves that the aromatic ring having phenolic moiety included completely in the HPα-CD cavity. This technique would be used to develop fast release activity of Umbelliferone.

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