# Spectral (UV-Vis, IR, NMR) and Thermal (Tg, DTG, ATD) Characterization of Some Synthesis Brom-isoflavanone and the Inclusion Compounds with beta-Cyclodextrin

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*The objectives of this study were to characterize a synthesis brom-isoflavanone (notated IF) with possible pharmacological activities, water insoluble and to examine the potential of beta-cyclodextrin to improve this property and obtain inclusion compounds that were analysed by different techniques: UV-Vis, IR, $^1$HNMR spectroscopy, thermal analysis. The presence of β-cyclodextrin rises the content of IF in water. The inclusion compounds were prepared by co-precipitation in 1:1 and 1:2 molar ratio substance-β-cyclodextrin. The UV-Vis, IR, $^1$HNMR analysis demonstrated the obtaining of inclusion compounds and the thermal analysis show that these compounds are more stable than the parent substance.*

*Keywords: UV-Vis, IR, NMR spectral analysis, thermal analysis, inclusion compounds, beta-cyclodextrin*

The substance (fig. 1) analysed, $C_{15}H_{17}O_3NBr_2$, 3 methyl, 3methylen-morpholino, 6,8 dibromo-isoflavanone, is a new compound from isoflavanone classes with 419 molecular weight, 158°C melting point, a white powder, insoluble in water, soluble in chloroform, DMSO, acetone.

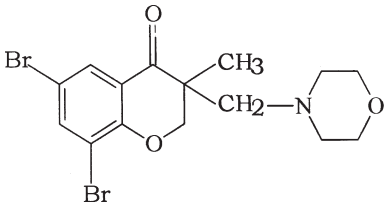


Fig. 1. Substance structure

Cyclodextrins (fig. 2) are cyclic oligosaccharides consisting of covalently linked α-D-glucopyranoside units by a 1,4-glycoside bound. The most important members of the cyclodextrin family are α, β and γ-cyclodextrin which possesses six to eight glucopiranoside units. Cyclodextrins are able to form inclusion compounds with many substances, these inclusion compounds being formed when a "guest" molecule is partially or fully included inside a "host" molecule.

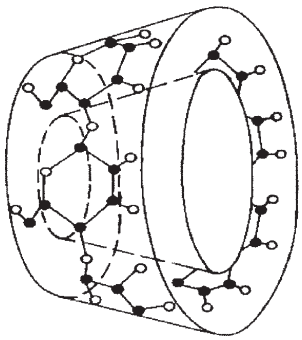

Fig. 2. β-CD structure

The complexation with cyclodextrins of active substances aims to: modification of physico-chemical properties of drugs, improvement of physical and chemical stability (against heat, oxidation, light induced decomposition in aqueous solution), enhancement of bioavailability, reduction of undesired side effects of drugs.

The present study describes the influence of beta-cyclodextrin on a new synthesis substance (notated IF) and demonstrates the inclusion compounds formation of IF with beta-cyclodextrin (β-CD). These inclusion compounds were performed by co-precipitation and then investigated by spectral and chromatographic methods.

## Experimental part

### *Materials*

β-CD was purchased from Fluka Chemica (Switzerland). All the solvents used were of quality standards of Farmacopeea Romana, X$^{th}$ edition.

### *Solubility studies*

Solubility studies were carried out according to the Higuchi and Connors methods [1, 2]. β-CD solutions of different concentrations (0.326 – 1.63 x $10^{-2}$ mol/L) were added to supersaturated solutions containing the same quantity of IF and shaken at room temperature for 48 h. After that, the solutions were filtered, diluted and spectrophotometricaly analyzed. We determined the concentration of IF in each solution, using external standard method.

The phase solubility studies were also performed similarly after incorporation of 0.25% w/v sodium carboxymethylcellulose (Na-CMC) to each of the above solutions.

### *Preparation of inclusion compounds*

The IF - β-CD inclusion compounds were prepared using the complexation in liquid medium, using 1:1 (noted IF1) and 1:2 (noted IF2) molar ratio. We prepared a saturated solution of β-CD in distilled water, then we added an equimolar concentration of IF. The mixture was stirred for 24 h at room temperature. The obtained precipitated was

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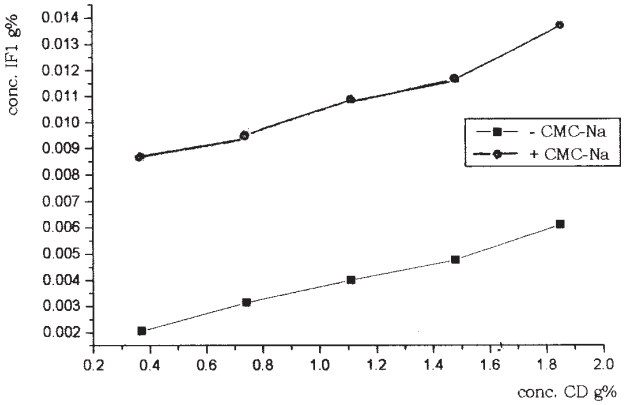


Fig. 3. Solubility diagram of IF in β-CD solutions

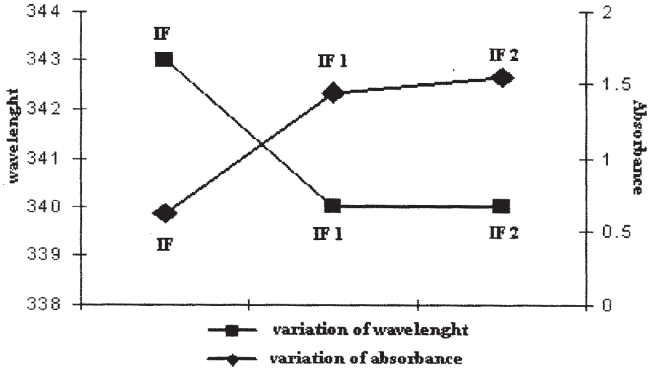


Fig. 4. Comparative presentation of absorbance and wavelength values for IF, IF1, IF2

filtered, washed with cold water and dried in a hot air oven at 40°C [3 - 5].

*Methods of analysis*

Ultraviolet-Visible absorption study

UV-Vis absorption spectra of IF and corresponding inclusion compounds were realized with a Jasco V530 spectrophotometer after proper dilution in ethanol. We compared the UV-Vis spectra of IF with those of the inclusion compounds.

Infrared spectral study

The IR spectra of IF, β-CD and the inclusion compounds were recorded with an Specord M 80 spectrophotometer after pastillation in bromide potassium. [6]

$^1$HNuclear Magnetic Resonance study

$^1$HNMR spectroscopy is one of the most useful techniques for investigating the host-guest systems [6, 7].

The inclusion compounds were characterized in deuterochloroform as solvent by $^1$HNMR, at room temperature. The spectra were obtained in a Jeol 60 MHz spectrophotometer, using internal standard trymethilsilan. For observing the modification that appear after IF - β-CD interaction, we represented the cyclodextrin influence on proton chemical displacement of IF.

Thermal analysis

The thermogravimetric curves (TG, DTG, DTA) were recorded on a Paulik-Paulik-Erdey type derivatograph, MOM, Budapest under the following operational conditions: heating rate 10° C/min, temperature range 25-700°C, film sample mass 50 mg in platinum crucibles. The estimation of kinetic parameters from thermogravimetric dates were calculated using Coats-Redfern (CR), Reich-Levi (RL) and Swaminathan-Madhavan (SM) methods [3, 7, 8].

## Results and discussions

*Solubility studies*

We performed the solubility studies of IF in aqueous solutions of different concentrations of β-CD alone and in the presence of Na-CMC. We represent the solubility diagram of IF in β-CD solution and then after incorporation of Na-CMC. (fig. 3)

We can say that the resulting curve can be classified as type $A_L$, indicating that complexes with 1:1 stoechiometry will be present in solution. Also, the presence of IF in solutions increased approximately 2,5-times in the presence of 0.25 % (w/v) Na-CMC.

Ultraviolet-Visible absorption study

From figure 4 we can observe that IF compound exhibited an intense maximum around 343 nm and the inclusion compounds showed a maximum peak around 340 nm so a hypocrom effect was observed on the addition of β-CD. Also, the absorbances of inclusion compounds were increased comparative with IF absorbance. So, the explanation of this modifications consist in possibility of formation of inclusion compounds.

Infrared spectral study

From IR spectra of IF, β-CD, IF1 and IF2 we can say that generally, in 1:1 inclusion compound characteristic cyclodextrin frequencies increase, and the most sensible are CH bending, piranosic ring vibrations, and for 1:2 inclusion compound the most sensible are OH deformation, CH bending and piranosic ring vibrations.

$^1$HNuclear Magnetic Resonance study

Table 1 present the chemical displacements of protons for inclusion compounds comparative with substance alone.

**Table 1**

CHEMICAL DISPLACEMENTS OF PROTONS ($\Delta\delta = \delta_{IF1-\beta\text{-}CD} - \delta_{IF1}$)

| ***Chemical displacements of protons in IF*** | **IF1** | **IF2** |
|---|---|---|
| H2 – 7.97 ppm | 0.02 | 0.02 |
| H5 – 6.87 ppm | 0.22 | 0.32 |
| H7 – 6.95 ppm | 0.25 | 0.55 |
| H ($CH_3$) – 3.7 ppm | 0.10 | 0.07 |
| H ($CH_2$) – 1.4 ppm | 0.15 | 0.175 |
| H2'– 2.2 ppm | 0 | 0.05 |
| H5' – 2.3 ppm | 0.15 | 0.20 |

We can say that the most evident displacements of the signals appears for dibrom-isoflavanone nucleus, for morpholino nucleus are very weak and for the methyl and methylen group are almost insesisable so the dibrom-isoflavanone nucleus can be included in cyclodextrin cavity by hidrophobe interactions and the second nucleus formed hydrogen bounds on β-CD surface. Also, the chemical displacement are function of quantity of β-CD. Generally the protons displacements are towards smaller fields comparative with the initial position.

**Table 2**
CINETIC PARAMETERS VALUES

| Sample | Ti ($^0$C) | Tm ($^0$C) | Tf ($^0$C) | ΔW (%) | $E_{CR}$ (Kj/mol) | $n_{CR}$ | $E_{SM}$ (Kj/mol) | $n_{SM}$ | $E_{RL}$ (Kj/mol) |
|---|---|---|---|---|---|---|---|---|---|
| IF | 117.2 | 236.7 | 285.8 | 31 | 72.4430 | 0.9 | 63.1870 | 0.9 | 82.8956 |
| IF1 | 158.5 | 218 | 321 | 30.6 | 12.2785 | 0 | 71.8715 | 1.7 | 72.5273 |
| IF2 | 174.5 | 231.7 | 349 | 31.6 | 15.6455 | 0 | 112.655 | 2.0 | 57.9556 |
| β-CD | 216.5 | 277 | 350 | 36 | 378.1692 | 2.9 | 615.064 | 4.6 | 222.751 |

Thermal analysis

The initial temperature of first step, corresponding to dehydration, for inclusion compounds decreses in these order: β-cyclodextrin > 1:2 inclusion compound > 1:1 inclusion compounds, so we can say that dehydration temperature rises with increasing β-cyclodextrin concentration. IF present only one step of decomposition (117-285°C), which contents also the maximum in mass loss, 31% better evidentiated on DTG curve. For the inclusion compounds the decomposition took place in three steps: in first step - both inclusion compounds present a peek on DTG curve on 100°C, second and third step are longer for IF1 than for IF2. The most important kinetic parameters values are presented in table 2.

## Conclusions

This study showed that the association of β-cyclodextrin and/or without Na-CMC can increase the content of IF in water and the preparation of inclusion compounds is possible. The inclusion can be proved by UV-Vis, IR, $^1$H NMR spectroscopy, and the inclusion compounds are more thermal stable than the parent substance.

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