Analele Universităţii din Oradea-Fascicula Chimie, Vol. XXX (30), p.5-10, 2023

THE STUDY COMPLEXATION OF β-CYCLODEXTRIN WITH SALICYLIC ACID

Mioara SEBEŞAN[1], Horea SEBEŞAN[1], Gabriela Elena BADEA[1], Radu SEBEŞAN[2], Sorin HODIŞAN[1]

[1]University of Oradea, Faculty of Informatics and Sciences, Universitatii 1st., RO-410087, Oradea, Romania
[2]University of Oradea, Faculty of Electrical Engineering and Information Technology, Universitatii 1st., RO-410087, Oradea,Romania
E-Mail: msebesan@uoradea.ro

Abstract: This paper presents a study of the process of formation of inclusion complexes between salicylic acid and *beta*-cyclodextrine (β-CD). Three inclusion compounds, resulting from complexation of salicylic acid and beta-cyclodextrin, were studied. The inclusion complexes have been prepared in different ratio of β-CD/ salicylic acid. The bioactive nanoparticles of complexes included different concentrations of salicylic acid. The inclusion complexes resulting were analysis, using UV-VIS spectrophotometry.

Keywords: *beta*-cyclodextrin, UV-VIS spectrophotometry, inclusion compounds.

INTRODUCTION

Cyclodextrins are chemical compounds, from the class of oligosaccharides, which have a cyclic structure. 3 types of natural cyclodextrins are known, α-cyclodextrin, β-cyclodextrin and γ-cyclodextrin, the difference between them being the number of linked glycosidic cycles. These compounds are obtained naturally from starch, by fermentation, in the presence of cultures of bacteria and fungi, [1].
The cyclic structure of cyclodextrins allows the formation of an internal cavity, in which a foreign molecule can enter, thus forming a new chemical compound. The obtained chemical compound is characterized by the physical interaction of two components: the "host" reactant, which is cyclodextrin, and the "guest" reactant, represented by the molecule that embeds itself inside the cyclodextrin cavity, [2].

In order for this process to take place, certain conditions need to be met: the "guest" molecules must have suitable dimensions to be embedded; to have a low solubility in water; the complexation method used have to give a good yield and lead to a stable inclusion complex over time.

So, due to the shape that cyclodextrins have, they are able to form inclusion complexes. The process is characterized by the mobilization of an external molecule, inside the non-polar cavity of the cyclodextrin. This molecule must be of the right size so that it can penetrate inside the cyclodextrin, have a low solubility in water and allow the formation of a stable complex, [3].

Through the reaction of β-cyclodextrin and salicylic acid (o-hydroxybenzoic acid), a complex is formed, which has different physical and chemical properties compared to the reagents. Obtaining the complex can be done by several techniques: in solution, in suspension, by mixing or by melting. The choice of one of the techniques is made according to the "guest" molecule, so that the yield of the reaction is as high as possible and

a large amount of complex is obtained.

Obtaining the complexes in solution is done by mixing an aqueous solution of β-cyclodextrin with the solution of a guest molecule. After mixing the two solutions, shake the contents and refrigerate for several hours. The formation of the complex can be seen by observing the formation of a turbidity of the obtained solution, [4].

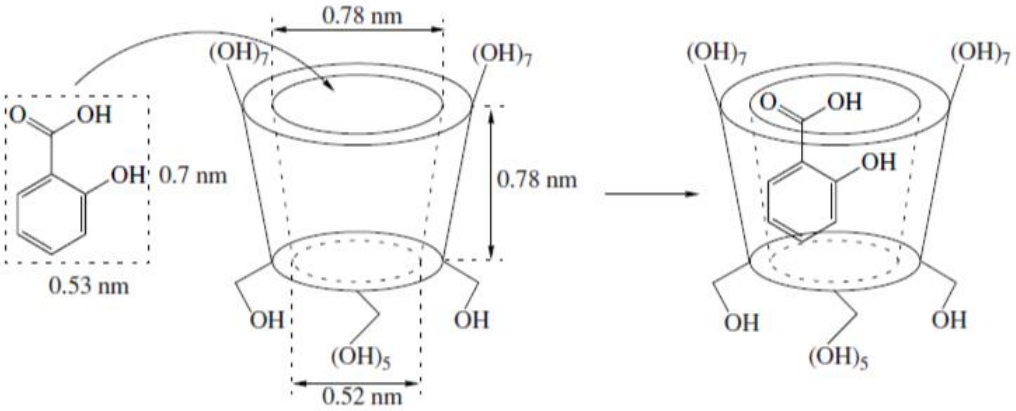

Figure 1. Schematic of the complexation between β-cyclodextrin and salicylic acid, [5]

The advantage of this method is the short reaction time, it only requires mixing the two reactant solutions, and then keeping cold for a few hours or days to let the complex precipitate. The reaction in this phase occurs in good yield, and the remaining uncomplexed compounds can be determined instrumentally or chromatographically.

EXPERIMENTAL PART

Due to the abilities of salicylic acid to be complexed by β-cyclodextrin, the method for chose for the preparation of inclusion complexes is that in solution because it is a method often used to obtain complexes, it is a method that have rezults and a good yield the ability to complex β-cyclodextrins can be calculating, [6].

The complexes were prepared in 3 samples, well determined amounts, both of β-cyclodextrin and of salicylic acid, to establish the optimal conditions of the process, i.e. when the complexation proceeded with a better yield and when a greater amount of complex obtained. Quantities used were determined based on stoichiometric calculations, [7-9].

Guest molecules of salicylic acid dissolved in ethanol are added to the solution of β-CD. The balance is achieved by intense agitation and then cooled for several hours. The reagents to use were of analytical purity and chromatographic use. Preparation of β-CD/ salicylic acid inclusion complexes was made in three ways , obtaining 3 samples, as following:

1) 0.5675 g of β-CD was dissolved in 6 ml of distilled water at 55 ° C, to hot solution was added an ethanol solution of salicylic acid, namely, 0.2072 g salicylic acid in 3 ml of ethanol. The molar ratio: β-CD and salicylic acid is 1:3, in sample **1**.

2) 0.5675 g of β-CD was dissolved in 4 ml ethanol and 2 ml of distilled water at 50 ° C, to hot solution was added an ethanol solution of salicylic acid, namely, 0.1035 g salicylic acid in 1 ml of ethanol. The molar ratio: β-cyclodextrin / salicylic acid is 1:1.5, in sample **2**.

3) 0.5675 g of β-cyclodextrin was dissolved in 3 ml of ethanol and 3 ml of distilled water at 50 ° C, to hot solution was added an ethanol solution of salicylic acid, namely 0,1381 g salicylic acid in 2 ml of ethanol. The molar ratio: β-cyclodextrin / salicylic acid is 1:2, in sample **3**.

The three samples were kept under stirring for 20 minutes, at 50 ºC in a round-bottomed flask equipped with condenser upward. After maintaining the samples at 22°C for 5 hours for slow cooling, they were cooled in a refrigerator at 5°C for 36 hours.

The complexes of β-ciclodextrin / salicylic acid that were formed in the three samples were filtered.

RESULTS AND DISCUSSIONS

Results from UV-VIS spectrophotometric analysis, the absorption spectra of salicylic acid, β-cyclodextrin, and of the three inclusion complexes are shown in figure 2, 3 and 4.

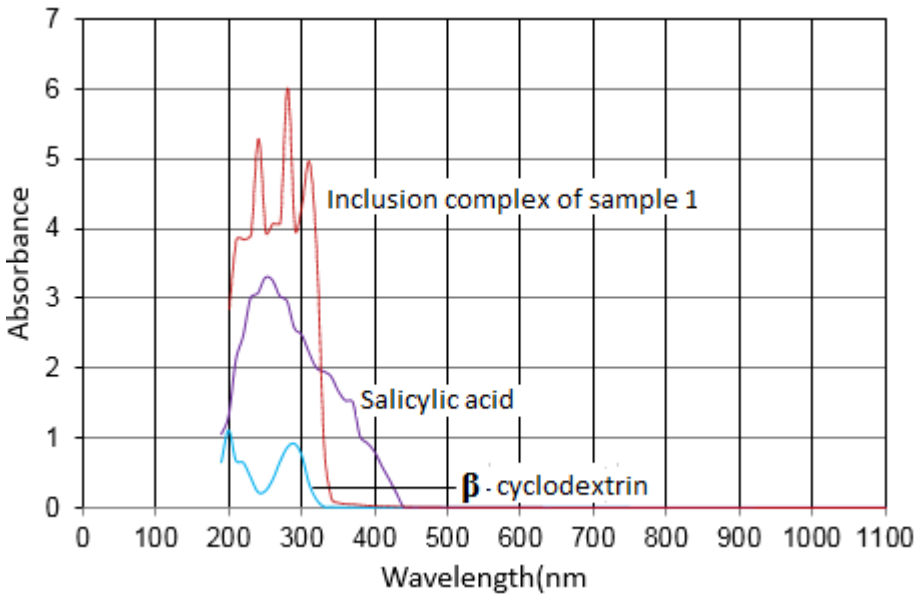

Figure 2. UV-VIS absorption spectra for: inclusion complex of samples 1- red, β-cyclodextrin (β-CD)-blue and salicylic acid - mauve.

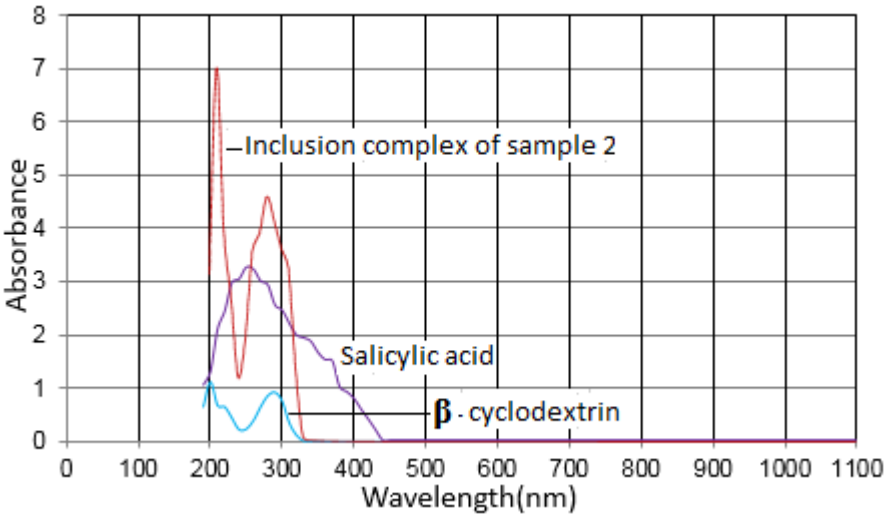

Figure 3. UV-VIS absorption spectra for: inclusion complex of samples 2- red, β-cyclodextrin (β-CD)-blue and salicylic acid - mauve.

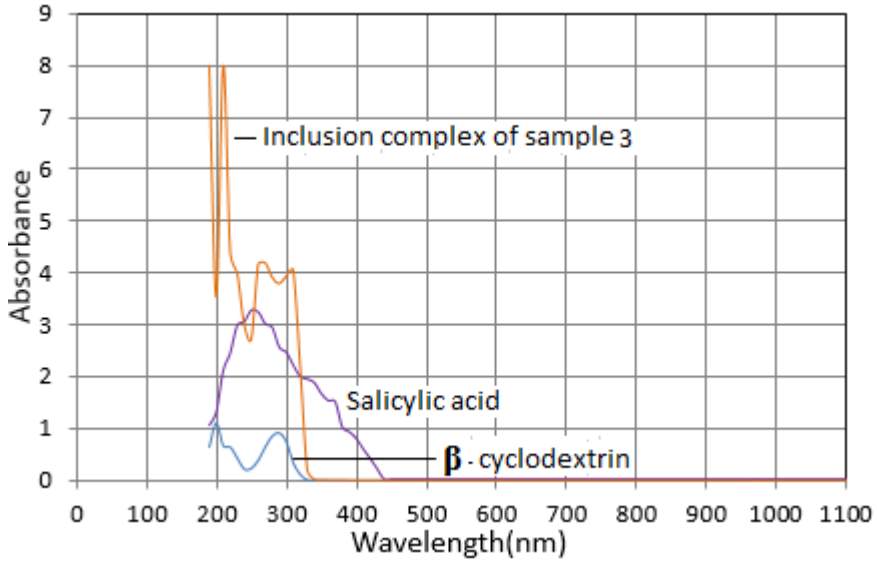

Figure 4. UV-VIS absorption spectra for: inclusion complex of samples 3- red, β-cyclodextrin (β-CD)-blue and salicylic acid - mauve.

The study of Ultraviolet-Visible Absorbtion (figures 2, 3 and 4) revealed that the salicylic acid shows an maximum absorption at around 262 nm, β-CD has two maximum absorption, the second one is sharper, around 300 nm.

Inclusion complex that it is formed in sample 1, exhibits maximums between 200 and 370 nm, the highest being 280 nm and the last around in 360 nm. We found that, after complexation with salicylic acid, the absorption spectrum of β-CD is modified. By adding β-cyclodextrin the absorbance of the inclusion complex, increases significantly compared with salicylic acid. Similar results are also obtained and by examining figures 3 and 4.

The absorption peaks of the inclusion complexes between β-CD/

salicylic acid are located far above those of β-CD. Inclusion compound between β-ciclodextrin and salicylic acid formed in sample 2 has an absorption peak between 200 and 300 nm, the highest being at 200 nm and the most well defined maximum is around 300 nm, the above the β-cyclodextrin.

In sample 3 we obtained a peak for inclusion compound by salicylic acid with β-ciclodextrină at about 220 nm and two absorption peaks for the inclusion complex, in the spectral absorption area of the β-cyclodextrin at 270-320 nm.

CONCLUSIONS

The study of inclusion complexes of cyclodextrins is one of the most important processes for the synthesis of compounds with new uses.

This study is based on the formation of a new compound, starting from two reactants, cyclodextrin and a "target" molecule, which will have new properties, [10-12].

What is specific to this process is the fact that it is not a chemical process, there is no chemical reaction between the reactants, but they physically interact and form the complex.

The interaction takes place by embedding the "guest" molecule in that of the cyclodextrin, being dependent on the structure, dimensions, polarity and solubility of the "guest" molecule.

Inclusion complexes are characterized by a stability constant, therefore the choice of the formation process must be aimed at obtaining a stable complex, a complex inert to the action of the surrounding environment and have properties protected against the reactant molecule, [13,14].

Synthesis of the inclusion complex of β-cyclodextrin with salicylic acid led to the discovery that it is a compound with uses in the pharmaceutical industry.

When forming the complex, the most practical method of synthesis is chosen, the path with the highest yield and the one in which the stability of the complex is as good as possible.

Following the formation of the complex in solution, it can be seen that the formation of the complex occurs rapidly, occurs in good yield, and that the process does not involve a complicated and expensive process. In all 3 cases realized, the complex was obtained, its formation being identified by UV-VIS spectrophotometry.

Obtaining and identifying the obtained complex, under the conditions carried out in the experimental part, indicates that upon the interaction of a salicylic acid solution with a β-cyclodextrin solution, based on a physical complexation process, a new compound with new properties is obtained, in a state of solid aggregation and which is both physically and chemically different from the two reactants.

The tests carried out were done in the same way, but the amounts of reactants are different, to see in which case, the complexation occurred better. From the results obtained, in sample 1, when the β-cyclodextrin:salicylic acid ratio was 1:3, the reaction yield was the best, the amount of complexed salicylic acid being the highest.

In this sense, we can say that the inclusion process depends a lot on the amount of "guest" molecule

introduced, on the reaction conditions, on the solubility and polarity of the molecule, the resulting chemical complex having new physical and chemical properties.

REFRENCES

[1] A. Liptak, P. Fügedi, Z. Szurmai, J, Imre, P. Nanasi and J. Szejtli (1982). *The chemistry of cyclodextrin derivates*. I. Int. Symp. on Cyclodetrins Budapest, D. Reidel Publishing, Dordrecht, 275-287.
[2] J. Szejtli (1982). *Cyclodextrins and their Inclusion Complexes*. Akademiai Kiado, Budapest, 115–122.
[3] Marcel Dekker, Inc.,(1996) *Microencapsulation. Methods and Industrial Applications*, Benita, S. (ed.) New York - Basel - Hong Kong, 3.
[4] W. Saenger (1984). *Structural aspects of cyclodextrins and their inclusion complexes*. *Inclusion compounds*. Academic Press, London, vol.2, 231-259.
[5] D. Duchêne (1987). *Cyclodextrins and their industrial uses.* Editions de Santé, Paris.
[6] Janisse Crestani de Miranda, Tércio Elyan Azevedo Martins, Francisco Veiga, Humberto Gomes Ferraz (2011). *Cyclodextrins and ternary complexes: technology to improve solubility of poorly soluble drugs*. Brazilian Journal of Pharmaceutical Sciences, vol. 47, n. 4, 665-681
[7] J. Bergsma, P.M. Bruinenberg, H. Hokse and J.B.M. Meiberg (1988). *Cyclodextrins from potato starch, recent developments*. Proceeding of the fourth international symposium on cyclodextrins, Dordrecht, 41-46.
[8] Tablet C., Dumitrache L., Minea L., Hillebrand M, (2012). *Inclusion complexes of 3-carboxy- and 7-diethylamino-3-carboxy-coumarin with α-cyclodextrin: spectral study and molecular modeling*, Revue Roumaine de Chimie, 57(7-8), 665-673.
[9] M. Vikmon (1982). *Rapid and simple spectrophotometric method for determination of micro-amounts of cyclodextrins*. I. Int. Symp. on Cyclodetrins Budapest, D. Reidel Publishing, Dordrecht, 69-74.
[10] H. Hokse (1983). *Colorimetric analysis of cyclomalto-octaose (γ-cyclodextrin)*. Carbohydrate Res., 114, 303-305.
[11] M. Mäkelä, T. Korpela and S. Laakso (1987). *Colorimetric determination of β-cyclodextrin: two assay modifications based on molecular complexation of phenolphtalein*. J. Biochem. Biophys. Meth., 14, 85-92.
[12] Horia Iustin Naşcu și Lorentz Jäntschi (2006). *Chimie analitică şi instrumentală.* Academic Pres, Cluj-Napoca, 114.
[13] Sanjoy Kumar Das, Rajan Rajabalaya, Sheba David, Nasimul Gani, Jasmina Khanam, and Arunabha Nanda (2013). *Research Journal of Pharmaceutical, Biological and Chemical Sciences Cyclodextrins*. RJPBCS, Volume 4, Issue 2, 1694.
[14] Hadaruga N.G., Hadaruga D.I, Paunescu V., Tatu C., Ordodi V.L., Bandur G., Lupea A.X., (2006). Thermal stability of the linoleic acid/α- and β -cyclodextrin complexes, Food Chemistry, 99, pg.500–508.