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NOI COMPLECȘI AI Co(II), Ni(II), Cu(II) ȘI Zn(II) CU BAZE SCHIFF CA POTENȚIALI INHIBITORI AI VIRUSULUI CUCUMBER MOSAIC (CMV). METODA „MOLECULAR DOCKING”

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Rezumat. În scopul testării combinațiilor complexe ale Co(II), Ni(II), Cu(II) și Zn(II) cu o nouă bază Schiff, ca inhibitori potențiali ai virusului cucumber mosaic (CMV), a fost realizat un studiu utilizând tehnica "Molecular docking". Complexul $[Zn_2L(OH)_2(H_2O)_4] - CMV$, având energia totală cea mai mică (-1396.0 KJ/mol), a fost selectat ca un posibil inhibitor al virusului cucumber mosaic.

Cuvinte cheie: virusul cucumber mosaic, bază Schiff, complecși, metoda "Molecular docking", programul Hex.

NEW SCHIFF BASE COMPLEXES OF Co(II), Ni(II), Cu(II) AND Zn(II) AS POTENTIAL INHIBITORS OF CUCUMBER MOSAIC VIRUS (CMV). „MOLECULAR DOCKING” STUDIES

Abstract. Was achieved a study involving Molecular docking method for selection of new Schiff Base complexes of Co(II), Ni(II), Cu(II) and Zn(II) as potential inhibitors of Cucumber Mosaic Virus (CMV). $[Zn_2L(OH)_2(H_2O)_4] - CMV$ complex with the lowest total energy (-1396.0 KJ/mol) was selected as a possible inhibitor of CMV.

Keywords: Cucumber mosaic virus, Schiff base, complexes, molecular docking, Hex program.

Introduction

One of the most studied families of plant viruses that infects a wide range of plants, tree or shrubs is the family Bromoviridae.¹ This family includes the genera *Bromovirus*,^{1,2} *Cucumovirus*,^{1,3} *Iilarvirus*,^{1,4} *Alfamovirus*,¹ and *Oleavirus*^{1,5} containing spherical icosahedral or bacilliform viruses with a tripartite positive-sense RNA genome.^{1,2,5}

The most important members of each gender are cucumber mosaic virus (CMV), brome mosaic virus (BMV) and alfalfa mosaic virus (AMV).

Cucumber mosaic virus (CMV) is the most studied member of the genus *Cucumovirus*, first information on this disease of cucurbits occurring since 1916 in Doolittle's research⁶ in Michigan and Jagger's research⁷ in New York.

Important results were obtained in 1934 when CMV was found in cucumbers (*Cucumis sativus*) causing mosaic symptoms, hence the name *Cucumber mosaic*.⁸

CMV is hosted by a wide variety of species and can attach many plants, vegetables and ornamentals (as many as 191 host species in 40 families).^{1,2,9}

Among vegetables affected by CMV are mentioned peppers (*Capsicum annum L.*), tomatoes (*Lycopersicon esculentum Mill.*), bananas (*Musa L. spp.*), muskmelon, squash, spinach and many other vegetables.^{1,2,9}

Among the most important ornamental hosts for CMV are: chrysanthemum, salvia, geranium, morning glory, petunia, tulip and many other ornamental hosts.^{1,2,9}

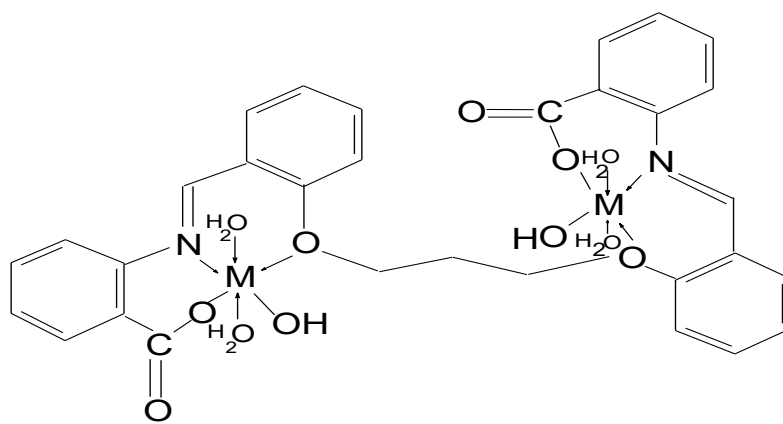
Symptoms caused by this virus are leaf mosaic or mottling, yellowing, ringspots, stunting, leaf, flower and fruit distortion.² CMV determine the "Shoestring" effect of young leaves with subsequent narrow and the entire plant to be stunted.²

The structure of cucumber mosaic virus (CMV) has been obtained by X-ray crystallography¹⁰ (code 1F15 – Protein Data Bank).

In the present paper we report a study involving Molecular docking method for selection of new Schiff Base complexes of Co(II), Ni(II), Cu(II) and Zn(II) as potential inhibitors of Cucumber Mosaic Virus (CMV).

Results and Discussion

Motivated by the results obtained by Meng et al.¹¹, in our laboratory were synthesized and characterized four transition metal complexes (Zn(II), Co(II), Cu(II), Ni(II)) with the ligand, a new Schiff Base derived from 1, 3-bis(2'-formylphenyl)-1,3-dioxopropane and 2-aminobenzoic acid.¹² The complexes will be tested as potential inhibitors of CMV using "Molecular docking" technique. The structure of complexes is presented in Figure 1.



M: Cu(II), Ni(II), Co(II) or Zn(II)

Fig. 1. The structure for the complexes with new Schiff base

Both CMV structure (Protein Data Bank code-1F15) and new complexes structures were prepared for „molecular docking” process using the Hex 5.0 program.¹³

Table 1. Total energy values of Schiff base-metal-CMV complexes

Complex	E _{total} (KJ/mol)
[Co ₂ L(OH) ₂ (H ₂ O) ₄]	-678.4
[Ni ₂ L(OH) ₂ (H ₂ O) ₄]	-660.6
[Cu ₂ L(OH) ₂ (H ₂ O) ₄]	-684.5
[Zn ₂ L(OH) ₂ (H ₂ O) ₄]	-1396.0

Structures are modeled using 3D parametric functions which encode both surface shape, electrostatic charge and potential distribution. These parametric functions are based on orthogonal spherical or polar basis functions.

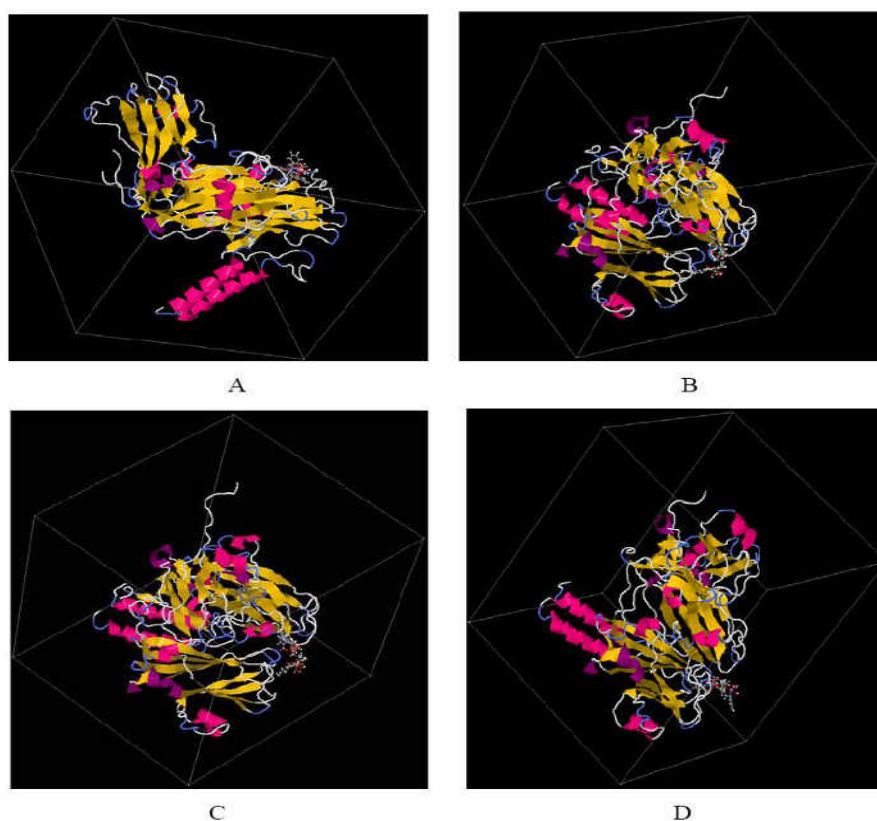


Fig. 2. The structure of Schiff base-metal-CMV complexes (Metal: Co(II)(A), Ni(II)(B), Cu(II)(C), Zn(II)(D))

To obtain of some effective results was used Fourier algorithm allowing accelerated search of the most favorable orientations of the ligand in receptor molecule, with a translation of ligand and, the other hand, has been used the spherical polar

approximation allowing both translation and rotation of the ligand to generate and evaluate optimal orientations.^{14, 15}

Because by translation and rotation of the ligand, the docking process is more complete, in Table 1 will be presented the values of total energies for Schiff Base-metal-CMV complexes involved in this study.

The structure of Schiff base-metal-CMV complexes with Jmol program is presented in Figure 2.

Conclusions

„Molecular docking” technique is an effective tool in selecting of potential inhibitor agents. When the synthesis of chemical compounds involves high financial costs, researchers used this technique to have a verdict.

For the complexes synthesized in our laboratory, data presented in Table 1 show that the $[Zn_2L(OH)_2(H_2O)_4] - CMV$ complex has the lowest total energy and therefore may present a potential inhibitory activity of CMV.

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