Effects of piroxicam and meloxicam complexes of Co (II), Ni(II), Cu(II) and Zn(II) as inhibitors of cyclooxygenase-2 determined by Molecular docking

A. BETERINGHE*
Institute of Physical Chemistry of the Romanian Academy, Laboratory of Coordination and Supramolecular Chemistry, Splaiul Independentei 202, Bucharest, 060021, Romania

Was achieved a study involving Molecular docking method for selection of piroxicam and meloxicam complexes of Co (II), Ni(II), Cu(II) and Zn(II) as inhibitors of cyclooxygenase-2 (COX-2). $[Co(HMel)_2(H_2O)_2]$ – COX-2 complex with the lowest total energy (-1616.2 KJ/mol) was selected as a possible inhibitor of COX-2.

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1. Introduction

The classical nonsteroidal anti-inflammatory drugs (NSAIDs) like aspirin, ibuprofen or indomethacin are still the most common prescribe drugs for inflammatory diseases treatment such as rheumatoid arthritis, osteoarthritis, orthopedic injuries, postoperative pains or acute mylagias [1-3]. These nonsteroidal anti-inflammatory drugs exert a primary anti-inflammatory action by the inhibition of cyclooxygenase (COX), the enzyme which catalyses the conversion of arachidonic acid to prostaglandin $(PG)H_2$ and thromboxane [4-8] and subsequent at a number of other prostaglandins which they are potential mediators of the inflammation.

Fu and his co-workers discover in 1990 [9] the existence of two isoforms of this enzyme: COX-1 and COX-2. COX-1 is constitutively expressed in most tissues and is necessary for proper functioning of the kidney and stomach [10-14]. COX-2, the inducible isoform, plays a major role in prostaglandin biosynthesis in inflammatory cells and in the central nervous system [10-14].

Because classical NSAIDs such as aspirin, ibuprofen, flurbiprofen or naproxen inhibit both forms of COX and causes gastrointestinal ulcerations or renal failure [15-17], have been attempted many studies to help finding some selective inhibitors for COX-2 [18, 19].

In the present paper we report a study involving Molecular docking method for selection of piroxicam and meloxicam complexes of Co (II), Ni(II), Cu(II) and Zn(II) [20, 21] as potential inhibitors of COX-2.

Molecular Docking Technique is one of chemometric techniques widely used for diverse selection of bioactive compounds, advanced materials with different properties. The piroxicam and meloxicam complexes of Co (II), Ni (II), Cu (II) and Zn (II) are important precursors for the guided synthesis of advanced materials which not only have inhibitory activity for COX-2 but also various other properties.

The results presented in this paper represents an important start for both guided synthesis and from a theoretical perspective.

2. Results and discussion

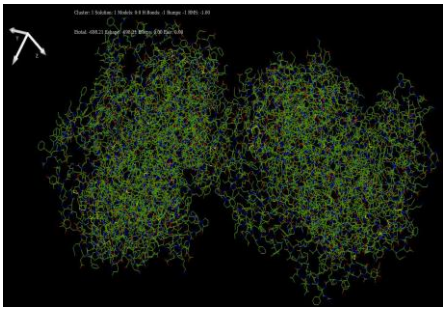
Both COX-2 structure (Protein Data Bank code – 5COX) [22, 23] and oxicam – metal complexes structures were prepared „molecular docking" process using the Hex 5.0 program [24]. Structures are modeled using 3D parametric functions which encode both surface shape, electrostatic charge and potential distribution. These parametric functions are based on orthogonal spherical or polar basis functions.

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 [25-28].

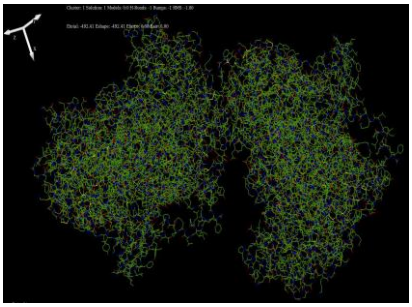
Because by translation and rotation of the ligand, the docking process is more complete in Table 1 will be presented the values of total energies for oxicam-metal-COX-2 complexes involved in this study.

Table 1. Total energy values of oxicam-metal-COX-2

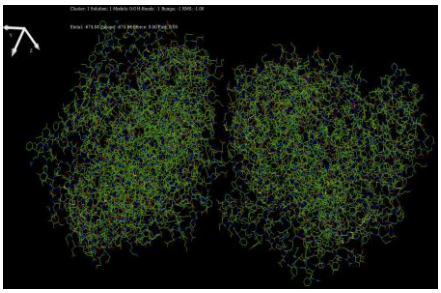
Complex	E_{total} (KJ/mol)
$[Co(HPir)_2(H_2O)_2]\cdot H_2O$	-698.21
$[Ni(HPir)_2(H_2O)_2]\cdot 2H_2O$	-674.84
$[Cu(HPir)_2(H_2O)_2]$	-363.25
$[Zn(HPir)_2(H_2O)_2]$	-634.21
$[Co(HMel)_2(H_2O)_2]$	-492.41
$[Ni(HMel)_2(H_2O)_2]\cdot H_2O$	-517.02
$[Cu(HMel)_2(H_2O)_2]$	-275.78
$[Zn(HMel)_2(H_2O)_2]$	-487.70



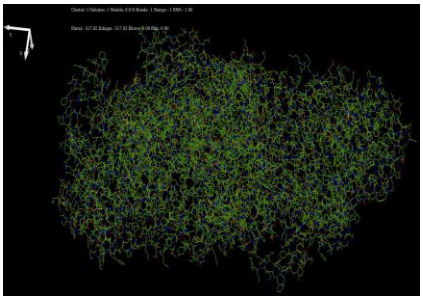
$[Co(HPir)_2(H_2O)_2]\cdot H_2O$



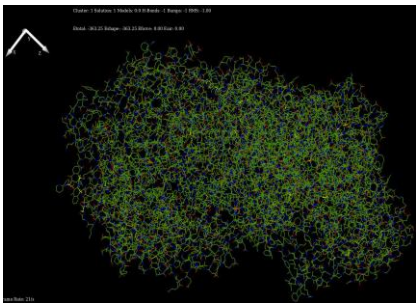
$[Co(HMel)_2(H_2O)_2]$



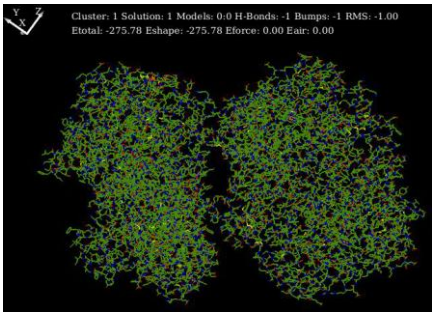
$[Ni(HPir)_2(H_2O)_2]\cdot 2H_2O$



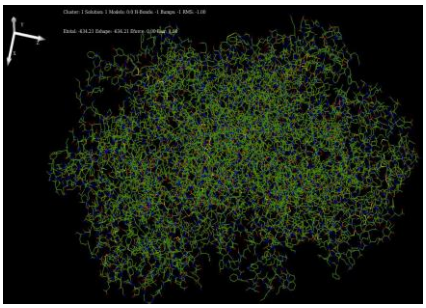
$[Ni(HMel)_2(H_2O)_2]\cdot H_2O$



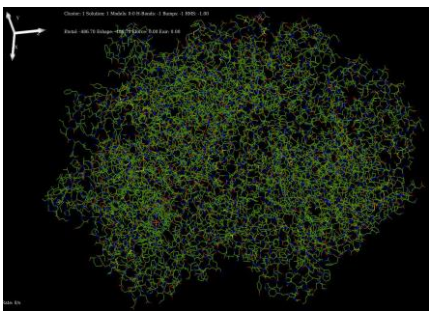
$[Cu(HPir)_2(H_2O)_2]$



$[Cu(HMel)_2(H_2O)_2]$



$[Zn(HPir)_2(H_2O)_2]$



$[Zn(HMel)_2(H_2O)_2]$

Fig. 1. Shows the structures of complexes shown in Table 1

3. Conclusions

Data presented in Table 1 show that the $[Co(HPir)_2(H_2O)_2]\cdot H_2O$ – COX-2 complex has the lowest total energy and therefore may present a potential inhibitory activity of COX-2.

On the other hand, the complexes with piroxicam as ligand have lower total energy and suggests that they may be used as potential COX-2 inhibitors.

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*Corresponding author: adrian.beteringhe@gmail.com