INTERACTION OF IBUPROFEN WITH POLYETHYLENE GLYCOL

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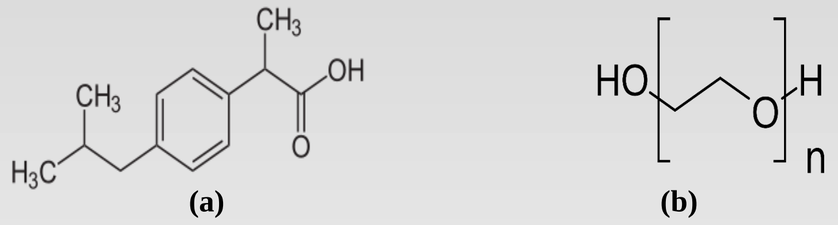
Ibuprofen (2-(4-isobutylphenyl)propionic acid) is a monocarboxylic acid that is a derivative of propionic acid. Since ibuprofen is a weak acid that is poorly soluble in water and has a flexible chemical structure, it can be divided into the following structures: an acidic side chain, a central aryl fragment, and a hydrophobic end. Ibuprofen is a non-steroidal anti-inflammatory drug, an antipyretic, and a medicinal allergen. The analgesic effect of ibuprofen is due to its ability to physically block the active site of the enzyme. This drug was patented in 1961.

Polyethylene glycol (PEG) is a synthetic polymer obtained by polymerizing ethylene oxide molecules in the presence of water and a catalyst under pressure. The molecular weights of polyethylene glycol vary depending on the duration of the polymerization process, and the weight itself represents a weight-averaged value of the individual molecules. Depending on the molecular weight, the polymer will differ in its physical and chemical properties. Polyethylene glycol has several properties: it contains primary hydroxyl groups that contribute to its weak bactericidal action; low sensitivity to pH changes (when electrolytes are introduced into its composition); low toxicity; resistance to light, temperature, and moisture; no noticeable side effects on the human body; solubility in polar solvents.



(a) **(b)**

Fig.1 Molecular structure: (a) – ibuprofen; (b) - PEG

Experimental spectrum of ibuprofen and PEG

At a frequency of 2500-3500 cm^{-1}, stretching vibrations (symmetric and asymmetric) of C-H bonds occur in the CH_2 and CH_3 groups. At a frequency of approximately 1708 cm^{-1}, stretching vibrations of C=O in the COOH group and C=C in the benzene ring occur. In the range of 500-1500 cm^{-1}, stretching vibrations of C-C in the benzene ring and deformation vibrations of C-O and C-H in COOH, CH_2, and CH_3 groups are observed. The band at 779 cm^{-1}, with the highest intensity, indicates these vibrations.

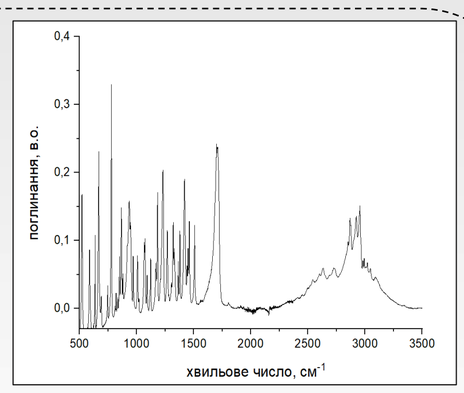
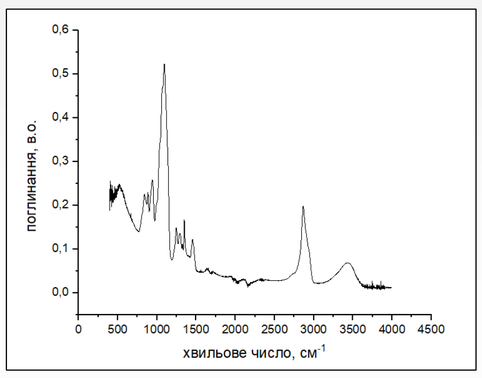


Fig. 2 Experimental IR spectrum of ibuprofen



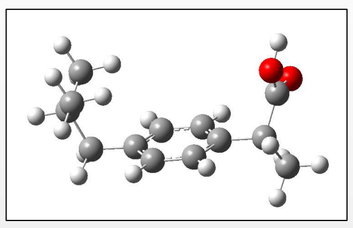
From the PEG spectrum, it can be concluded that in the range of approximately 500-1500 cm^{-1}, there are stretching vibrations for C-C and C-O, as well as deformation vibrations for C-H and O-H. In the range of 2500-4000 cm^{-1}, stretching vibrations of O-H and C-H are observed. The most intense absorption bands have wavenumbers of 1099 and 2868 cm^{-1}.

Fig. 3 Experimental IR spectrum of PEG

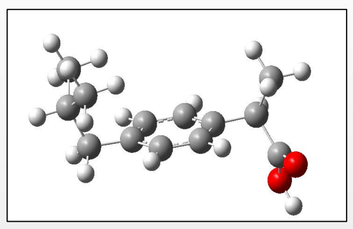
Quantum chemical calculations of ibuprofen

Using quantum chemical calculations, the IR absorption spectra of ibuprofen were computed using the DFT method (Ground State, Default Spin, Restricted, B3LYP, cc-pVTZ) and Hartree-Fock (Ground State, Default Spin, 3-21G). For the spectrum calculated using the Hartree-Fock method, the most intense bands correspond to the valence and deformation vibrations in the benzene ring and the carboxyl group (1211 and 1828 cm^{-1}). In the case of the density functional theory calculations, the most intense bands for the same vibrations have frequencies of 1145 and 1808 cm^{-1}.

Calculations were performed for two conformers of ibuprofen, which are shown in Figure 5. The calculations were carried out using the MP2 method (Ground State, Default Spin, 6-311+G (2d, p)). For the first conformer, the most intense absorption bands have wavenumbers of 1163, 1789 and 3137 cm^{-1}, and for the second conformer, they are 1159, 1784 and 3743 cm^{-1}.

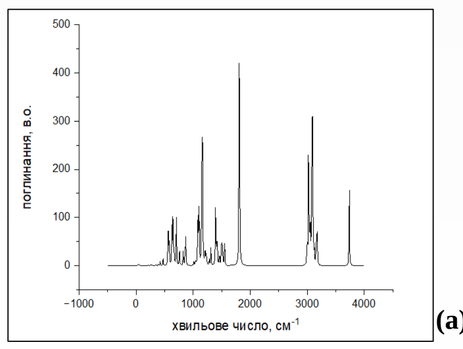


(a)

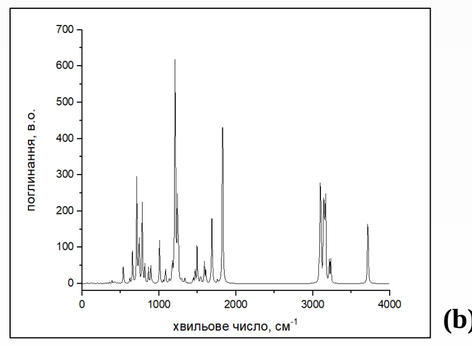


(b)

Fig. 5 First (a) and second (b) optimized conformers of ibuprofen

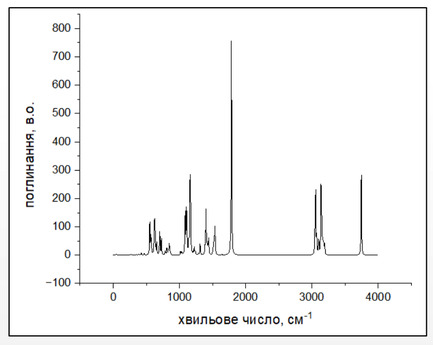


(a)

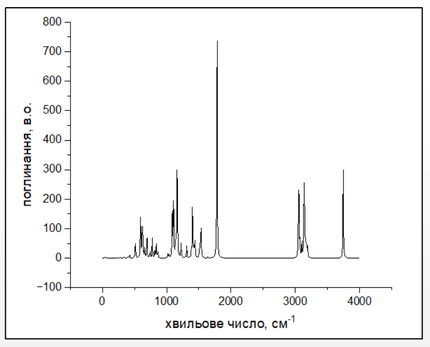


(b)

Fig. 4 IR spectra of the ibuprofen molecule: (a) – Hartree-Fock; (b) – DFT



(a)

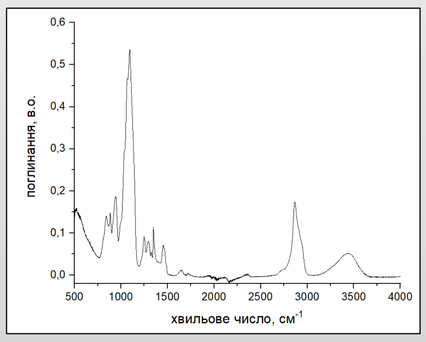


(b)

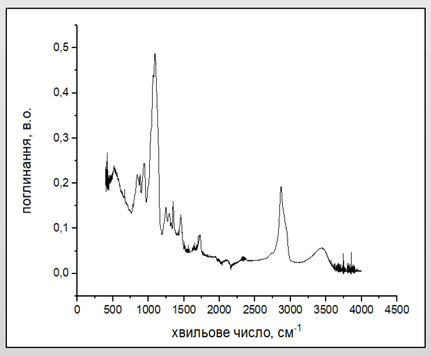
Fig. 6 Absorption spectra IR of the ibuprofen molecule using the MP2 method for the first conformer – (a), and for the second conformer – (b)

IR absorption spectra of polyethylene glycol with the addition of ibuprofen

The first mixture has a 4% concentration of ibuprofen, while the second mixture had a 30% concentration.



(a)



(b)

Fig. 7 IR spectrum of the PEG mixture with ibuprofen concentration of: (a) – 4%; (b) – 30%

From Fig. 7 (a), it can be concluded that the intense band in this spectrum is due to the fluctuation in the intensity of PEG. The given concentration is insufficient to detect the absorption bands of ibuprofen.

In Fig. 3.8 (b), it is clear that at 1730 cm^{-1}, there are valence vibrations for C=O and C=C. In the ~500-600 cm^{-1} range, there is increased absorption intensity compared to the pure PEG spectrum due to valence and deformation vibrations of C-C, C-O, C-H, and O-H groups, which are characteristic of ibuprofen. A similar situation occurs in the ~3700-3900 cm^{-1} range. Frequencies at 2954, 3744, and 3952 cm^{-1} are characteristic of valence vibrations of O-H and C-H bonds.

Conclusion

1. Comparing the IR spectra of ibuprofen calculated using three different quantum-chemical methods with experimental data shows that the MP2 method provides the most accurate results. This is due to MP2's superior ability to account for electron correlation compared to Density Functional Theory (DFT) or Hartree-Fock (HF).

2. The positions of the absorption band maxima in the IR spectra for the two different conformers of ibuprofen differ by only a few wavenumbers. This small difference makes it difficult to determine the specific conformer present in the experimental sample based on the recorded spectrum.

3. The IR spectroscopy results for the polyethylene glycol (PEG) and ibuprofen mixture (at 30% concentration) indicate potential for controlled release of ibuprofen in pharmaceutical formulations using a PEG matrix. This could lead to the development of new drug formulations that provide sustained and controlled release of the active ingredient, potentially enhancing therapeutic effectiveness and patient convenience.