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Removal of pharmaceuticals from aquatic environment using modified biomaterials

Ahmed M. Bayoumy [1], Amina Omar [1], El-Sayed M. El-Sayed [1], Medhat Ibrahim [2,*]

[1]Physics Department, Biophysics Branch, Faculty of Science, Ain Shams University, Cairo, Egypt
[2]Spectroscopy Department, National Research Centre, 33 El-Bohouth Str., 12622 Dokki, Giza, Egypt
*corresponding author e-mail address: ***medahmed6@yahoo.com*** | Scopus ID 8641587100

ABSTRACT

Pharmaceuticals in the environment are of growing interest as a result of continuous occurrence through human into municipal wastewater without adequate treatment. Green methods are needed to overcome this problem without adverse impact on the environment. In this work, modified nanobiopolymers have been dedicated to solve this problem. Accordingly, modified chitosan with nanosilica is proposed to mediate ibuprofen. Spectroscopic analysis was carried outbased on both experimental techniques such as FTIR spectrophotometry and theoretical approach represented in semiemprical calculations. QSAR descriptors were also conducted in order to quantify biological activities of both structures. Results of FTIR ensure that chitosan can be modified using silica through the formation of both chemical and physical bonds. Furthermore, FTIR shows that spectra of chitosansilica after interaction with ibuprofen suffers from a general reduction in all of its peaks and shifting in many bands. Significant reduction in bands of –NH bending and –CH stretching proposed that chitosan may interact with ibuprofen through electrostatic and hydrophobic mechanisms. PM6 calculations illustrate that amine group of modified chitosan is the most probable active site for interaction either in the complex or adsorb forms. The calculated vibrational frequencies ensure that the calculated structures correspond to minimum energy structures.

Keywords: *Chitosan; Ibuprofen; PM6; FTIR; Nanosilica; QSAR.*

1. INTRODUCTION

Chitosan is one of the bestvital products of chitin, the second abundant natural polymer on earth after cellulose [1]. It is characterized by having the highest amount of amine groups (NH_2) among biopolymers. Chitin can be extracted from the exoskeleton of terrestrials as well as aquatic animals [2]. Chitosan is the deacetyled product of chitin [3,4]. It has various characteristics related to its solubility in dilute acids, biodegradability, biocompatibility and its ability to construct strong hydrogen bonds with a broad range of structures [5]. Hence, it is reported that chitosan has several applications in various fields [6-13].

Ibuprofen or α-Methyl-4-(2-methylpropyl) benzene-acetic acid [14] is one of the common members of nonsteroidal anti-inflammatory drugs (NSAIDs). It is the most familiar analgesic medicine used worldwide where it has significant antiinflammatory and analgesic effects against pains of different body organs. However, in the last decades, ibuprofen has been recognized as one of the most frequent drugs found in several types of water [15-18]. Recently, chitosan has been emerged in wastewater treatment applications depending on its high adsorption capacities for both organic and inorganic species. This is always attributed to its numerous functional groups. Therefore, numerous research papers have utilized both pure chitosan, chitosan blends with organic and inorganic substances as well as modified chitosan in adsorbing organic and inorganic pollutants [19, 20].

However, chitosan has many physical and chemical drawbacks concerning its solubility in aqueous solutions and common solvents and its low mechanical strength. Therefore, chitosan modification processes always aim to enhance itssolubility and other chemical features. Several nanoparticles are utilized in order to enhance both itsphysical as well as itsmechanical featuressince nanotechnology can control materialmodification processes. It is well known that nanomaterials are utilized in functionalization among the focal points of advanced research papers [21-23]. Developing different substances with nanomaterials are stopped at techniques for preparation and characterization, but also involve the theories concerned with nanoscale interactions [24, 25]. With respect to bulk materials, those in the nanoscale possess increased surface to volume ratio, which in turn enhance their mechanical strength as well as their physicochemical properties [26]. Depending on nanoscale engineering technology, it is now possible to design biomaterials with specific dimensions and formulations [27, 28]. Silica is one of the most potential nanometal oxides used in the modification of natural polymers.

They always used due to their large specific surface area, their high stability in acidic media, their antimicrobial properties, their high thermal stability, their ease processing work and their low cost. Numerous research articles focused on the modification of chitosan using silica nanoparticles for environmental applications [29-35].

Several experimental techniques and theoretical tools have been utilized in investigating interactions between various species either organic or inorganic substances. FTIR technique is one of the most powerful tools used for identifying chemical structures where it provides principal information of interatomic bonding between atoms in the chemical structures. FTIR analyses strategieshavebeen knownto be the mastertool used for studying the interaction of chitosan and several species as a unique spectroscopic technique[36-38]. In addition, molecular modeling and computational simulations have proved their capabilities in studying the interactions between different chemical structures and provide reliable data concerning all biological, chemical and physical features [39-44]. Quantitative Structure Activity Relationships (QSAR) methodology is a computational tool that

can quantify the relationship between physicochemical properties of a certain biological structure and its biological activities [45]. It has become a basic concept to conduct some molecular QSAR descriptors in terms of mathematical equations that clarify directly and/or indirectly the investigated biological activities of the considered molecules [46, 47]. Recently, several researchers continue calculating QSAR parameters to evaluate the biological activityof many biosystems [48-52].

Therefore, this work aims to investigate the interaction between chitosan modified with silica nanoparticles and ibuprofen on spectroscopic basis depending on both FTIR technique and semiemprical quantum mechanical calculations. This is carried out on the two experimental and molecular modeling approaches.

2. MATERIALS AND METHODS

2.1. Chemicals.

Chitosan of medium molecular weight (from Sigma Aldrich), ibuprofen in the powder form received from SEDICO Pharmaceutical Co. and amorphous silica nanoparticles of particle size 25 nm obtained from the Building Physics and Environment Institute, Housing and Building National Research Center (HBRC).

2.2. Synthesis of microspheres.

Chitosan microspheres were prepared using ionotropic-gelation method [53]. Viscous solution of chitosan was treated by crosslinker solution, containing polyvalent ions, which can form bonds with chitosan [54] through dropping 2% chitosan solution into sodium hydroxide solution of concentration 2M [55]. Silica nanoparticles are added to chitosan with ratio chitosan: silica (96%: 4%). The final concentration of the chitosan-silica mixture is kept at 2% w/v.

2.3. Instruments.

Pristine chitosan and nanosilica modified chitosan microsphere were analyzed with ATR technique which implemented with VERTEX 70 FTIR spectrometer BRUKER, Germany at Spectroscopy Department, National Research Centre in the wavelength range from 4000 to 400 cm^{-1}.

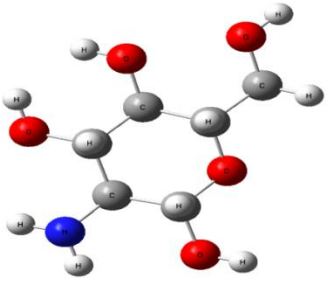
2.4. Calculation details.

The computations were calculated at semiemprical quantum mechanical calculation at PM6 method [56] via SCIGRESS 3.0. Software that is implemented at Spectroscopy Department, Physics Division, National Research Centre, NRC [57]. Geometry optimization calculations for the built-up model molecules of pure chitosan monomer and ibuprofen as well as five proposed interaction possibilities as illustrated in figure 1 were conducted at PM6 level. Some physical parameters are considered such as charge (C), dipole moment (TDM) and HOMO/LUMO band gap energy (ΔE). In addition, QSAR descriptors are calculated such as Final heat of formation (FF), Ionization potential (IP), Log P, Molar refractivity (MR), Surface area (A) and Volume (V) at the same level. Finally, vibrational frequencies are also calculated in the same theoretical method.

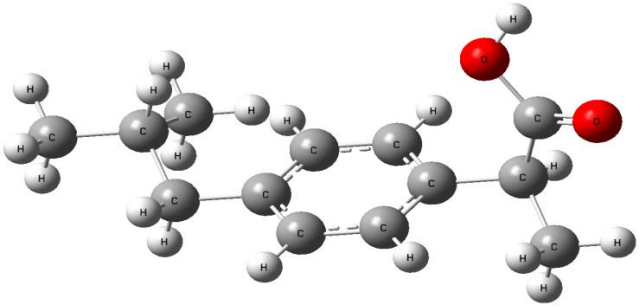
3. RESULTS AND DISCUSSION

3.1. Building model molecules.

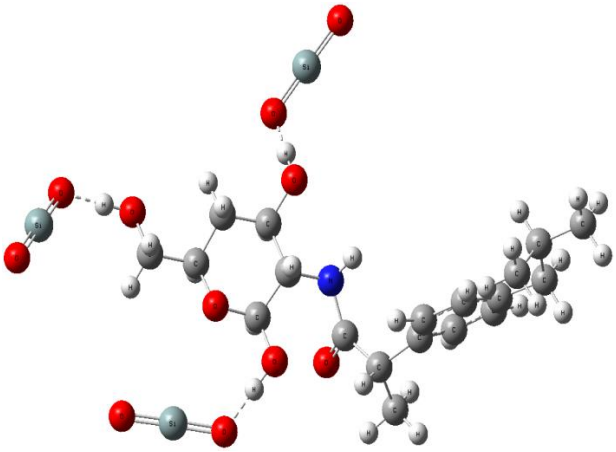
Model molecules of chitosan monomer, ibuprofen molecule and their proposed interaction probabilities are demonstrated in figure 1. The active sites of chitosan and ibuprofen, as well as their interactions, were previously illustrated at [58]. Figures 1(c-g) present the interaction of modified chitosan with silica at its non-bonding active sites as adsorb state and ibuprofen molecule.



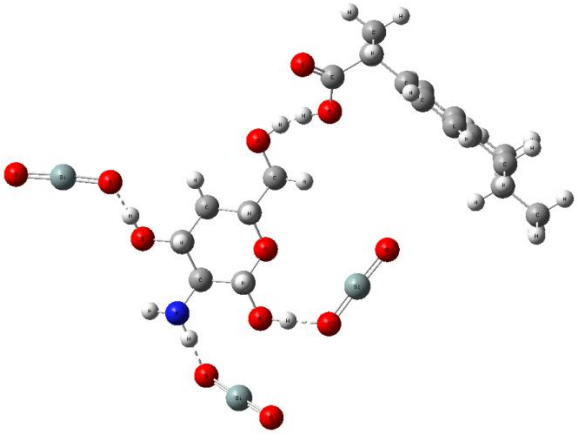
(a) Cs monomer



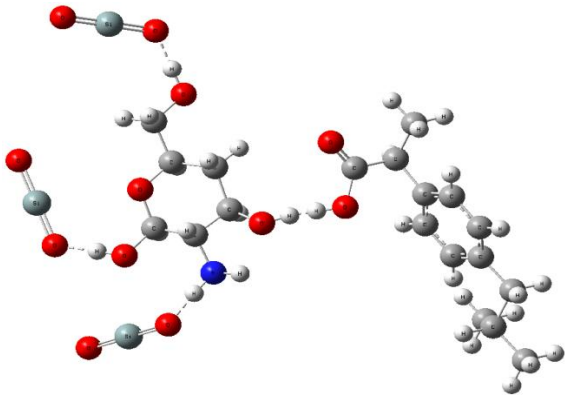
(b) IBP molecule



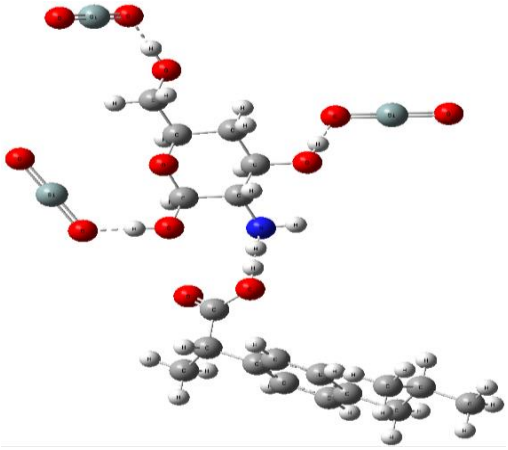
(c) Cs-Si-IBP (P_1)



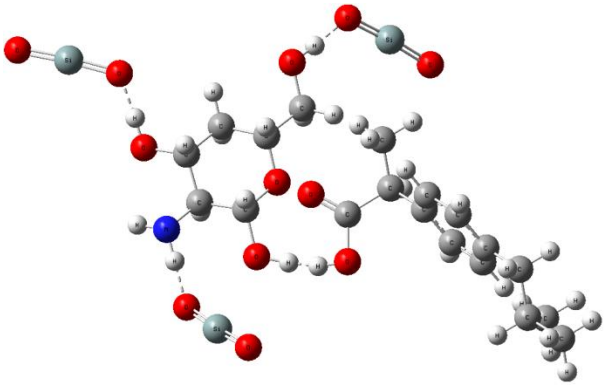
(d) Cs-Si-IBP (P_2)



(e) Cs-Si-IBP (P_3)



(f) Cs-Si-IBP (P_4)



(g) Cs-Si-IBP (P_5)

Figure 1. Optimized molecular structures of (a) chitosan monomer, (b)ibuprofen and its interaction with silica modified chitosan at PM6 level. (c) Cs-Si- IBP as a complex state P_1 and (d-g) Cs-Si- IBP as adsorb state (P_2-P_5).

3.2. Geometry optimization of model molecules.

Geometry optimization processes of chitosan, ibuprofen and their interactions in the presence of silica molecules were conducted at PM6 level. Table 1 presents some of the considered physical parameters such as energy (E), total dipole moment (TDM) and HOMO/LUMO band gap energy (ΔE).

The considered structures are all in the ground state, therefore they all possess no electric charge and are neutral. Energy is calculated as a good indicator of the stability of the calculated compounds. Interaction of chitosan modified with silica and ibuprofen decreases the energy of all the resultant structures in either complex state or in the adsorb one reflecting highly stable structures. It is obvious that interacting modified chitosan with ibuprofen through physical interaction is more preferred than chemical complex state regarding their energies. The total dipole moment is always considered as an excellent reference for the reactivity of chemical structures. TDM of chitosan monomer is greater than that of ibuprofen which seems reasonable since it has four functional groups with respect to only one for IBP [52]. TDM of both P_1 and P_4 are the highest among all the proposed structures where their TDM are 16.013 and 12.875 Debye, respectively. It is worth noticing that the considered possibilities are both related to the amine group of chitosan monomer which is well known by its high TDM value and hence its reactivity. However, the complex chemical reaction produces a structure of higher reactivity with respect to the adsorbed state. Furthermore, HOMO/LUMO band gap energy is calculated to reflect the electrical conductivity of the considered structures and hence their activity. Although chitosan owns four functional groups, its band gap is larger than that of IBP which has only one. Interacting modified chitosan with IBP reduces the calculated band gap energies of all the computed molecules. ΔE of both P_2 and P_4 is the smallest in comparison with those of other structures where they have 6.699 and 6.867eV, respectively. Based upon the considered physical parameters, interacting with modified chitosan with IBP is most probable to occur through the amine group of chitosan through either chemical or physical interactions.

3.3. QSAR descriptors.

Quantitative structure-activity relationship (QSAR) present simple and accessible scheme for forecasting biological activities of structures. It lasts to be one of the hottest topics of research work when judging the biological activity [59-61]. QSAR descriptors are calculated for the proposed structures at PM6 theoretical level. Table 2 presents the computed QSAR descriptors such as final heat of formation (FF), ionization potential (IP), Log P, molar refractivity (MR), polarizability (P), molecular weight (MW), surface area (SA) and volume (V).

Regarding FF that is usually termed as the change in heat resulting from the formation of a certain compound from its constituents [62]. The calculated FF of chitosan is lower than that of IBP where their values are -231.219 and -102.601kcal/mol, respectively. Their interaction together after chitosan modification with silica significantly lowers their FF magnitudes and P_3 possesses the lowest value of -730.741kcal/mol.Ionization potential is one of the QSAR descriptors that reflect the electrical conductivity of chemical structures and hence their reactivity. It is defined as the quantity of energy required to remove an electron away from its nucleus. The resultant IP of chitosan is smaller than that of IBP indicating that Cs is easier to be ionized than IBP that may be attributed to its numerous functional groups. However, modification of chitosan with silica and its interaction with IBP either in the complex or the adsorb states has no significant impact on the IP values of the proposed structures where they are more or less equal to that of IBP. Log P is the abbreviation for the logarithm of the partition coefficient which is useful in detecting whether the compound is hydrophilic or hydrophobic. It is usually defined as the proportion of the quantity of a substance dissolved in organic solvent to that does in aqueous one. Therefore, positive values indicate hydrophobic structures and negative ones reflect hydrophilic ones. Results in table 2 ensure that chitosan is a hydrophilic structure while IBP is a hydrophobic one. Their interaction with silica produces a slightly hydrophobic chemical structures.Addition of modified chitosan to IBP reduces its hydrophobicity.

Molar refractivity (MR) is also calculated as one of the QSAR descriptors. MR of chitosan is smaller than that of IBP and

their values equal 37.581 and 60.732. MR of the proposed interactions of modified chitosan and IBP increases greatly and they all have nearly the same MR values. Molecular weight is also calculated for chitosan, IBP and their interactions. MW of chitosan is lower than that of IBP as a reasonable result for their well-known structures. Interaction of modified chitosan with IBP in the complex state equals 531.690 au while that of all the adsorb states is 549.705 au. Surface area and volume are calculated as one of the geometrical QSAR descriptors that are usually conducted to evaluate the effect of silica on the interaction between chitosan and IBP in adsorb or complex states. The surface area and volume of IBP is greater than those of chitosan. In the same manner, those structures result from adsorbing state interaction are greater than those result from chemical interaction between modified chitosan and IBP.

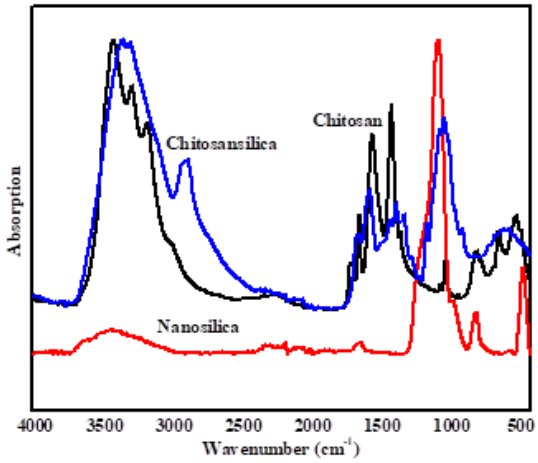


Figure 2. FTIR spectra of chitosan (Cs), silica and chitosan modified with nanosilica (Cs/Silica) microspheres.

These results are logical since those of adsorb states contain all the atoms forming both modified chitosan and IBP. Polarizability (P) can be defined as the ease of a chemical structure to be polarized in response to external forces. It reflects somehow the reactivity of chemical structures and it depends on volume of them. Interaction of modified chitosan with IBP has no significant effect on the polarizability of the resultant structures.

3.4. FTIR Spectra.

Figure 2 illustrates the FTIR spectra of pure chitosan (Cs), nanosilica and modified chitosan with nanosilica microspheres (Cs/silica). FTIR spectra of chitosan composed of a broad band at 3408-3277cm^{-1} for the stretching vibration of -NH group overlapped with -OH one [63]. A peak at 3162cm^{-1} for -NH symmetric stretching. Vibration of –CH arises at 2985cm^{-1}. The peak around 1636cm^{-1} represents the -C=O stretching vibration [64]. -NH bending is noticed around 1546cm^{-1}. -CH bending band in both CH_2 and -CH_3 groups appears at 1404cm^{-1}. Symmetric bending vibrations CH in CHOH group arise at 1336cm^{-1} [1]. -CO stretching is at 1022cm^{-1} [65]. The spectra of silica consist of few numbers of peaks. The peak at 1069cm^{-1} is assigned for the asymmetric Si-O-Si stretching. SiOH stretching peak can be distinguished at 964cm^{-1} band. Band at 794cm^{-1} can be due to SiO_4 tetrahedron ring. The peak at 460cm^{-1} is assigned for the presence of Sulphur [66]. A broad band around 1100-1000cm^{-1} represents the C-O-C functional group [67].

Interacting chitosan with silica increases the intensity of C-O-C band indicating the presence of Si-O-C bonds. Si-O stretching appears at the same wave numbers of C-O stretching. However, it is found at 1064cm^{-1} in chitosan spectra and at 1056cm^{-1} in chitosan modified with silica making a shift to lower wavenumber. In addition, the SiOH stretching band of silica disappears in its spectra. However, most of the characteristic bands of chitosan still present even interacting with nanosilica. It proves the probability of having two types of interactions; chemical and physical ones. Not only have forming chemical bonds with chitosan chains, but silica also seemed to be adsorbed on the pores of chitosan microspheres [68].

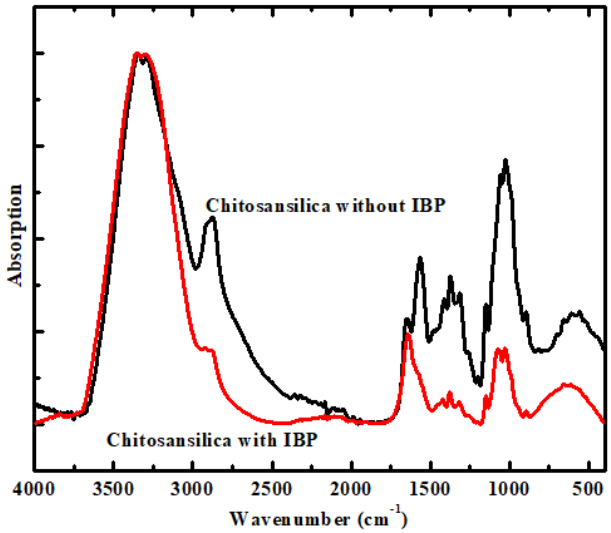


Figure 3. FTIR spectra of chitosansilica microspheres before and after interacting with IBP for 24h.

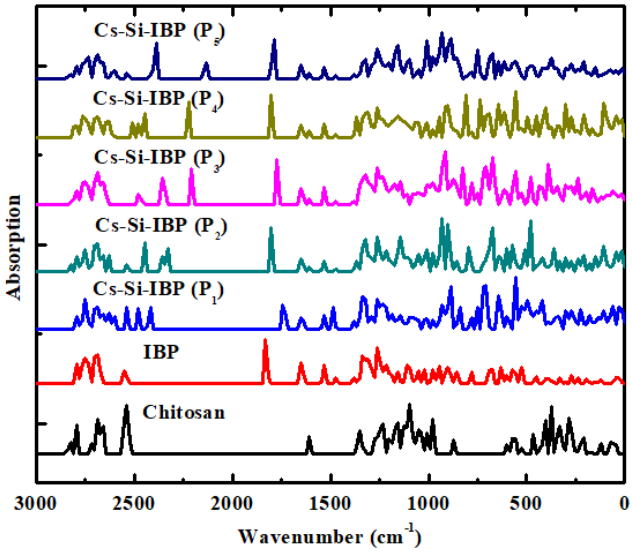


Figure 4. PM6 calculated vibrational IR frequencies of chitosan (Cs), ibuprofen (IBP) and their proposed interactions in the presence of silica (P_1-P_5).

Figure 3 presents the FTIR spectra of chitosan modified with nanosilica microspheres before and after their interaction with IBP solution for 24 hours. A general reduction in the chitosansilica peaks can be observed after interacting with IBP as well as shifting in many bands. -NH band shifts to a higher wavenumber around 1584cm^{-1}.This ensures that there is interaction occurs between chitosansilica and IBP which results in reducing its intensity that can be attributed to its consumption in IBP interaction. Figure 3 also shows the great reduction occurs in the –CH band as well as its shift to 2921cm^{-1} which may reflect hydrophobic interactions between chitosansilica and IBP. Significant reduction in bands of –NH bending and –CH stretching proposed that chitosan may interact with ibuprofen through electrostatic and hydrophobic mechanisms. In other words, this may ensure what is stated previously in

geometry optimization section that both chemical and physical interactions through amine groups of chitosan can take place.

3.5. Calculated vibrational spectra.

Figure 4 demonstrates the calculated vibrational IR frequencies of chitosan, IBP and their proposed interactions at the same PM6 theoretical level. The aim of calculating the IR vibrational frequencies of the proposed structures is not the assignment of the resultant spectra because PM6 theoretical method is not sufficient to provide accurate IR spectra of the calculated structures, hence experimental FTIR assignment is provided in the previous section [69]. The aim is whether the proposed interactions correspond to real optimum structures or not. Having positive frequencies means that the calculated structures correspond to their minimum energy structures, since these IR frequencies result from the second derivative of energy with respect to nuclear positions and hence thermochemical parameters can be obtained. As obvious from figure 4, all the resultant IR frequencies are positive which ensures that all the proposed structures correspond to optimum minimum energy state and real structures as presented in FTIR analysis.

Table 1. PM6 calculated energy (E) as kcal, total dipole moment (TDM) as Debye and HOMO/LUMO band gap energy as eV for chitosan (Cs), ibuprofen (IBP) and their proposed interactions in the presence of silica (P_1-P_5).

Structure	E (kcal)	TDM (Debye)	ΔE (eV)
Cs	-70856.219	2.811	10.839
IBP	-69159.347	2.041	9.466
Cs-Si-IBP (P_1)	-175643.364	16.013	7.084
Cs-Si-IBP (P_2)	-184427.558	5.610	6.699
Cs-Si-IBP (P_3)	-184646.734	4.554	7.499
Cs-Si-IBP (P_4)	-184198.439	12.876	6.867
Cs-Si-IBP (P_5)	-184512.475	7.925	7.695

Table 2. PM6 computed QSAR parameters including final heat of formation (FF) as kcal/mol, ionization potential (IP) as eV, Log P, molar refractivity (MR), molecular weight (MW) as au, surface area (SA) as A^2 volume (V) as A^3, and polarizability (P) as A^3 for chitosan (Cs), ibuprofen (IBP) and their proposed interactions in the presence of silica (P_1-P_5).

Structure	FF (kcal/mol)	IP (eV)	log P	MR	MW (au)	SA (A^2)	V (A^3)	P (A^3)
Cs	-231.219	-10.038	-2.108	37.581	179.171	177.65	144.23	10.168
IBP	-102.601	-9.279	3.830	60.732	206.281	240.13	205.65	15.779
Cs-Si-IBP (P_1)	-546.710	-9.679	0.656	102.581	531.690	474.39	414.53	34.091
Cs-Si-IBP (P_2)	-673.614	-9.102	0.039	105.873	549.705	518.15	431.94	33.559
Cs-Si-IBP (P_3)	-730.741	-9.348	1.284	105.688	549.705	497.14	429.42	33.958
Cs-Si-IBP (P_4)	-608.061	-9.434	0.661	105.780	549.705	501.84	435.05	34.293
Cs-Si-IBP (P_5)	-689.548	-9.728	1.947	102.907	549.705	503.41	430.30	34.730

4. CONCLUSIONS

This work aims to investigate the interaction between modified chitosan with nanosilica and ibuprofen as one of the organic pollutants. Spectroscopic analysis was carried outbased on both experimental techniques such as FTIR spectrophotometry and theoretical approach represented in semiemprical calculations. Semiemprical quantum mechanical calculations at PM6 method as well as QSAR descriptors were conducted. QSAR parameters are useful in quantifying the biological activities of both modified chitosan and IBP structures.

Results of experimental FTIR spectra ensure that chitosan can be modified using silica through formation of both chemical and physical bonds. Furthermore, FTIR shows that spectra of chitosansilica after interaction with ibuprofen suffers from a general reduction in all of its peaks and shifting in many bands. Significant reduction in bands of –NH bending and –CH stretching proposed that chitosan may interact with ibuprofen through electrostatic and hydrophobic mechanisms.

PM6 calculations illustrate that amine group of modified chitosan is the most probable active site for interaction either in the complex or adsorb forms. The calculated vibrational frequencies ensure that the calculated structures correspond to minimum energy structures.

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