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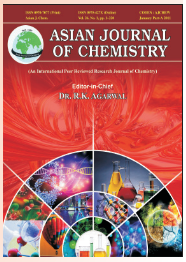

Investigation of Adsorption of 5-Fluorouracil and 5-Bromouracil onto Sepiolite and Loughlinite: An IR Spectroscopic Study

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The adsorption of 5-fluorouracil (5FU) and 5-bromouracil (5BrU) by sepiolite and loughlinite (natural Na-sepiolite) has been investigated using FT-IR spectrometry. The spectroscopic results indicate that 5-halogenouracils adsorbed on sepiolite and loughlinite are coordinated to surface hydroxyls and/or to Lewis acidic centers by hydrogen bonding interaction through the oxygen lone pairs. Some intensity and frequency changes in the OH stretching and deformation bands of surface hydroxyls (Si-OH) of the 5-fluorouracil and 5-bromouracil treated sepiolite and loughlinite were observed. Adsorption capacity of the sepiolite is found to be higher than loughlinite for 5-halogenuracils. Moreover adsorption capacity of clays were found to decrease in the order 5-fluorouracil > 5-bromouracil.

Keywords: Adsorption, 5-Bromouracil, Clays, 5-Fluorouracil, IR spectroscopy, Loughlinite, Sepiolite.

INTRODUCTION

Uracil and derivatives play important role in basic biological processes. 5-Fluorouracil (5FU) and 5-bromouracil (5BrU), (5-X-2,4(1*H*, 3*H*)-pyrimidinedione; where X = F or Br), are halogenated derivatives of uracil which are known to affect the growth of viruses, bacteria and other microorganisms. Moreover, they effectively block the replication of DNA viruses in cell culture systems[1,2]. They act as an antimetabolite or base analog. They have been found to exert profound effects in a variety of microbial and mammalian agents and are used as antitumor, antibacterial and antiviral drugs. Substitution of thymine with 5-bromouracil or fluorouracil in DNA is known to change interaction between DNA and proteins, thereby inducing various biological phenomena. Both molecules have the ability to coordinate with metals or to bind to tissues *via* metals, which interface with the growth of cancer cells. 5-Bromouracil is also used to treat inflammatory tissues. 5-Fluorouracil, is one of the oldest chemotherapy drugs, was first synthesized in 1957 and it is being used since then for the treatment of solid tumors[3,4].

Sepiolite and loughlinite belong to palygorskite-sepiolite group of phyllosilicates class of clay minerals. The structures of the minerals consist of talc-like chains (ribbons) parallel to the fiber axis and are formed by an alteration of blocks and channels that grow up in the fiber direction[5] (c-axis). Loughlinite is known as natural Na-sepiolite and is virtually identical in appearance to sepiolite[6]. They have micro-channels and have the ability to adsorb selectively both polar and non-polar organic molecules and ions[5,7,8]. Sepiolite group of clays have been widely used as catalysts for oxidation and/or polymerization reactions of aromatic molecules[5,9]. Recently clays have been investigated as drug carries[10,11]. In previous studies adsorption of 2-aminopyridine and 2,2'-bipyridine onto loughlinite were investigated[12,13]. It was shown that IR spectroscopy is a valuable technique for shedding light on the nature of the surface species formed on clays. Previously[14,15] we have investigated the adsorption of 5FU and 5BrU into the layers of montmorillonite. Continuing our studies on the adsorption of drugs on the clay surfaces, in this study the adsorption of 5FU and 5BrU onto sepiolite and loughlinite (natural Na sepiolite) from Anatolia has been investigated using FT-IR spectrometry. To our best of knowledge no study has been reported on the adsorption of 5BrU or 5FU onto sepiolite group of clays. The objective of this study is to investigate sorption properties of halogenated uracils by sepiolite group of clay minerals using vibrational spectrometry.

EXPERIMENTAL

In the present work, natural sepiolite and natural loughlinite from Mihalliccik-Eskisehir region of Anatolia (Turkey) were employed. The clay samples were ground to fine powder of < 0.5 mm particle size and were analyzed by X-ray diffraction, differential thermal and IR spectroscopic techniques for purity.

The results indicate that loughlinite is associated with analcime (approximately 8 %) and Al_2O_3 (approximately 6 %) and has detectable calcite impurity (IR; 1435 cm^{-1}). The chemical compositions of starting clays are as follows: Sepiolite: 58 % SiO_2, 25.5 % MgO, 0.5 % Al_2O_3, 0.5 % K_2O, 0.5 % CaO, 0.05 % TiO_2, 0.05 % Na_2O, 0.01 % P_2O_5, 0.01 % MnO, 0.05 % $\Sigma(FeO + Fe_2O_3)$, 14.5 % loss on ignition, loughlinite: 55.0 % SiO_2, 12.5 % MgO, 7 % Na_2O, 6.5 % Al_2O_3, 2.8 % $\Sigma(FeO + Fe_2O_3)$, 1.1 % K_2O, 1 % CaO, 0.30 % TiO_2, 0.1 % P_2O_5, 0.05 % MnO, 14 % loss on ignition.

The adsorbates (5BrU and 5FU) were reagent grade and were used as received. 5-Bromouracil or 5-fluorouracil treated clays were prepared by immersing clays in aqueous solution of 5BrU/5FU in sealed bottles at room temperature for 2 days, after then clay organic suspension was washed and centrifuged at 7000 g for 10 min. Samples were also prepared by solid-solid reactions[16].

The IR spectra (4000-400 cm^{-1}) of self-supporting films, prepared according to Madejova[17], oriented films supported onto a CaF_2 window or KBr discs of samples were recorded on a Bruker Tensor 27 FT-IR spectrometer (0.5 cm^{-1} resolution) based on averaging 70 sample and 16 background scans.

RESULTS AND DISCUSSION

The molecular model of 5BrU /5FU is given in Fig. 1. The FT-IR spectra 5BrU and 5FU treated sepiolite and loughlinite are given in Fig. 2. The FT-IR spectrum of 5FU treated sepiolite in comparison to those of starting sepiolite and solid 5FU is given in Fig. 3. The 1870-1233 cm^{-1} region of the IR spectrum of 5FU treated sepiolite, after subtracting the vibrational bands of the natural sepiolite, in comparison to that of solid 5FU is given in Fig. 4.

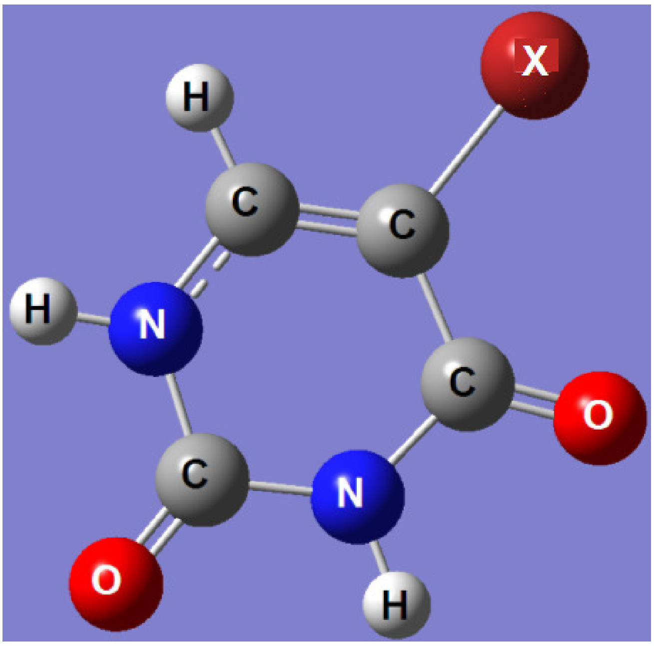

Fig. 1. Molecular model of 5-halogeneted uracils (X= Br or F)

Theoretical studies[18,19] have shown that keto-enol tautomerism exists in 5BrU and 5FU. But although in the isolated state 5BrU and 5FU may exhibit tautomerism, in the solid

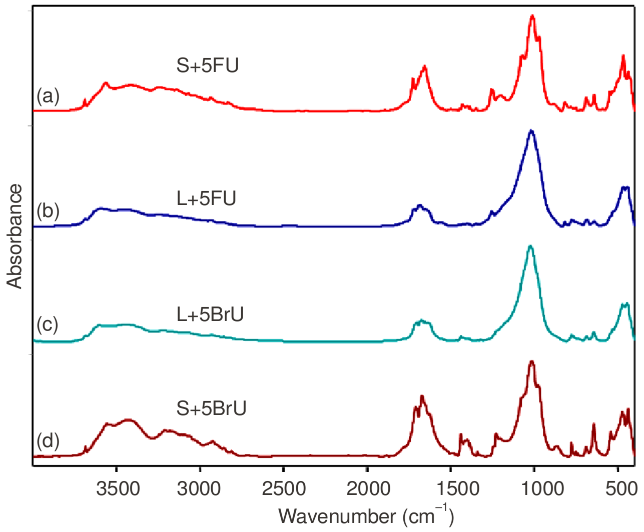

Fig. 2. FT-IR spectra of 5FU (a, b) and 5BrU treated (c, d) sepiolite (S) (a, d) and loughlinite (L) (b, c)

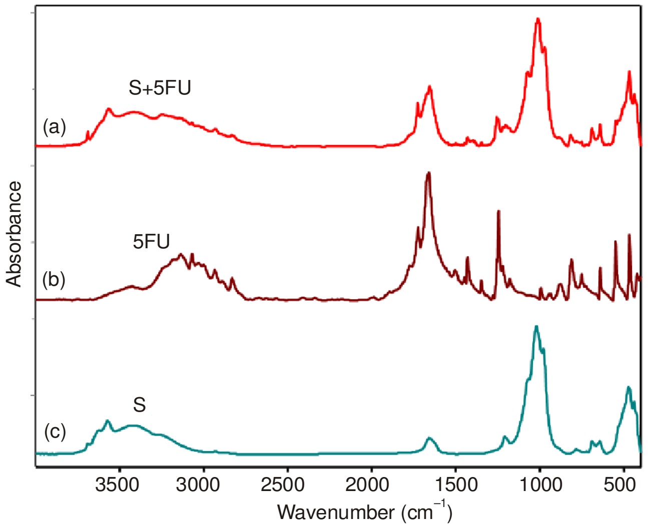

Fig. 3. FT-IR spectra of 5FU treated sepiolite (S + 5FU) (top), solid 5FU (5FU) (middle) and natural sepiolite (S) (bottom)

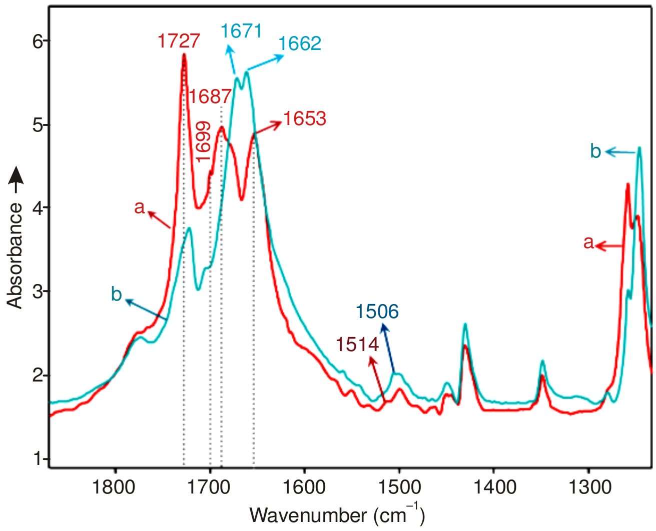

Fig. 4. 1870-1233 cm^{-1} region of the IR spectra of 5FU treated sepiolite, after subtracting the vibrational bands of the natural sepiolite (a), and solid 5FU (b)

state they exist only in keto form. In the IR spectra of solid 5BrU and, 5FU, OH stretching band around 3700-3500 cm^{-1} is not observed and presence of strong C=O stretching bands indicate that 5BrU and 5FU in solid state are in keto form. On the other hand we also observed strong C=O stretching bands in both 5BrU and 5FU treated sepiolite and loughlinite, indicating that adsorbed 5BrU/5FU molecules are in the keto form as like as in the solid phase (Fig. 1).

In solid 5FU and 5BrU, the oxygen atoms are known to involve in strong hydrogen bonding interactions, therefore we compare the 5FU/5BrU vibrational wavenumbers adsorbed on clays, to those of 5FU/5BrU in an argon matrix[20-22]. The C=O stretching wavenumbers of 5BrU and 5FU adsorbed on clays are found to be lower that those in Ar matrix, but slightly higher than those of solid phase, indicating that adsorbed 5BrU/5FU oxygens involve H-bonding interaction but less than in solid case. For example in the IR spectra of the C=O stretching wavenumbers of adsorbed 5FU onto sepiolite are found to be 1727 and 1687 cm^{-1}, corresponding wavenumbers are 1754 and 1742 cm^{-1} in Ar matrix[20] and 1715 and 1671 cm^{-1} in solid state. Tables 1 and 2 list the adsorbed 5FU and 5BrU wavenumbers onto clays, in comparison with those of in Ar matrix[20] and in solid state.

TABLE-1
INFRARED BANDS (cm^{-1}) OF ADSORBED 5FU ONTO SEPIOLITE AND LOUGHLINITE AND WAVENUMBERS OF 5FU IN ARGON MATRIX AND SOLID 5FU

5FU		5FU on clays		Approximate description[14]
Ar[20]	Solid[14]	Sepiolite	Loughlinite	
3468	3141vs	3144	3148	NH stretch
3468	3141vs	3144	3148	NH stretch
3416	3001vs			NH stretch
	3069vs	3073	3060	CH stretch
1754	1715s	1727	1721	CO stretch
1742	1671vs	1699sp 1687	1699 1673	CO stretch
1685	1662vs	1653	1653	Ring stretch
1477	1506m	1514	1514	Ring stretch
1412	1430s	1430	1422	Ring stretch
1334	1349m	1349	1341	NH i.p. bend
1247	1246m	1249	1244	CF stretch + ring stretch
807	813s	819m	816	i.p. ring def.
757	771w	779m	779	CO o.p. bend + o.p. ring def.
750	751m	755	755	Ring stretch
731	730w	741	740	CO o.p. bend + o.p. ring def.
653	643m	647	647	NH o.p. bend

i.p. = in plane; o.p. = out of plane

TABLE-2
INFRARED BANDS (cm^{-1}) OF ADSORBED 5BrU ONTO SEPIOLITE AND LOUGHLINITE AND WAVENUMBERS OF 5BrU IN ARGON MATRIX AND SOLID 5BrU

5BrU		5BrU on clays		Approximate description
Ar[20]	Solid	Sepiolite	Loughlinite	
3459	3168	3176	3172	NH stretch.
3413	3055	3056	3058	NH stretch.
3040	3032	3031	3029	CH stretch.
1761	1699	1710	1706	CO stretch.
1729	1674	1699 1676	1700 1676	CO stretch.
1635	1623	1653	1653	Ring stretch.
1463	1497	1514	1512	Ring stretch.
1400	1419	1421	1424	Ring stretch.
1327	1342	1344	1341	NH i.p. bend.
760	778	779	779	CO o.p. bend.+ o.p. ring def.
753	755	755	756	Ring stretch.
714	742	742	742	CO o.p. bend.+ o.p. ring def.
656	647	647	647	NH o.p. bend.

The most probable binding sites of sepiolite group of clays[5] are expected to be surface hydroxyls and Lewis acidic centers. It is well known that the broken Si-O-Si bonds of the terminal silica tetrahedra on the external surfaces of sepiolite compensate their residual charge by accepting a proton or hydroxyl group and form Si-OH groups[5]. The Si-OH bond stretching band is observed at about 3700 cm^{-1} in the IR spectra of sepiolite group of clays[23]. Alteration of this band indicates interactions of the adsorbate with the silanol groups. The major changes, observed in the IR spectrum of 5FU and 5BrU treated sepiolite, are the increase in the intensity and the decrease in the wavenumber of the Si-OH stretching vibration. The alteration due to the adsorption of 5FU/5BrU, observed in the Si-OH stretching band of loughlinite, was found to be lesser extend than that of sepiolite, probably because the surface Si-OH groups in loughlinite appear to be less abundant than in sepiolite. The OH stretching region of 5FU and 5BrU treated sepiolite are given in Figs. 5 and 6, respectively, in comparison with those of natural sepiolite. If adsorbed 5FU/5BrU molecule interacts with surface silanol groups of sepiolite, alterations in the Si-OH stretching band is expected. Thus, the spectroscopic results indicate that 5FU/5BrU molecules adsorbed on sepiolite and loughlinite are mostly coordinated to surface hydroxyls by H-bonding interaction. On the other hand frequency decrease on OH stretching vibration of zeolitic water of the sepiolite structure upon adsorption of 5-halouracils was also observed (Figs. 5 and 6). Alterations of the vibrational wavenumbers of zeolitic water molecules may indicate the

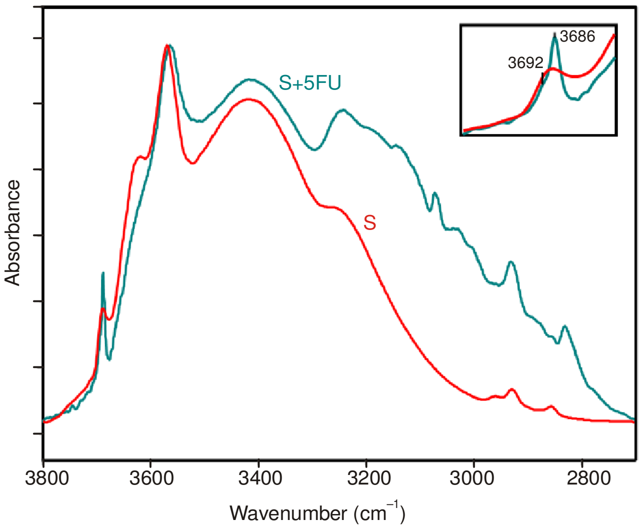

Fig. 5. 3800-2700 cm^{-1} region of the IR spectra of 5FU treated sepiolite (S + 5FU) and natural sepiolite (S). The detail part of the 3735-3655 cm^{-1} region is given in the upper frame

penetration of some of 5FU/5BrU molecules into the channels of sepiolite-loughlinite structure. On the other hand we also observed the slight changes in bandwidth and wavenumber of Si-O stretching mode (Fig. 7) which is a further proof of the penetration of some of 5FU/5BrU molecules into the channels of sepiolite-loughlinite structure, because this mode is known to be significantly affected by changes in swelling and orientation clay platelets[24].

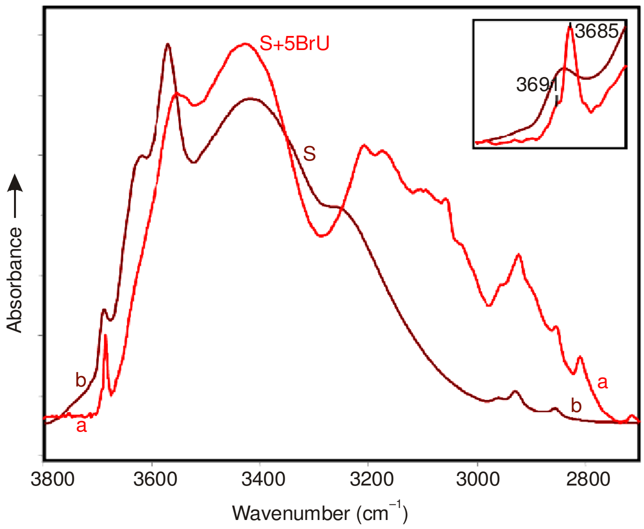

Fig. 6. 3800-2700 cm^{-1} region of the IR spectra of 5BrU treated sepiolite (S + 5BrU) and natural sepiolite (S). The detail part of the 3735-3655 cm^{-1} region is given in the upper frame

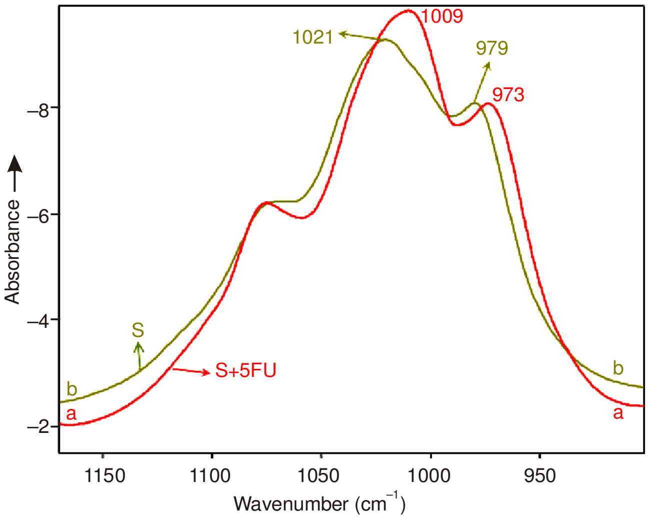

Fig. 7. 1200-900 cm^{-1} region of the IR spectrum of 5-FU treated sepiolite (a), and natural sepiolite (b)

Conclusion

The comparison of the IR spectra of the adsorbed 5BrU/5FU to that of free corresponding free molecules offered data on the nature and characteristics of the formed clay-organic complexes. 5-Bromouracil (5BrU) and 5-fluorouracil (5FU) were adsorbed on the sepiolite and loughlinite due to coordination of halogenated uracils through one of the C=O group oxygen by hydrogen bonding through the surface hydroxyl groups and/or Lewis acidic centers. Alterations of the vibrational wavenumbers of zeolitic water molecules may indicate the penetration of some of the 5BrU and 5FU molecules into the pores. Adsorption capacity of the sepiolite is found to be higher than loughlinite for 5-halogenuracils. Moreover adsorption capacity of clays were found to decrease in the order 5FU > 5BrU.

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