

## Constrained synthesis of 5-Fluorouracil entrapped poly amino alkyl siloxane, an organic in-organic hybrid

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**Abstract.** Controlled drug carriers are important for the treatment of chronic illnesses. They are classified based on their physicochemical properties, release mechanism and preparation methods employed. Mesoporous materials with surface functionalization have attracted many researchers for drug carrier applications, among them amine functionalized mesoporous materials are largely studied. A disadvantage is costly organic templates are used during the hydrothermal synthesis of the mesoporous materials to control both the pore and particle size; the templates are subsequently removed by calcinations. The present study is focused to employ a novel, simple, one spot synthesis of poly aminoalkyl siloxane, an organic inorganic hybrid, by the hydrolysis and condensation of triethoxy aminopropyl silane that can entrap 5-fluorouracil (5-FU), a model drug. The synthesized material was characterized by FT-IR spectroscopy. The data strengthening that it can be a convenient substitute for hitherto reported several mesoporous materials to take-in and release slowly of any potentially toxic drugs to treat colo-rectal cancer like diseases.

**Keywords:** 5-Fluorouracil, poly amino alkyl siloxane, organic-inorganic Hybrid, colon cancer, drug delivery

### 1 Introduction

The common drug delivery systems which are conventionally used for delivering drugs are cross-linked polymer matrices, like hydrogels and supra-molecular polymer aggregates apart from the different forms of microencapsulation carriers [1-4]. The controlled release systems can be classified according to their physicochemical, pharmaceutical aspect, release mechanism and preparation methods [5]. Naturally available polymers and synthetic polymers [6-10] are being competitively used in the sustained release drug delivery system along with the many mesoporous functionalized silica materials as a nanoparticles or nanofiber or in the microgel forms with their own safety aspects and advantages. Mesoporous materials have attracted many researches in relation to its synthesis and various aspects of application since from the discovery of M41S mesoporous materials [11, 12]. Since the silica

mesoporous materials are being with high surface area ( $>800 \text{ m}^2/\text{g}$ ), large pore volume ( $1 \text{ cm}^3/\text{g}$ ) and large pore size (20 to  $100 \text{ \AA}$ ) extensive research has been carried on it for making it to use as drug carrier [13, 14]. There is also a possibility for making surface functionalization of the silica mesoporous materials depending on the requirement [15]. But, while synthesizing the silica mesoporous materials the pore size should be seriously taken into considerations because, if the drug molecule size is more than the intended pore size then the special template material is required for the synthesise of mesoporous materials which is not a cost effective one. Total particle size should also under consideration while intending the mesoporous silica material as a drug carrier, because if the total particle size is more than 300 nm due to aggregate formation will lead to thrombosis [16].

Usually, the templates determine the particle size of the silica mesoporous materials, while the chain length of the hydrophobic domains and the processing procedures alter the particle size [17, 18]. In order to occupy the drug molecule inside the mesopores, the specific interactions should be achieved by making functionalization of the mesopores wall. So, apart from the usage of costly templates, surface modification is also to be practiced which can be possibly affected by post synthesis grafting or co-condensation. In recent years, amine functionalized silica mesoporous materials have attracted many researchers [19, 20].

In the present work, we have developed a fast, simple synthesis for the drug carrier with amine functionality; amino alkyl silane is hydrolyzed in water to form a silica gel matrix which can entrap any drug regardless of their size, polarity, etc. Tetra ethyl ortho silicate is also co-hydrolyzed and condensed with the above compound to obtain solids enriched with voids. This solid matrix with the drug swells in water and permits sustained release of the drug through diffusion. The same method can be applied to uptake of any drug irrespective of size and nature.

## 2 Experimental

### 2.1 Synthesis of drug entrapped amino alkyl siloxane

The synthesis is carried out through sol-gel route in which Tetra ethyl ortho silicate, Amino ethyl tri-ethoxy silane, 5-Fluorouracil model drug were mixed with water with different ratios, allowed to form precipitate and dried it to obtain the solid substance.

### 2.2 Characterization

The FT-IR spectrum (Fig. 1) of 3-aminopropylsiloxane (APS) solid illustrates the characteristic peaks for amino alkyl and siloxane groups. The  $-\text{NH}_2$  stretching vibrations yielded a broad envelope in the high energy region; it is due to hydrogen bonding. In this envelope, the stretching vibration of defective SiO-H groups and water are blocked; the  $-\text{CH}_2-$  stretching vibrations of the alkyl group which generally occur just below  $3000 \text{ cm}^{-1}$  were largely blocked. The  $-\text{NH}_2-$  bending vibration occurred at  $1569 \text{ cm}^{-1}$ . Of the  $-\text{CH}_2-$  bending modes resolved at  $1387 \text{ cm}^{-1}$  and

1488  $\text{cm}^{-1}$ , the former is very weak and sharp illustrating burial of the alkyl groups in the solid matrix. The peak at 1335  $\text{cm}^{-1}$  is assigned to  $-\text{C}-\text{N}$  vibration. The peak at 1134  $\text{cm}^{-1}$  is due to asymmetric stretch of  $\text{Si}-\text{O}-\text{Si}$  group and its symmetric vibration occurred at 779  $\text{cm}^{-1}$ ; the corresponding bending mode occurred at 441  $\text{cm}^{-1}$ . The residual unhydrolyzed  $-\text{OCH}_2\text{CH}_3$  is evidenced by the intense sharp peak at 1033  $\text{cm}^{-1}$ .

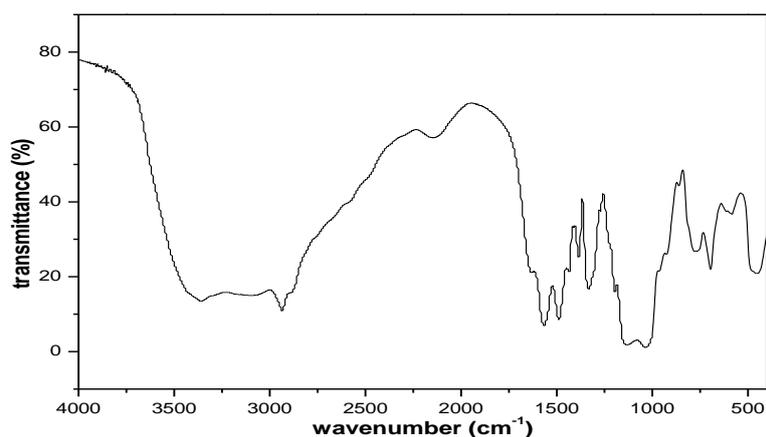


Fig. 1. FT-IR Spectrum of APS

The FT-IR spectrum (Fig. 2) of 5-Fluorouracil (5-FU) is as follows.

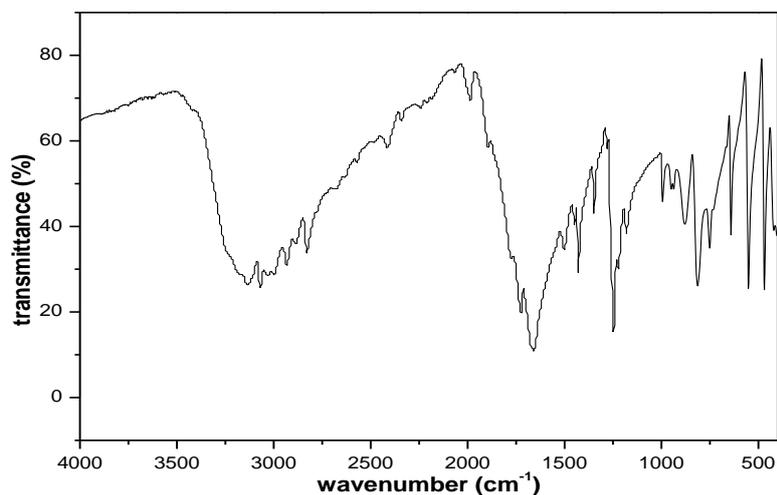


Fig. 2. 2. FT-IR Spectrum of 5-FU

The FTIR spectrum of 5-FU trapped 3-aminopropyl siloxane matrix is shown in Fig. 3. It is expected that the amino group of siloxane can interact with the 5-FU moiety via hydrogen bonding, and so its vibrational characteristics might be affected. It is evidenced by the change in the characteristic change in the shape of the envelope due to  $\text{-NH}_2$  stretching in the high energy region. The amino group bending vibration at  $1566\text{ cm}^{-1}$  of is shifted to  $1561\text{ cm}^{-1}$  supporting interaction with the 5-FU. The  $\text{C=O}$  stretching vibration of 5-FU occurred at  $1660\text{ cm}^{-1}$ , but it is shifted to  $1637\text{ cm}^{-1}$  confirming strong interaction of it with the amino groups of aminopropyl siloxane. In addition, the free  $\text{C=O}$  stretching vibration of 5-FU which occurred at  $1723\text{ cm}^{-1}$  is completely absent illustrating the interaction of all of it with the amino groups. The  $\text{-C-N-}$  stretching vibration of aminopropyl siloxane supported 5-FU illustrates strengthening of the bond as its peak at  $1247\text{ cm}^{-1}$  in 5-FU is shifted to  $1333\text{ cm}^{-1}$ . The  $\text{C-F}$  group vibration is not exempted, as its original vibration at  $813\text{ cm}^{-1}$  in 5-FU is shifted to  $816\text{ cm}^{-1}$  due to change in its orientation. Compared to changes in the peak positions of  $\text{-NH}_2$  groups, the symmetric and asymmetric stretching vibrations of  $\text{-Si-O-Si-}$  are very much affected; the asymmetric stretch is shifted from  $1134\text{ cm}^{-1}$  to  $1133\text{ cm}^{-1}$ , and the symmetric stretch from  $753\text{ cm}^{-1}$  to  $779\text{ cm}^{-1}$ . The  $\text{-O-CH}_2\text{-CH}_3$  vibration is changed from  $1028\text{ cm}^{-1}$  to  $1033\text{ cm}^{-1}$ . Such changes illustrate the strengthening of siloxane links presumably due to interaction with the 5-fluorouracil. So, 5-fluorouracil is verified to experience significant interaction inside the amino siloxane matrix and it is the cause for a dramatic change in the morphology of the matrix.

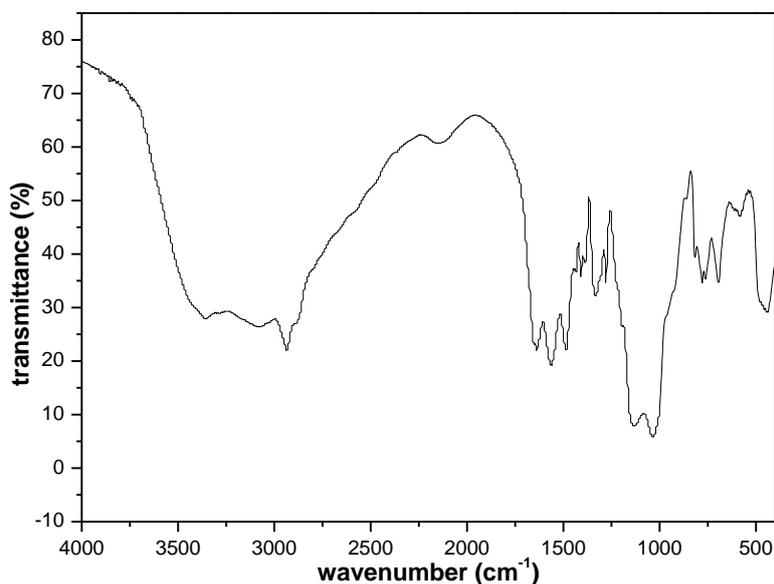


Fig. 3. FT-IR spectrum APS + 5-FU.

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