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Development of pH Independent Cyclodextrin Capped Silica Hybrid as Nanocarrier

F. Tariq* and U. Rafique
Fatima Jinnah Women University, Department of Environmental Sciences, 46000, Rawalpindi, Pakistan

Porous silica base hybrids have great potential for useful application such as drug delivery due to their high stability and hydrophilicity. Silica hybrids also serve as an outstanding host for guest molecules after gatekeeper attachment under specific pH conditions. It is proposed that variations in pH (a measure of hydrogen ion concentration), acidic (< 7) or basic (> 7), strongly affects the hydrophilicity of silica materials. The present study is designed to prepare silica hybrid by adapting the sol–gel protocol, follows the functionalization with vanadium by mixing method. The functionalization of silica hybrid thus enhances and improves the hydrophilicity of material without pH dependence. The functionalized hybrid is further loaded with drug (cisplatin) and grafted with cyclodextrin (gatekeeper) to achieve control drug release from the carrier. The formation of synthesized product is confirmed by characterizing it through different analytical techniques such as the Fourier transform infrared and scanning electron microscopy. The Fourier transform infrared method confirms the development, modification, and grafting of loaded silica hybrid by the appearance of peaks at 956, 1637, 1109, and 3165 cm^{-1}. Scanning electron microscopy image of the product clearly reveals irregular, non-porous scales particles with random dispersion of loaded drug. The activity (release) of the drug from loaded material can be investigated by dialysis membrane experiment for 72 h under dark and uncontrolled pH conditions.

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1. Introduction

In past, nanotechnology has flourished with advancements in biomedical research, leading towards designing of biocompatible silica based carriers for controlled and targeted drug delivery [1]. In the field of drug delivery, various inorganic and polymeric materials are widely acknowledged due to the significant increase in solubility, reduced cytotoxicity, and improvement of the of hydrophilicity of both carrier and drug. Among the class of inorganic polymer, polysialates (aluminosilicates) are the preferred choice because of their affinity to chemically bound or absorbed drug on the targeted site. In addition, drug release from polymeric carrier displays highly pH sensitive release rates, for instance, polyacidic polymers show significant release at low pH but increasing pH swell the carrier [2]. In spite of eco-friendly and economical aspects of these materials. It is proposed that the biocompatible nature of silica particles play a significant role in nanomedicine applications [3] but sometimes, acidic nature of silica matrix restrict their use in biological systems. However, these conventional materials did not gain wide acceptance due to their sophisticated properties such as high pH sensitivity, acidity, and hydrophobic nature may hinder the continual drug release. The limitation associated with material's properties led to the modification of silica particles with inorganic materials. The modification thus enhances hydrophilicity and provides an alternative to achieve rapid release rate without depending upon pH. The present study is an exertion toward the synthesis of silica-vanadium (SiV) hybrid using simple, economical, and an environmentally viable means i.e., sol–gel and mixing method. The material will serve as an efficient carrier for the rapid release of cisplatin drug showing no dependence on pH.

*corresponding author; e-mail: fatimatariq86@gmail.com

2. Material and methods

2.1. Reagents

Sodium silicate was procured from Riedel-de-Haen, vanadium(III) chloride, cetyl tri-methyl-ammonium chloride (CTAC) was purchased from BDH, phosphate buffer saline (PBS) from Caisson, and β-Cyclodextrin was purchased from Calbiochem.

The present research work provides with a cost-effective and successful synthesis of silica hybrid for determining controlled drug release. The adapted sol-gel has proven to be an economical alternate approach for synthesizing silica hybrid. Furthermore, the use of sodium silicate in place of expensive chemicals such as TEOS is also advancing the present study.

The protocol of Zheng et al. [4] was adapted for hybrid formation, leading towards the drug loading and gatekeeper grafting. For synthesis, sodium silicate was hydrolysed, followed by the addition of 0.78 mg/l of CTAC (cetyltrimethylammonium chloride). The solution was heated (2 h), cooled, washed, filtered [5], and calcined for 5 h at 700 °C [6]. For fictionalization purpose, the different ratio (3:1) of silica and vanadium were hydrolysed and mixed with CTAC to form gel. The crude product was filtered, washed repeatedly with ethanol, and oven dried at 100 °C [7]. The product is coded as "SiV".

2.2. Drug loading and gatekeepers attachment

The pre-synthesized silica hybrid was loaded with drug by dissolving 1 g of SiV powder in 100 ml of drug solution. This mixing ensues the continuous stirring of slurry for 48 h in dark conditions. The successful loading of the drug pursued gatekeeper attachment by adding a known amount of cyclodextrin into drug loaded solution and vigorously stirring for 72 h on the hotplate. The solution is filtered, washed, and vacuum dried (70 °C) overnight [8].

3. Results and discussion

3.1. FTIR

The Fourier transform infrared FTIR (FTIR-8400 Schimadzu, Japan) results of loaded (SiV) hybrid obtained are presented in Table I. The intense peak recorded at 956 cm^{-1} indicates hybrid formation (SiV) [9], whereas shoulder peak at 1109 cm^{-1} confirms gatekeeper attachment. In addition, drug loading on the synthesized hybrid is confirmed by a peak at 1637 cm^{-1} [10]. The broad peak at 3165 cm^{-1} represents OH, clearly indicating that hydrophilicity is induced and enhanced.

TABLE I

FTIR peaks of loaded silica hybrid (SiV)

Important frequencies of recorded spectra	Assignment
956 cm^{-1}	hybrid formed
1637 cm^{-1}	drug loaded
1109 cm^{-1}	cyclodextrin attached
3165 cm^{-1}	OH (hydrophilicity induced)

3.2. SEM

The SEM scan of (SiV) revealed irregular, non-porous scales particles randomly dispersed with void spaces, resulting in relatively increase particle size (11 nm). Low dispersion of cisplatin (see Fig. 1) was likely due to enhanced hydrophilicity and attachment of cyclodextrin as elongated structures embedded within the silica matrix.

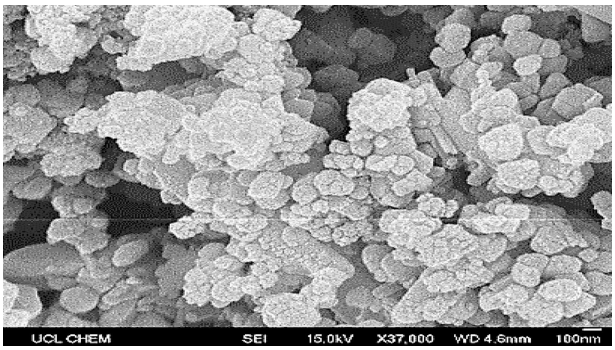

Fig. 1. SEM image of loaded silica hybrid (SiV).

3.3. Drug release experiments and discussion

The potential of the loaded synthesized product was tested as a drug carrier for the controlled release. The mechanism involved the pH-independent release rate of the drug from synthesized hybrid and effect of the activity of gatekeeper during release. The dialysis membrane experiment was performed by suspending the loaded particles in dialysis bags by immersing loaded material in phosphate buffer saline by keeping the other end closed. Each synthesized material (10 mg) was added separately to 12 ml of drug solution and stirred for 24 h at room temperature. This was followed by the addition of a known amount of cyclodextrin and stirring for another 72 h. For drug release experiments, the loaded dialysis bag was immersed in a glass beaker containing 50 ml of phosphate buffer solution (PBS). Aliquot of the released solution was drawn after regular intervals of contact time (2, 4, 6, 8, 12, 24, 48, and 72 h) and analysed on UV-visible (UV-1601, Shimadzu, Japan) spectrophotometer at $\lambda_{max} = 705$ nm [11].

The graphs plotted for pH dependent and independent drug release are observed in Fig. 2. It shows significant increase in the drug release (75–85%) with the increase in time (initial 72 h) for pH independent experiment. It is attributed to gatekeeper grafting which initiate the drug release due to the creation of repulsive forces between free silica and ammonia groups (cisplatin) and OH groups (hydrophilicity) [12]. Comparatively pH-dependent drug showed gradual drug release (35–40%) due to the effect of pH (acidic and basic sites on the loaded carrier).

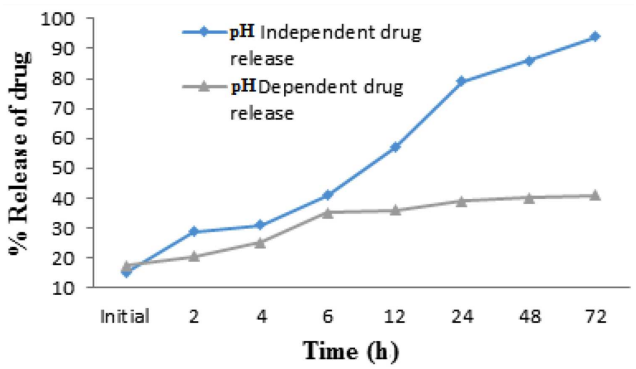

Fig. 2. Comparative study of pH independent and dependent drug release.

4. Conclusion

It is concluded that a number of factors contribute towards the significant drug release (75–85%) due to vanadium functionalization, improved hydrophilicity, and gatekeeper attachment, creating repulsive forces between loaded drug and substrate. The present study is a successful attempt to achieve pH independent drug release by enhancing the hydrophilicity of synthesised material (SiV).

Acknowledgments

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