RESEARCH ARTICLE

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Facile and Green Synthesis of Silica Based Hydrogel for Drug Loading Application

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In this study, we have chosen chitosan as capping and stabilizing agent for silica-based hydrogel synthesis. Chitosan, a biomaterial linear polysaccharide gives the pathway to greener synthesis. The source of Silica that has been chosen is sodium silicate which is very cheap when compared to other silanating agent. But the more important feature of these hydrogels is that they shows the similar properties in the qualitative and quantitative analysis. The applications of these nanoparticles are also like another silane reagent. The hydrogel was characterized by UV-Visible, FTIR, XRD, and SEM with EDX analysis. The prepared nanoparticle in presence of acidic medium shows the behavior of hydrogel and they swell in water because of hydrophilicity of water. The hydrogel is applicable in drug loading such as isoniazid.

Introduction

The development of silica-based hydrogel was several reported methods for their synthesis. But the greener approach for the synthesis, now days is becoming more interesting for R& D is promising because of eco-friendly nature of starting materials applying principle of Green Chemistry for use of safe chemicals, renewable feed stock and minimizing the potential for accident causing less harm to the environment. Also, the cost-effectiveness can focus if the starting material is easily available and cheaper as compared to any other source available then it is more useful from the industrial point of view. In the present work, chitosan is selected as capping agent in the synthesis of silica hydrogel and reaction is just simply catalyzed in alkaline medium. The biopolymers are less toxic and more bio-compatible in nature [**1**]. The chitosan is an example of biopolymer which can be obtained from natural resources or recycled shrimps and crab shells. Chitosan is a cationic natural polymer obtained from deacetylation of biopolymer chitin which is present in crustacean shells of crabs, lobsters, insects, and other lower plants [**2,3**]. Chitosan is a mucoadhesive cationic polymer at acidic pH and is non-toxic [**4-6**]. Chitosan also has a fungicidal effect, wound healing properties, and ability to cut down cholesterol level [**7**].

Although chitosan has several advantages, its potential application is limited by its low solubility in aqueous media. It is insoluble in aqueous solutions above pH 7 and soluble in dilute acids like acetic acid due to the protonation of its free amino groups [**8**]. To overcome the problem of solubility, several water-soluble derivatives of chitosan have been synthesized, which act over a wide range of pH examples such as carboxymethyl chitosan (CMC) and N-trimethyl chitosan chloride [**9**]. CMC is a key derivative of chitosan and has exceptional chemical, physical, and biological properties such as low toxicity, biocompatibility, good antimicrobial activity, film-forming ability, and capacity to interact with different substances and solubility in the wide range of pH. It is used in medical and pharmaceutical areas, mainly for the controlled release of the drug [**10-12**]. The chitosan is more promising material for hydrogel preparation because of hydrophilic nature and presence of functional groups such as amino and hydroxyl [**13**].

The biopolymer is responsible for gelation in the method and the synthetic method preferred here is a sol-gel method. The gel formed in the reaction mixture is dried in an oven that dried gel responsible for a porous nature of hydrogel. The silica nanoparticle or silica composite generally forms a spherical morphology outer layer to this morphology or porous network to same is developed due to the chitosan only. Due to the porosity of the hydrogel, it finds application in drug loading and drug release study [**14**]. In the pores, the drug is completely loaded to hydrogel so that the drug release study is more effectively carried out. The drug selected for this study is isoniazid which acts as an anti-tuberculosis drug, the application suitable for pharmaceuticals [**2**]. The smaller drug molecule, the antibiotic release by hydrogel of the chitosan-coated molecule is because of hydrophilicity [**15**]. Mesoporous silica nanoparticles are having a promising role in hydrogel preparation because of pore volume, tunable particle size and biocompatibility [**16-18**].

In the present work silica source is sodium silicate which produces silica nanoparticle morphology in hydrogel is spherical and another important material of synthesis is chitosan biopolymer and the synthesis becomes complete greener approach towards hydrogel preparation. The number of a method known for synthesis of hydrogel but by use of sodium silicate is less commonly reported. The good porosity observed in morphology is applicable in drug loading study.

Experimental

Materials

The sodium silicate (water glass) is purchased from SD fine chemicals. The Chitosan is purchased from SD fine, Acetic acid, Sodium hydroxide is taken as purity grade, and de-ionized water is used.

Method: The method of synthesis involved the Sol-gel method

1) Chitosan solution

The chitosan dissolution was performed by using 1 gm of Chitosan in 1% of the acetic acid solution. The same solution allowed to stir for 24 h at room temperature. The clear solution of chitosan was formed.

2) Silica hydrogel synthesis

The sodium silicates 20 mL was mixed with distilled water and continuously stirred for 30 min. To the complete clear solution formed 2 mL of 0.1 N NaOH is added. The precipitate formation is observed in this solution by drop-wise addition of chitosan solution till gel formation is observed. The gel was washed with ethanol and water. The gel was then dried at 80 °C for 3-4 hrs.

3) Drug release study

To study the release profile of the isoniazid loaded silica hydrogel, dried drug loaded samples were immersed in a solution of pH 1.2 and stirred continuously. At scheduled time interval, the 1-5 mL solution was withdrawn, filtered, and assayed spectrophotometrically at 200-600 nm by using UV-Visible spectrophotometer for the determination of the cumulative amount of drug release up to a time t. Each determination was carried out five times. To maintain a constant volume, 5mL of the solution having the same pH was returned to the container [**19**].

Characterization

The ultraviolet and visible spectra of silica hydrogel was carried out by adjusting pH of the solution up to 1.2 at this point the powder material had completely dissolved and a clear solution was obtained. The drug release study was performed at room temperature in the wavelength range of 200-600 nm on a UV-Vis spectrometer (Shimadzu UV-1700). The Fourier transform infrared spectroscopy was carried out with KBr pellet method by using Shimadzu FTIR-8400 in the range of 400-4000 cm^{-1}. The crystallinity of hydrogel was determined by using XRD pattern. X-ray diffraction (XRD) patterns, recorded using a Rigaku Rotalflex RU-200B diffractometer with a CuKα (λ = 1.5418A°) in the scanning angle of 20 to 80 degrees. The morphology of hydrogel has been determined using the Scanning electron microscopy using S-4800, Hitachi, Japan operated at 15kV. The elemental detection carried out by Brucker.

Results and discussion

The visual observations: The color of the silica hydrogel is pale yellow in color. The SiO_2 nanoparticles are usually insoluble in water but in our synthesized sample, they show the clear solution in distilled water having pH value 1.2. The solubility in water was one of the important features of hydrogel synthesis.

Ultraviolet and visible spectroscopy

The UV-visible spectra carried out for optical property study. The absorbance value is also responsible for paramagnetic and non-paramagnetic nature of the hydrogel in the broad range of UV spectra [**20**]. The UV-Visible spectra of prepared hydrogel from acidic solution sample forms a clear solution and gives a good absorption in spectra as shown in **Fig. 1** and the optical properties in **Fig. 2.** The characteristic peak of hydrogel shows the value of 290 nm. This band shows the non-paramagnetic behavior of silica also known as a B2 band this is because of deficiency of oxygen on the surface of silica network [**21**]. The silica nanomaterial usually does not show the absorption in the visible range. But we got the very good results 290-310 nm range for silica nanomaterial reported in an earlier study [**22**]. The band gap observed for hydrogel is calculated as 2 eV by using Taucs plot method. This value is for silica materials. This result may find useful application in solar device fabrication also.

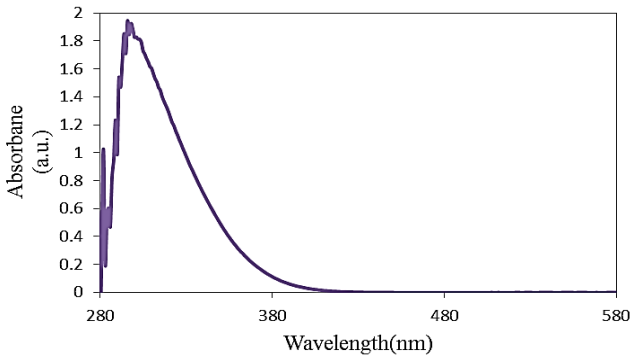

Fig. 1. UV-Visible spectra of Hydrogel

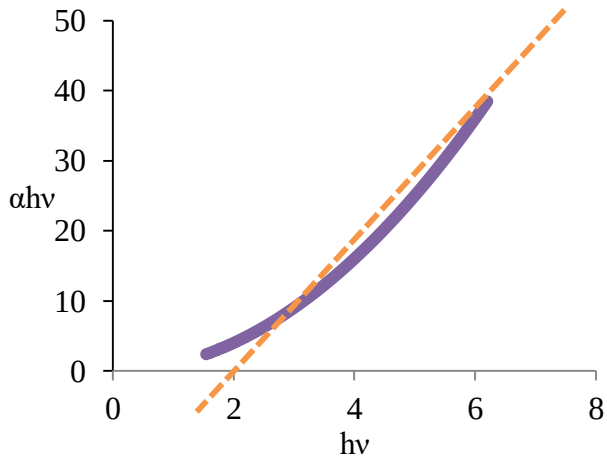

Fig. 2. Optical image of band gap spectra of Hydrogel.

Drug loading (Isoniazid) study on silica hydrogel

In this study, we took a prepared solution of silica-based hydrogel and added 1M solution to the given hydrogel at a ratio fixed 1:1 to 1:5 mL of isoniazid loaded on the surface of the hydrogel. The loading here shows that the drug loading of isoniazid increases there is decrease in the absorbance of the sample. The decrease in intensity of absorbance shows that more amount of drug is loaded on its surface. The amount of drug loading increases the decrease in intensity of hydrogel sample i.e. effective drug loading as shown in **Fig. 3** and **Fig. 4**. The kinetics study shows that given mechanism of drug loading obeys equation of straight line and shows first order of reaction as shown in **Fig. 5**. This hydrogel can be more suitable for many antimicrobial drugs, protein and any other small drug moiety. The given results prove the effective drug release study.

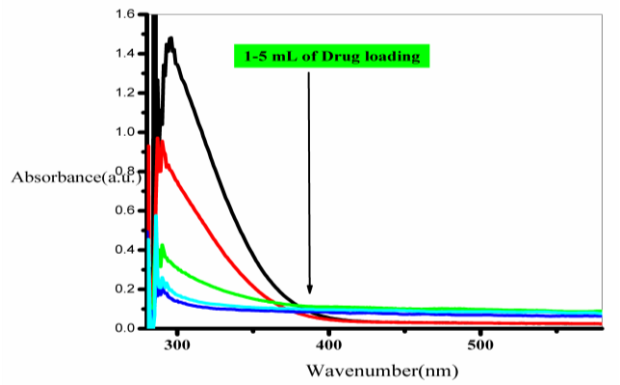

Fig. 3. UV-Visible spectra of Isoniazid loading study on Hydrogel.

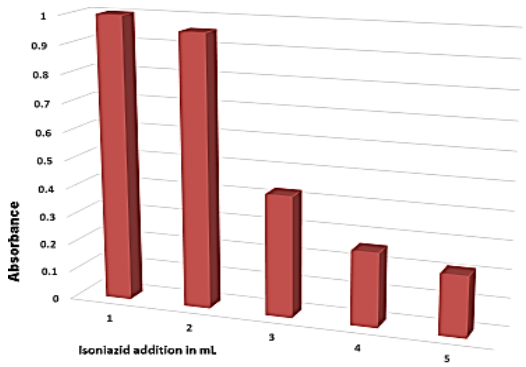

Fig. 4. Activity of Isoniazid loading study.

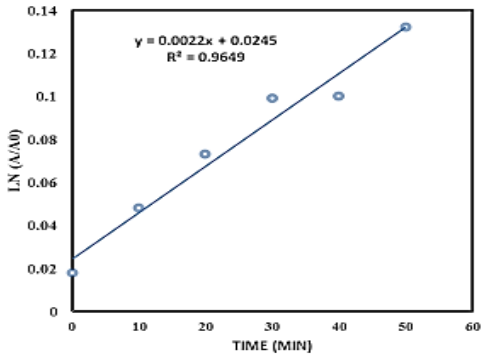

Fig. 5. Kinetics of Isoniazid loading study.

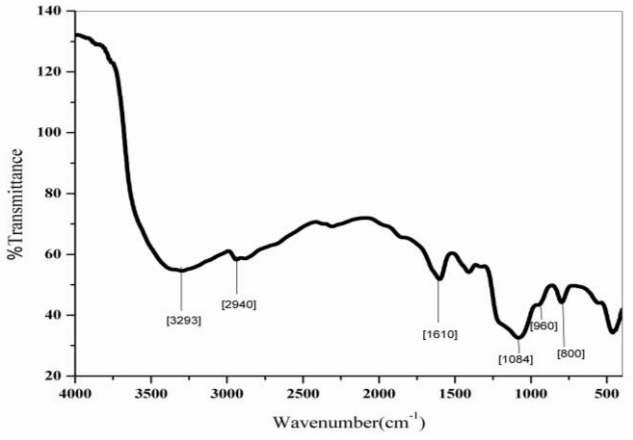

Fig. 6. Fourier transforms infrared Spectra of hydrogel.

Fourier transforms infrared spectroscopy

Major regions of the FTIR spectra of chitosan-silica hydrogel are depicted in **Fig. 6**, characteristic absorption regions of chitosan with O-H (stretching, 3293 cm^{-1}), C-H (2940 cm^{-1}), C=O (1610–1670 cm^{-1}), N-H (hydrogen-bonded 1557 cm^{-1}) and C-O (stretching 1084 cm^{-1}) [**23**]. Basically, these results for pristine chitosan indicate hydrogen bonding exists within the molecular chain. As in situ silica was incorporated, most of the typical absorption bands remained largely unchanged. The intensity of the interaction of hydrogen bonding between Si-O on silica and functional groups on chitosan decreases in the N-H regions as well. The appearance of a new absorption band at 967 cm^{-1} associated with the stretching of Si-OH bonds was observed. Further, the characteristic absorption band of Si-O specified at 1000-1100 cm^{-1} band becomes sharp as silica concentration increases. The two strongest IR absorption bands at ~800 and 480 cm^{-1} initiates from the extension and flexural vibrations of Si-O-Si bonds. FTIR analysis also shows that the band at 960 cm^{-1} was slightly shifted towards lower wave number as the particle size is reduced. This observation suggests a change in the local bonding structures of Si and O atoms at smaller particle size [**24,25**].

X-ray Diffraction (XRD)

The XRD of hydrogel as shown in **Fig. 7** that the 54.5% amorphous nature and remaining crystalline in nature. The more amorphous nature is suitable for drug release study. In this XRD two peaks show the chitosan characteristic this is at 2θ = 10° and 20.2° due to [020] and [100] plane [**26,27**]. Apparently, some crystalline form was disrupted due to the interaction of chitosan and silica, which caused the region of 2θ from 5 to 30° to become broad. The remaining crystalline peaks are due to silica nanomaterials. The average crystallite size is obtained from the broadening effect of the most intense peak employing the Scherer formula:

$$D = k\lambda/\beta Cos\theta \quad [1]$$

where, β was the full width half maximum (rad), λ was the wavelength of the X-ray, θ is the angle between the incident and diffracted beams (degree) and D is the particle size of the sample (nm). By using the above formula [1], 36 nm grain size of hydrogel material was obtained. The sharp peak observed in

XRD pattern reveals face-centered cubic lattice and the peak value matches in the given JCPDS file no.78-2500 and 80-0018 [**28,29**].

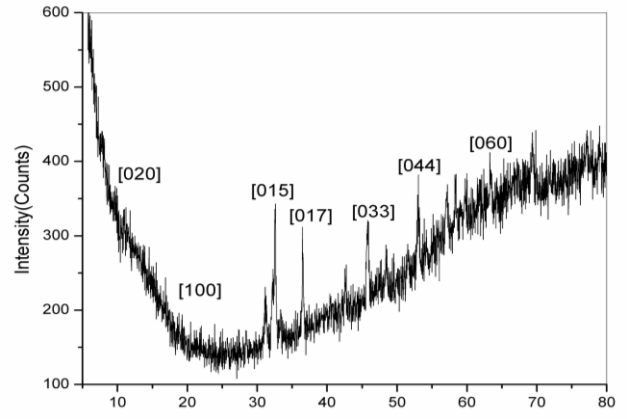

Fig. 7. X-ray diffraction Spectra of Hydrogel

Scanning Electron Microscopy (SEM)

The scanning electron microscopy of silica hydrogel as shows in **Fig. 8** that the spherical silica nanoparticles. The aggregation of spherical nanoparticles with white color chitosan is observed at outermost surfaces. The well-coated silica with chitosan as capping and stabilizing agent for hydrogel is formed. Also, in the elemental analysis of hydrogel the more percentage of oxygen as compared to silica material, confirms the SiO_2 formation [**30**]. Here the hydrogel shows the morphology matches with another method of silica nanomaterial formation.

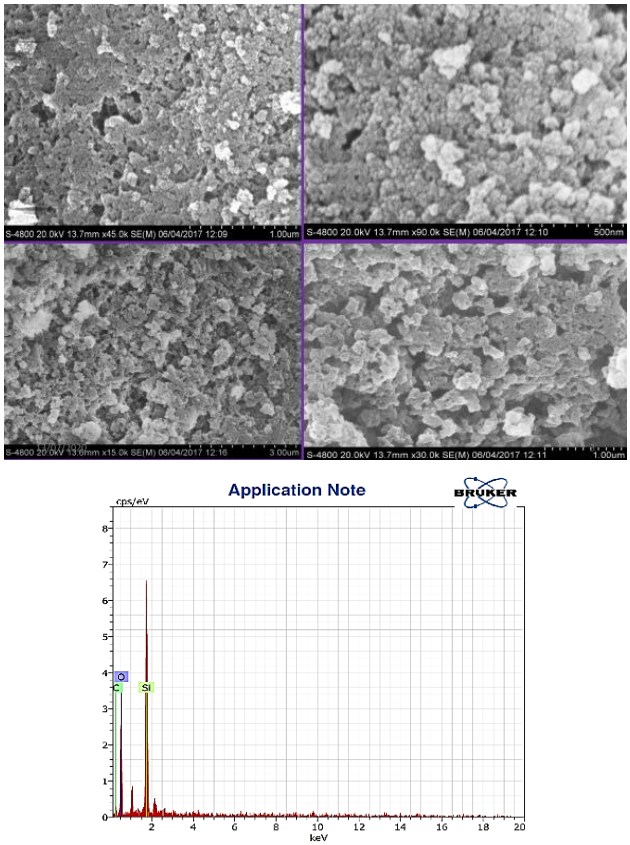

Fig. 8. FE-SEM of Hydrogel with EDX.

Conclusion

This work demonstrated the successful preparation of chitosan loaded silica hydrogel by using the sol-gel method. The silica source for hydrogel preparation is sodium silicate which is more cost effective than any other silica precursor. The UV, FTIR, XRD, and FE-SEM with EDX show the confirmation of hydrogel preparation. The porous nature observed in SEM morphology will be useful in drug loading study not only for isoniazid, but for other drugs also. The drug loading of isoniazid from the hydrogel were found to enhance. It is also confirmed by kinetics study. Therefore, it is more useful in various drug release study also because of cost effectiveness, easy method and eco-friendly.

Acknowledgements

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Conflicts of interest
"There are no conflicts to declare".

Keywords

Hydrogel, sodium silicate, chitosan, hydrophilicity, drug loading.

References

1. Bin, H.; Yarmo, M.; Rahman, M.; Zainal, Z.; Liang, A.; *MJAS*, **2001**, *7*, 35.
2. Raphae, R.; He, R.; Anne des, R.; Nicolas, D.; Christine, J.; Veronique, P.; *Adv. Polym. Sci.*, **2011**, *244*, 19.
3. Banik, N.; Ramteke, A.; Maji, T.; *Polym Advan Technol.*, **2014**, *25*, 1580.
4. Alves, N.; Mano, J.; Int. J. Biol. Macromol., **2008**, *43*, 401.
5. Shirosaki, Y.; Tsuru, K.; Hayakawa, S.; Osaka, A.; Lopes, M.; Santos, J.; Fernandes, M.; *Biomaterials*, **2005**, *26*, 485.
6. Venter, J.; Kotze, A.; Auzely-Velty, R.; Rinaudo, M.; *Int. J. Pharm*, **2006**, *313*, 36.
7. Denkbas, E.; Ottenbrite, R.; *J. Bioact Compat Pol.*, **2006**, *21*, 351.
8. Kumirska, J.; Weinhold, M.; Thöming, J.; Stepnowski, P.; *Poly.*, **2011**, *3*, 1875.
9. Sieval, A.; Thanou, M.; Kotze, A.; Verhoef, J.; Brussee, J.; Junginger, H.; *Carbohydr. Polym.*, **1998**, *36*, 157.
10. Qie L., Chen W., Wang Z., Shao Q, Li, X., Yuan L. and Huang Y.; *Adv. Mater.*, **2012**, 24(15): 2047-2050.
11. Pang, H.; Chen, G.; Park, H.; Cha, D.; Kennedy, J.; *Carbohydr. Polym.*, **2007**, *69*, 419.
12. Vaghani, S.; Patel, M.; Satish, S.; Patel, M.; Jivani, P.; *Bull. Mater. Sci.*, **2012**, *35*, 1133.
13. Di Martino, A.; Sittinger, M.; Risbud, M.; *Biomaterials*, **2005**, *26*, 5983.
14. Zhu, Y.; Shi J.; Shen W.; Chen, H.; Dong, X.; Ruan, M.; *Nanotechnology*, **2005**, *16*, 2633.
15. Vermonden, T.; Censi, R.; Hennink, W.; *Chem. Rev.*, **2012**, *112*, 2853.
16. Trewyn, G.; Giri, S.; Slowing, I.; Lin, V.; *Chem. Comm.*, **2007**, *31*, 3236.
17. Wu, S.; Hung, Y.; Mou, C.; *Chem. Comm.* **2011**, *47*, 9972.
18. He, Q.; Shi, J.; *J. Mater. Chem.*, **2011**, *21*, 5845.
19. Jafarzadeh, M.; Rahman, I.; Sipaut, S.; *Cera. Int.*, **2010**, *36*, 333.
20. Skuja, N.; Streletsky, N.; Pakovich, A.; *Solid State Commun.*, **1984**, *50*, 1069.
21. Tohmon, R.; Mizuno, H.; Ohki, Y.; Sasagane, K.; Nagasawa, K.; Hama, Y.; *Phy. Rev. B.*, **1989**, *39*, 1337.
22. Rabea, M.; Mohseni, M.; Mirabedini, S.; Tabatabaei, M.; *Appl. Surf. Sci.*, **2012**, 258, 4391.
23. Liu, Y.; Su, H.; Lai, J.; *Polymer*, **2004**, *45*, 6831.

24. Rahman, A.; Vejayakumaran, P.; Sipaut, S.; Ismail, J.; Chee, C.; *Mat. Chem. and Phy.*, **2009**, 114, 328.
25. Li, X.; Cao, Z.; Zhang, Z.; Dang, H.; *Appl. Surf. Sci.*, **2006**, *252*, 7856.
26. Banik, N.; Hussain, A.; Ramteke, A.; Sharma, K.; Maji, T.; *RSC Adv.*, **2012**, 2, 10519.
27. Mukhopadhyay, P.; Sarkar, K.; Soam, S.; Kundu, P.; *J. Appl. Polym.*, **2013**, *129*, 835.
28. Won, C.; Nersisyan, H.; Won, I.; Lee, H.; *J. Solid State Chem.*, **2009**, *182*, 3201.
29. Scriba, R.; Britton, D.; Arendse, C.; van Staden, M.; Härting, M.; *Thin Solid Films*, **2009**, *517*, 3484.
30. Cai, X.; Riedl, B.; Zhang, S.; Wan, H.; *Composites Part A: Applied Science and Manufacturing*, **2008**, 39, 727.

Authors biography

Ujwala S. Tayade is completed her Ph.D. in Kavayitri Bahinabai Chaudhari North Maharashtra University, Jalgaon, India. She did her M.Sc degree in (Organic Chemistry) from the same university. Her research is focused on synthesis of the nanomaterial's and their applications.

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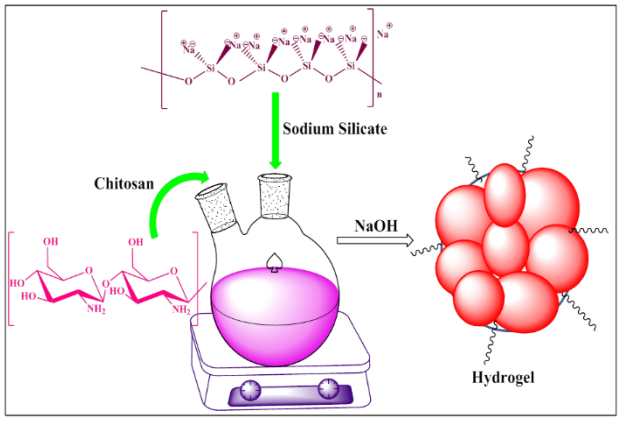
Jyotsna S. Meshram is Professor and currently working as Head in Department of Chemistry, Rashtrasant Tukadoji Maharaj University, Nagpur, India. She had Published 115 National and International Papers in reputed Journals. Her current research is focused on Green Chemistry, Polymers, Macromolecules, Nanomaterials, Synthesis etc.

Graphical abstract



Schematic image of Hydrogel preparation.