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A STARRING ROLE OF BIOGENIC NANO SILICA FOR DRUG DELIVERY AND PHOTOCATALYTIC DEGRADATION

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ABSTRACT

Amorphous silica nanoparticles were rapidly synthesized in a simple and cost effective way using a sol-gel technique from rice husk- a waste product of rice mill. Greener approach is used with low chemical energy utilization along with easily scaled up technique, thus minimizing the risk leading to harmful hazards. The silica nanoparticles were investigated for the surface topography and amorphous phase by SEM and XRD techniques. In the present research work, silica nanoparticles produced by green method were successfully revealed a good potential for the drug delivery application with inclusion of model drug onto mesoporous silica by calcination technique and also to act as a photocatalyst for methylene blue dye degradation.

KEYWORDS: Amorphous silica; Green method; Rice husk; Sol-gel.

1. INTRODUCTION

Nanotechnology has become a fascinating field providing the applications ranging from biosensors, photonics, photocatalyst to the recent development in drug delivery. There are three routes for synthesis of nanoparticles namely chemical, physical and biological (greener approach). Greener route of synthesis explores natural resources with different molecular background and diversity. It is a cost effective, facile and easily scaled up technique which minimizes the risk of endangering the environment.[1] Rice husk is a waste product found in rice mills. Obtaining silica from rice husk ash is a step towards green synthesis. Various research works have been published on use of rice husk as a starting material for nanoparticle synthesis.[2] Silica is a polymer of silicic acid consisting of inter-linked SiO_4 units in a tetrahedral fashion with the general formula SiO_2. Naturally synthesized silica is crystalline in nature, whereas synthetic silica is amorphous in nature. Amorphous silica synthesis is generally preferred, as these become the benign approach utilizing lower chemical energy. Silica is synthesised using a sol-gel technique with rice husk ash as a precursor. Sol-gel method enables synthesis at low temperature and nanoparticles of various sizes can be obtained.[3] Amorphous silica is Generally Recognized as Safe (GRAS) by USFDA.[4] Among various target specific drug delivery agents, mesoporous silica nanoparticles have taken a drift towards biomedical application in recent years. Mesoporous silica is an ordered porous structure which allows uniform drug loading. Considering the superior features including high surface area, orderly arranged porous interior, mesoporous silica can be use as a suitable carrier for delivery of poorly soluble drugs.[5] Over the recent years photocatalyst semiconductor were highlightened due to their wide range applications in water and air treatment. Few of them are ZnO, TiO_2 etc. There is very less literature available about SiO_2 which act as a photocatalyst for methylene blue dye degradation.[6,7]

An attempt is made to synthesize, characterize silica from an economical source and its application as mesoporous material for drug delivery and photocatalytic degradation are discussed.

2. MATERIALS AND METHODS

Rice husk was obtained from the rice mill in thane district. All chemicals were purchased from Molychem, India. Cetyl-trimethylammonium bromide (CTAB) and Ibuprofen were obtained as gift samples from Acme Sujan Chemicals, Jalgaon and Teva Pharmaceuticals, Ambernath, Maharashtra respectively.

UVspectrophotometer used: Shimadzu (UV-1800) Particle size analyser: Horiba partica size analyser (SZ-100 nanopartica)

2.1 Amorphous silica by green synthesis

Washed and dried rice husk was processed in a furnace at a temperature of 650°C for four hours to convert into the ash. Ten gm of the ash was suspended in 70 ml of distilled water, 1N HCl was added drop wise to attain pH 7 and then stirred for 2 hrs at room temperature on a

magnetic stirrer. Subsequently washing was given with distilled water followed by addition of 60 ml of 1N NaOH and reaction was stirred at 65° C for 1hr. The filtrate obtained was then titrated with 1N HCl till pH 7 where gel formation occurs. Gel was aged for 14 hr and was then broken into slurries by addition of distilled water, which later was centrifuged at 2500 rpm for 20 min. The xerogel thus obtained was placed in a hot air oven at 80°C for 12 hr to obtain pure silica nanoparticles.

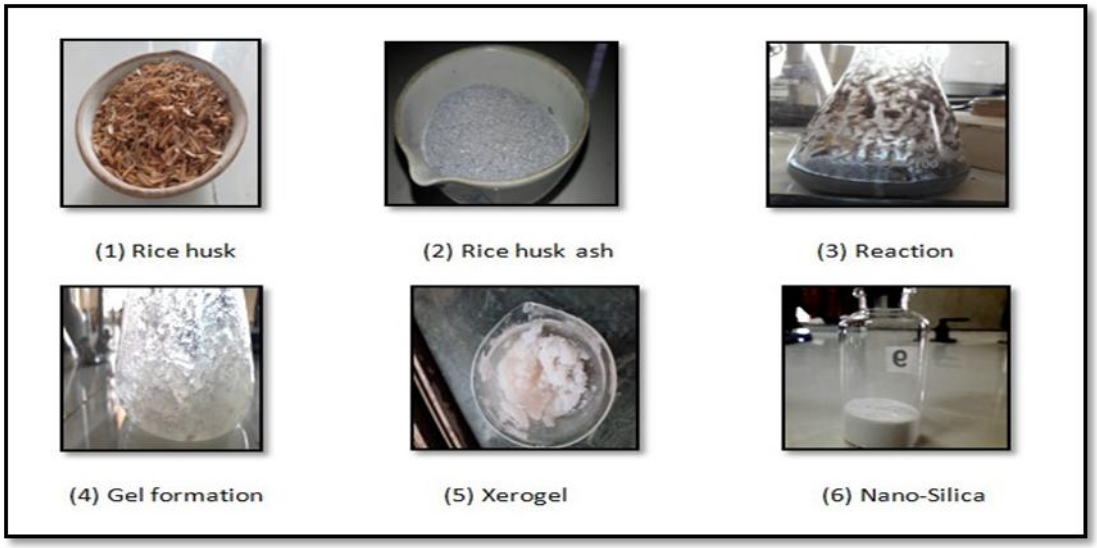


Figure 1: Silica Extraction Process.

The above fig.1 explains the process of silica extraction, which begins with processing of rice husk to obtain ash to its final conversion into pure amorphous nano silica.

2.2 Preparation of drug loaded Mesoporous Silica nanoparticles

Ten grams of silica was added to a stirred solution of $7.5x10^{-2}$ mol of Cetyltrimethylammonium bromide (CTAB) and sodium hydroxide (NaOH) in 200ml distilled water at following ratio H_2O/NaOH/CTAB/SiO_2 = 20 : 0.3 : 0.15 : 1. Place the sample in a hot air oven for 18 hr, the resulting white powder after filtration was washed with water and ethanol and dried at 50°C and finally in furnace at 550°C for surfactant removal to obtain mesoporous silica.

Mesoporous silica 0.5 gm was soaked twice with 2 ml solution of Ibuprofen in ethanol of concentration 65mg/ml. **S**olvent evaporation is done after each impregnation at 50°C. To achieve pore filling 100 mg of ibuprofen was added in excess and washed with 5 to 10ml of ethanol for removal of ibuprofen molecules at edges. The impregnated material was dried at 50°C to obtain mesoporous silica loaded with model drug – Ibuprofen.

2.3 Photocatalytic dye-degradation of methylene blue dye using nano silica

A 100 ppm, 20 ml solution of methylene blue dye was prepared to which 0.2gm silica nanoparticles (SiO_2) added and sample was placed on the magnetic stirrer in presence of sunlight. A 2 ml aliquot was taken each time at a frequent interval of 10 sec. This was then centrifuged for 5 minutes to separate the suspended silica nanoparticles. The decrease in methylene blue dye concentration was estimated using a UV spectrophotometer at the λ_{max} of 622nm.

3. RESULTS AND DISCUSSION

Extraction of amorphous silica from rice husk ash occur by low temperature alkali extraction as solubility of amorphous silica is less at pH<10 and it distinctly increases when pH>10. Thus this peerless solubility behaviour enables the extraction of pure silica by solubilising under alkaline condition followed by subsequent precipitation at low pH. Also at pH 7 sufficient negative charge is present on silica surface which prevents it from aggregation. The charges are then neutralised due to the presence of ionised salts.

SiO_2 (ash) + NaOH $\longrightarrow$ Na_2SiO_3 + H2O

Na_2SiO_3+ HCl $\longrightarrow$ SiO2 + NaCl + H2O

The synthesized amorphous silica nanoparticles were confirmed by various analytical techniques.

3.1 Characterization of Nano silica

3.1.1 Fourier transform infrared spectroscopy studies (FTIR)

The major chemical functional groups present in silica were identified through FTIR studies. Prominent peaks were observed at 785.24 cm^{-1} for Si-O symmetric vibration, at 1050.31 cm^{-1} for siloxane (Si-O-Si) and broad peak at 3377.51 cm^{-1} assigned for OH stretch in H-bonded water. Also 1637.45cm^{-1} is the bending vibration of molecular water.

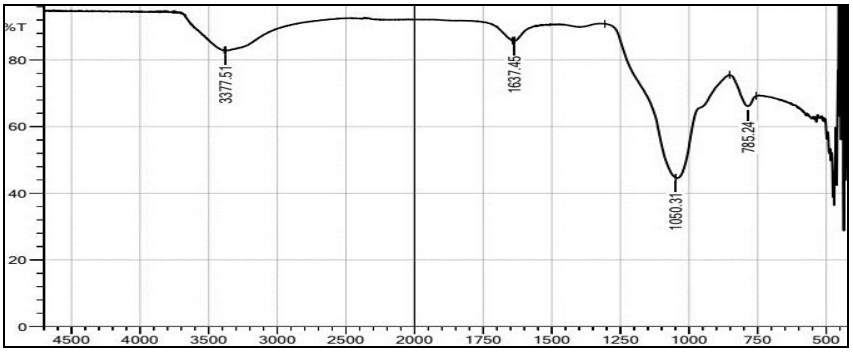


Figure 2: FTIR spectrum of synthesized amorphous silica from Rice husk ash.

3.1.2 Particle size analysis

The particle size measured by particle size analyzer (Horiba) was in the range from 900 to 1500 nm. Dynamic light scattering method determines the dynamic diameter particle sizes of SiO_2 NPs dispersed in water. The zeta potential was -25.3mV and PI was 0.554. This denotes the stability of Nano silica.

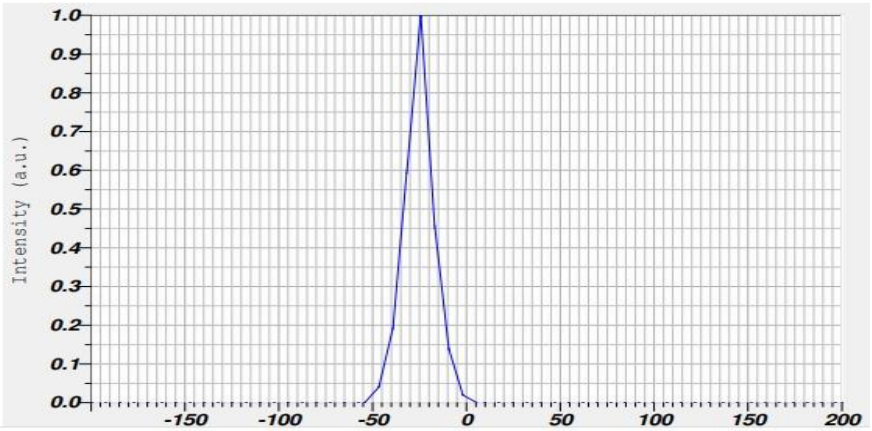
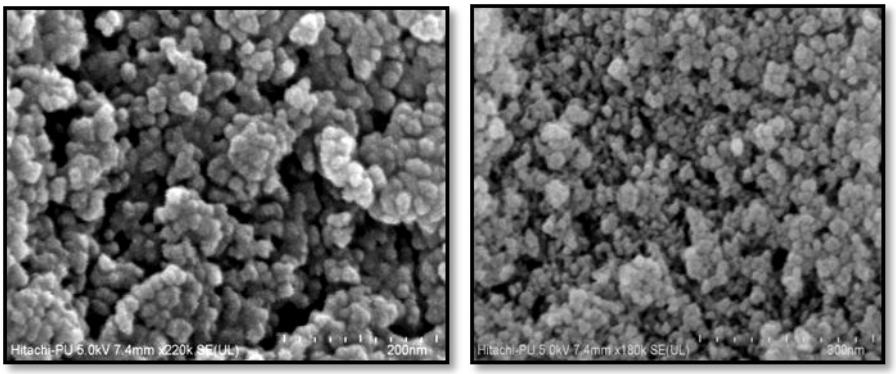


Figure 3: Zeta potential for synthesized silica nanoparticles.

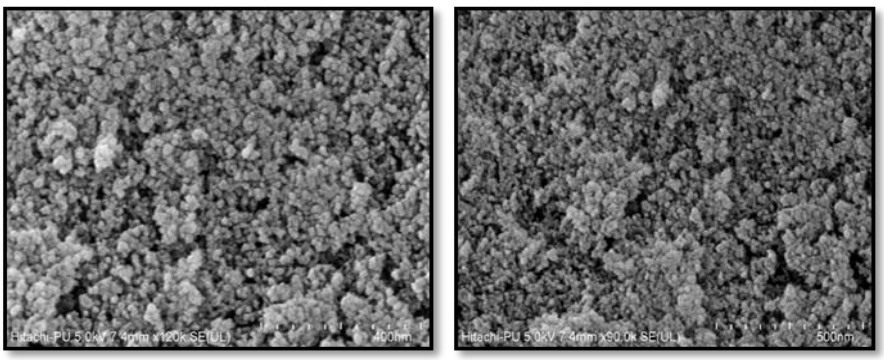
3.1.3 Scanning electron microscopy (SEM)

The FESEM images show clustered - circular shape irregular arrangement of silica nanoparticles. The Nano silica does not show clear margins as they are in agglomerated and amorphous form. Hence from SEM analysis we can conclude that silica nanoparticles synthesized from rice husk ash are in nano- range.

Fig.4 shows the scale of resolution scale from 200-500 nm for a, b, c and d respectively. It is observed that SiO_2 nanoparticles are porous and are linked to each other.



(a) **(b)**



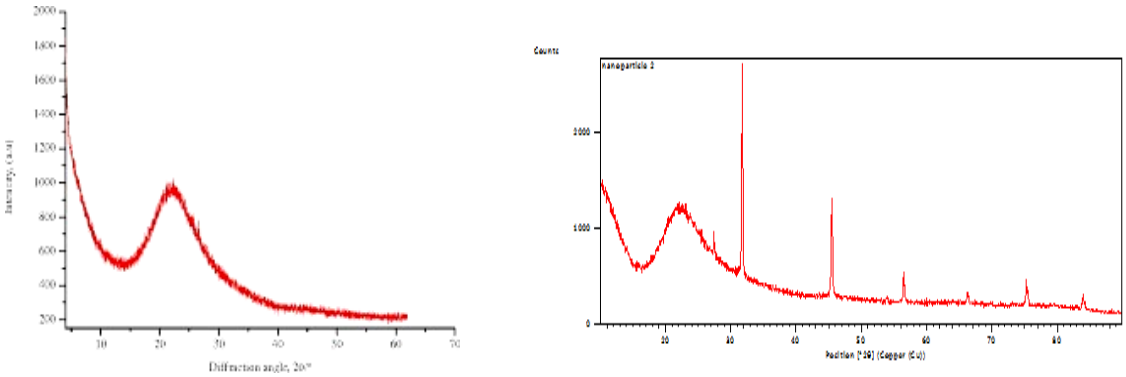
(c) (d)

Figure 4: SEM images obtained for synthesized silica.

3.1.4 X-ray diffraction studies (XRD)

In XRD studies, X ray intensity is measured as a function of scattering angle (2θ) for the material silica. The diffraction angle was scanned from 10^o to 90^o using a current of 40mA and accelerated voltage of 45 kV.

An X-ray diffraction pattern indicates a single broad peak at $2\theta=22^o$ which confirms the presence of amorphous silica. It is a highly disordered structure signifying the amorphous property of silica nanoparticles. Very less or negligible amount of crystalline silica must be present. Fig 5.a and 5.b represent the comparison between standard amorphous silica.[8] and synthesized amorphous silica respectively. The additional peaks appeared in synthesized silica (fig 5.b) can be attributed to the minerals present in the natural source of the rice husk and possibly moisture entrapped.



(a) Standard silica **(b) Synthesized silica**

Figure 5: XRD spectra of standard and synthesized silica.

3.2 Applications of silica nanoparticles

3.2.1 Silica nanoparticles as drug delivery system

The mesoporous silica nanoparticles (MSNs) were synthesized by self-assembly of silica and the surfactant micelles. This is hydrothermal synthesis in presence of cationic surfactant such as cetyltrimethylammonium bromide. These ordered mesoporous structure results from the interaction between negatively charged silicates and positively charged quaternary ammonium micelles. The porosity is achieved after the successful removal of surfactant using calcination. Due to the well-defined and good inner porosity along with the large surface area mesoroporous silica act as a promising carrier for drug delivery.

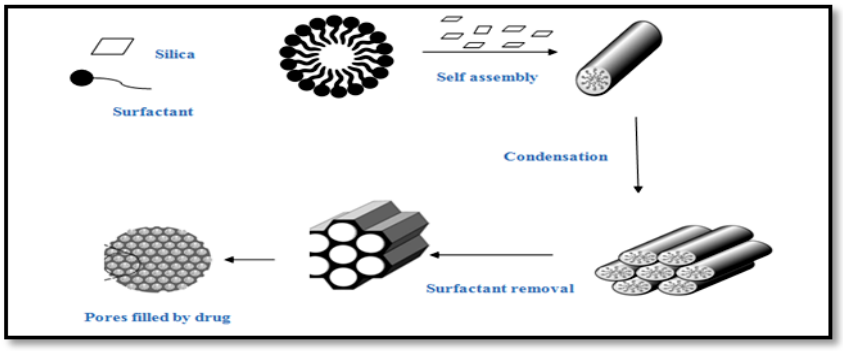


Figure 6: Schematic synthesis process of mesoporous silica.

Fig.6 represents the schemetic diagram for synthesis of mesoporous silica.[9]

The textural properties associated with mesoporous silica nanoparticles have capacity to load high amount of drug as there are large numbers of silanol group on the internal and external domain of mesoporous silica, facilitating surface functionalization for a better control of drug diffusion kinetics. MSNs with high colloidal stability attracts attention of researchers for their use as a target specific drug delivery carrier and also suitable for bio imaging devices. MSNs as a drug delivery system has capability to act as a nanocarrier with zero-premature cargo release by blocking the pores with different guards through external or internal stimulus.

3.2.1.1. Selection of model drug and loading on mesoporous silica

The synthesis of mesoporous silica nanoparticles was carried with an aim to demonstrate their ability to load poor water soluble drug and to characterize the same. Ibuprofen was selected as a model drug having anti-inflammatory property.

Ibuprofen belongs to BCS Class II (low solubility, high permeability) which is used as short duration therapy. Moreover drug is rapidly eliminated through systemic circulation resulting in short half life. Thus several dosages are required to achieve effective results. However to achieve prolonged drug release and reduced frequency of dosing it is necessary to incorporate such drugs into a nanoparticulate system. Mesoporous silica nanoparticles exhibit various interesting properties such as controllable pore size, large specific area and also prevent crystallization of encapsulated drug which therefore enhances solubility. It also avoids digestion in GI tract and control the release of incorporated drug. Thus loading of ibuprofen into mesoporous silica would enhance the efficacy as well as aqueous solubility of the drug.

Fig (7a) and (7b) displayed the FTIR spectrum of mesoporous silica before and after loading with the model drug. Through the FTIR spectrum it was clear that drug loading has taken place. Fig (7a) represents the FTIR spectrum for mesoporous silica. Additional peaks after the drug loading fig (7b) was observed at 1507cm^{-1} for aromatic C=C stretch, 1705cm^{-1} for C=O vibration and 2954cm^{-1} for CH_3 stretching of Ibuprofen drug molecule.

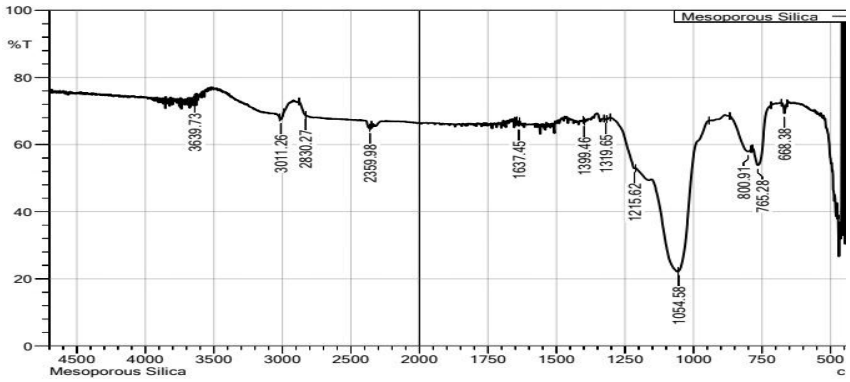


Figure 7.a. FTIR spectra of synthesized mesoporous silica.

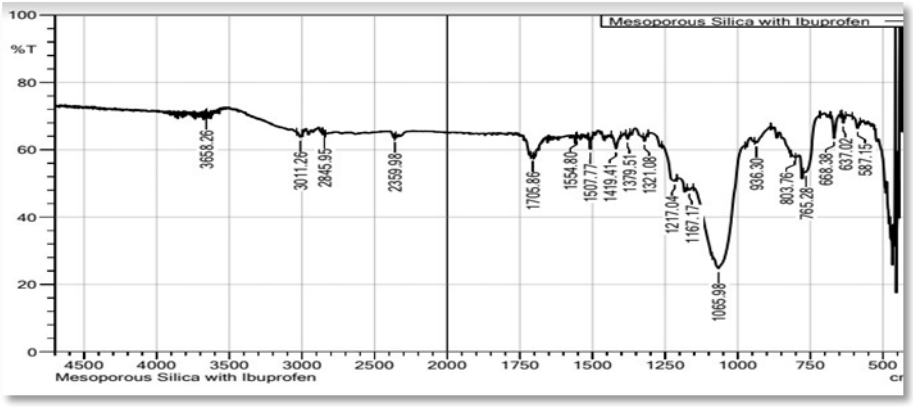


Figure 7.b. FTIR spectra of drug loaded with mesoporous silica.

For successive drug loading, excess amount of the model drug was added with frequent washing using solvent such as ethanol followed by drying.

The impregnation method was used to synthesize the mesoporous silica so that it helps to enhance the inclusion of Ibuprofen within the pores. Successive

impregnations enable to ensure the pore filling and the significant improvement in the amount of drug encapsulated. Impregnation is dissolving active pharmaceutical ingredient in an organic or aqueous solvent and then mixed with dry support (mesoporous silica) in these case so that solution will be drawn into the pores through capillary action and solvent evaporation will take place simultaneously resulting in the drug loaded nanoparticles. The advantage of this method is we can load sufficient amount of a drug into the carrier.

3.2.1.2. Drug release study

Although targeted delivery of nanoparticles increases the potency of drug, but sometimes issue related to elevated toxicity due to the carrier material reduces the safety. Thus drug release becomes a crucial aspect during development of nanoparticulate system. Invitro drug release pattern procure attention as an alternate test for product performance.

Once drug loading is achieved, in-vitro release of drug can be performed by using dialysis bag or dissolution apparatus. When drug release study was performed using a dialysis membrane placed in a beaker having same dissolution media (phosphate buffer pH 7.4) as that in the dialysis membrane the results were not conclusive. This can be attributed to the assumption that media being the same, half of the drug release would have taken place in the dialysis membrane itself so very less amount of drug release was achieved at end.

Finally the in vitro drug release was performed using Type II dissolution test apparatus (paddle type) with phosphate buffer pH 7.4 (intestinal fluids). The absorbance was taken at λ_{max} 222nm.

The in vitro release of Ibuprofen was carried in intestinal fluid (pH 7.4) for a period of ninety minutes using a type II dissolution apparatus. At the end of ninety minutes it was around 100% drug release observed. Aqueous solubility of ibuprofen at pH 7.4 results the transfer of drug molecules from silica matrix into the buffer solution. Morever phosphate buffer pH 7.4 was chosen as a dissolution media because of the high aqueous solubility of ibuprofen within the media also it is easy to maintain the sink condition which therefore allows the transport of drug substance from mesoporous silica to the buffer solution. The release kinetic profile presents a great interest in pharmaceutical industries to improve the drug delivery of poorly water soluble drugs. Fig.8 shows drug release in phosphate buffer over a period of 90 minutes. On y-axis, time (min) is observed whereas on x-axis percent cumulative release is observed.

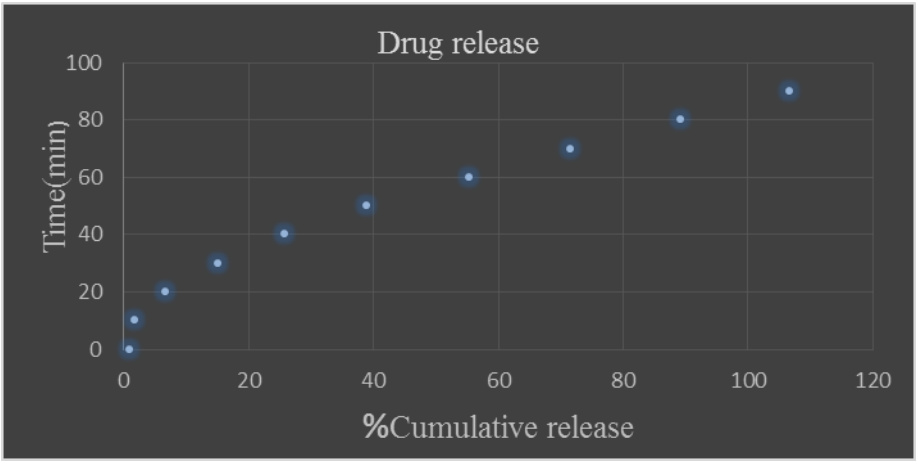


Figure 8: Drug release study in Phosphate buffer.

3.2.2 Silica nanoparticles showcasing photocatalytic dye degradation

Organic dyes are considered as one of the major group of dyes widely used in industry, textiles, and medicines etc which have hazardous effects on environment and have become a major concern leading to pollution crisis. Various industries make use of dyes containing high amount of colour effluents for different purposes on daily basis. These dyes are more toxic and have become resistant to conventional methods used for destruction. The massive heap of dyes in water bodies endangers the aquatic life by retarding infiltration of sunlight, also reducing the re-oxygenation capacity. Thus removal of dyes from water bodies cannot successively achieve by conventional methods which includes adsorption or ultra filtration. Photocatalytic degradation grabs attention from few decades resulting in destruction of dyes by quick oxidation which become superior over conventional methods for the removal of dyes from water. In the recent years researchers have put their efforts to improve photocatalytic activity by incorporating nanoparticles which in turn effectively degrade the dyes.

3.2.2.1 Methylene blue dye degradation by silica nanoparticle

Methylene Blue is an azo dye used in textiles, laboratory assays and commercial products etc. It may cause eye irritation or sometimes creates serious problems when inhaled or swallowed thus degradation of the dye is a

crucial aspect. Photocatalyst semiconductors recently have proved to its proficiency in dye degradation. Nevertheless silica nanoparticles are essentially inert for various reactions, amorphous silica proved to remote photocatalytic reactions under UV radiations. A fixed concentration of methylene blue was prepared. The reaction was carried out in sunlight so as to obtain the desired results. It was observed that as time increased the dye colour slowly started disappearing indicating the decrease in concentration of dye and at the end of 1 min, colourless solution was seen resulting in dye degradation.

Fig. 9 demonstrates decrease in colour of dye with increase in time.

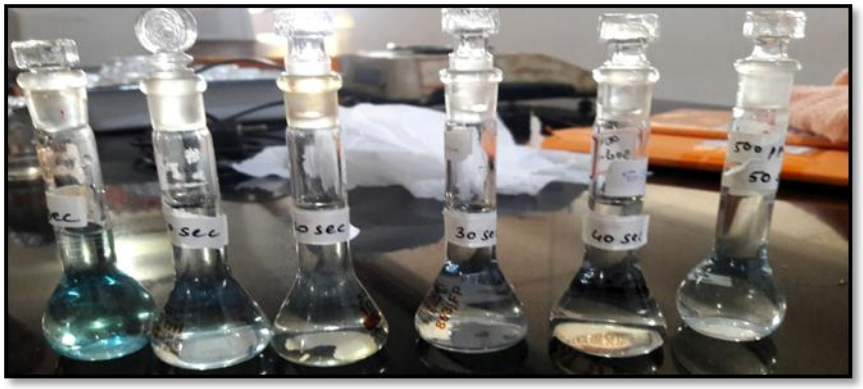


Figure 9: Image to depict change in colour of samples.

Dye degradation process was carried in 2 ways,
1. Dye degradation in absence of UV source in presence of silica.
2. Dye degradation in presence of UV source with silica.

Blue colour indicates photo catalytic degradation of dye in presence of UV source.
Red colour indicates degradation in absence of sunlight.

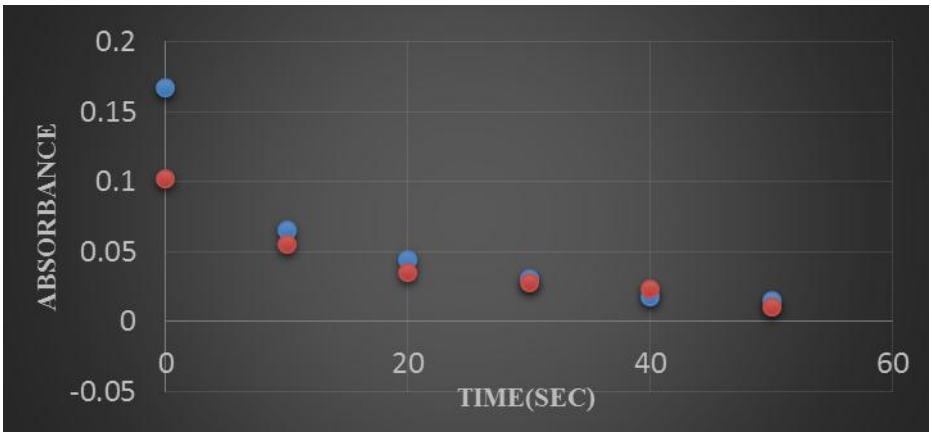


Figure 10: Spectra to depict dye degradation occur before and after exposure to UV source.

Dye degradation obtained without exposure to a UV source in presence of silica, was about 88.23% which then lifts to 91% in presence of sunlight.

From (fig.10) On Y-axis time (sec) whereas on X-axis absorbance is placed: It clearly states that, the absorbance was found to decrease so do the concentration with the increase in time. So it can be said that when there is decrease in absorbance the degradation dye increases predominantly. The entire process was carried within 1min. Approximately 91% of dye degradation was achieved within 1 min in presence of UV source. From the results obtained it was concluded that maximum degradation was achieved when sample was exposed to a UV source as compared to a sample without its exposure to a UV source in presence of silica nanoparticles.

3.2.2.2 Mechanism of dye degradation by silica nanoparticles

Silica nanoparticles are found to be photo-excited which results in charge transfer from Si-O bonding orbital to the 2p non bonding orbital of the non-bridging oxygen. A photon of UV light when strikes the SiO_2 surface an electron from valance bond jumps to the conduction bond which leaves behind a positively charged hole, thus then the negative increases in conduction band. As a result of this photo catalytic active centres get formed on the SiO_2 surface. The valance bond hole then further reacts with the chemiabsorbed H_2O molecule which then

forms reactive $OH^{\cdot}$ radical species when later reacts with dye to form their complete degradation. Fig 11 explains how the dye degradation takes place in presence of a UV source.

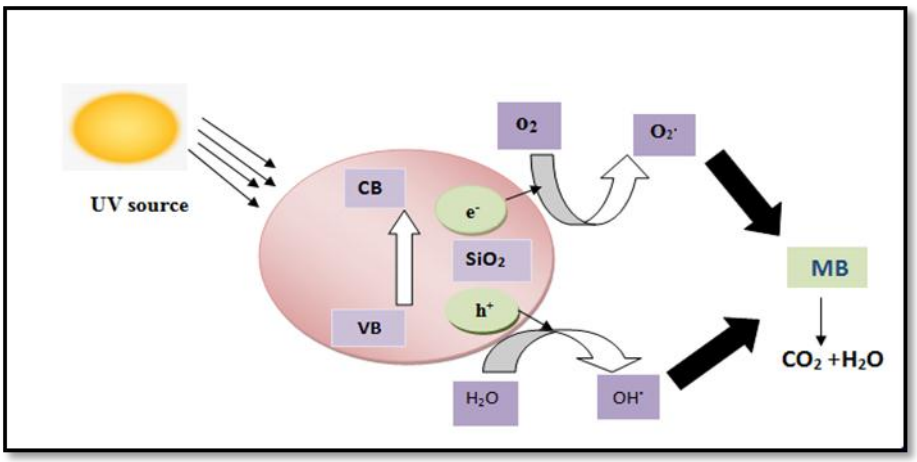


Figure 11. Mechanism of dye degradation.

CONCLUSION

Synthesis of nanoparticles from natural source is thus a facile, cost effective and sustainable approach. Silica nanoparticles were successfully synthesized from rice husk ash using the sol- gel technique and characterized by instrumental methods.

Mesoporous silica with its large surface area, good drug loading and releasing property has become a promising drug delivery candidate in nanotechnology research. These nanocarriers have been successfully adopted for release of poorly water soluble drugs. Moreover applications of silica nanoparticles in drug delivery and dye degradation were successfully achieved. It is expected in the near future that nanoparticles in pharmaceutical analysis will play a major role in next generation pharmaceutical technologies.

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