Iranian Journal of Pharmaceutical Sciences
2024: 20 (4): 324- 335
https://journals.sbmu.ac.ir/IJPS

Original Article

Improved Method for Imparting Porosity in Mesoporous Silica and its Applicability as Slow-release Carrier

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Abstract

Removing polyethylene oxide and polypropylene oxide co-polymer template to generate porosity is critical in synthesizing SBA 15 (MSN). Porosity generation among silica nanoparticles is in high demand due to its wide applications. Different physical treatments like calcination, solvent extraction ultrasonication, and a combination of methods were implemented to remove organic templates from pores. The particles obtained were characterized using FTIR to expose silanol functional groups. The PSL-5 particles were obtained via combination treatment, which was economical and was selected to formulate mosquito repellent cream. The optimized cream formulation with and without an MSN carrier was evaluated for mosquito repellency using diurnal mosquitoes and blank active citronellol using the arm cage method. The uniformity of particle size distribution and hexagonal porosity represented by crystallinity were evident from the SEM and XRD data. The zeta potential of -16.8 mv of SBA 15 indicates the stability of the particles. Comparison of FTIR of carrier SBA 15 and citronellol shows no incompatibility. The mesoporous material effectively deters mosquitoes for more than 3 hours. The novel template removal process utilizes mild temperature and a less solvent ratio of 1:3. Thus, the obtained MSN material showed prolonged mosquito repellency in the laboratory assay.

Keywords: FTIR, Mesoporous materials, Mosquito repellant formulation, SBA 15, Template removal, XRD.

1. Introduction

Porous materials are categorized based on pore diameter into Macroporous (d>50 nm), Mesoporous (2nm<d<50 nm), and microporous (d<2nm). The mesoporous materials offer several advantages that better suit them as carriers. SBA 15 is a mesoporous Silica nanoparticle (MSN) type with distinctive features like large surface area, flexible pore size, a tendency to undergo surface modification, stability, and biocompatibility [1]. Electrostatic attraction makes it possible to multifunction and increase the loading capacity of these mesoporous

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Cite this article as: Vakkanti VS, Guntuku GS. *Improved Method for Imparting Porosity in Mesoporous Silica and its Applicability as Slow-release Carrier*. Iran. J. Pharm. Sci., 2024, 20 (4): 324- 335.

DOI: https://doi.org/10.22037/ijps.v20i4.45582

materials [2]. Mesoporous materials are widely applied in different areas. Using triblock co-polymers, they can serve as carriers and catalytic centers with controlled pore diameter [1-3]. MSNs are widely employed in drug delivery and as biosensors [4-5]. Mesoporous silica materials are functionalized with tracking and imaging agents and are widely used in Nanomedicine [6-8]. These ordered structures are used in batteries and supercapacitors as energy storage reserves [9]. These materials exhibit widespread utilization in separating gases, membrane permeation, and even oil recovery [10-11]. These materials find wide biocatalytic applications [12]and are used even in targeted medication to individuals via theranostic application [13] and as controlled release agents in transfection studies [14]. MSNs are extensively used in agricultural fields [15]. These materials as carriers can also be employed in conserving cultural heritage structures [16]. These highly ordered materials in tissue engineering have recently gained momentum [17]. The efficiency of managing diabetes mellites and targeted delivery of anti-diabetic drugs is made possible using nanocomposites based on Mesoporous structures. Heat transfer and conductivity of fluids can be significantly enhanced by incorporating Mesoporous materials [18]. Owing to the boundless applicability of these materials in varied fields, the synthesis of well-ordered SBA 15 containing mesopore structure is in high demand. The removal of the block co-polymer template during the synthesis of MSNs by exposure to a high temperature of around 145°C -360°C was in practice [3]. As the temperature and time of exposure are high, more template removal was efficient during calcination. However, it resulted in drastic shrinkage of pores and loss of functional groups, compromising its applicability [19-20]. Template removal procedures also implemented the combination of solvent extraction and calcination [21]. The template removal efficiency is less with solvent extraction. With the available methods, there is one or the other disadvantage. In current research, we have tried to develop a more economical method so that these particles' many applications can be easily exploited. The prepared mesoporous materials were used to develop a mosquito-repellent formulation to check its efficacy as a slow-release material. One of the terpenoid components of citronella oil, Citronellol, is associated with Insect repellent properties [22-23]. The protection offered by these natural repellents is for about 20 minutes due to their volatility [24]. Nanoemulsion formulations can prolong the mosquito-repellent activity for about 2-3 hours. [25]. Nanostructured lipid carriers were employed to prolong the effect of citronella oil as a repellant cream [26]. The present work aims to impart porosity in the silica particles using mild conditions like low temperature and less solvent ratio to minimize the drawbacks associated with the existing methods. Though nanoemulsions and nanostructured lipid carriers were employed to formulate Citronella Oil Mosquito repellents, simple carriers like MSN were not used in the earlier works. The SBA 15 carrier in Citronellol cream formulation was tested for its effectiveness as a prolonged-release material.

2. Materials and Methods

2.1. Chemicals used

TEOS, Pluronic 123 surfactant, HCl, methanol, citronellol (CO), Stearic acid, Cetyl alcohol, Stearyl alcohol, Glycerin, Propylene glycol, Potassium hydroxide, Methyl paraben, propyl paraben is purchased from Sigma Aldrich Chemicals. All the chemicals used in the present work are of analytical grade and were used as such without any further purification.

2.2. Synthesis of MSN-SBA-15

The sol-gel method was employed for the synthesis of SBA-15 by using TEOS as a precursor and Pluronic 123 triblock co-polymer ($EO_{20}PO_{70}EO_{20}$) as surfactant as per Zhao protocol [3]. The obtained particles were labeled as PSL-1.

2.3. Removal of organic template

2.3.1. Method I

The dried Silica particles obtained were subjected to different physical treatments to remove the surfactant and obtain ordered mesoporous silica material. About 50 g of dried silica was calcinated at 400^0C for 5 hrs. The obtained particles were labeled as PSL-2.

2.3.2. Method II

Five volumes of methanol solvent were added and refluxed to the dried silica particles at 60^0C for about 6 hrs. About 50 gm of silica particles were taken in a 500 ml RBF, and 250 ml of methanol was added and refluxed [27] After six hours the mixture was filtered under vacuum and subjected to vacuum drying at 80^0C. The obtained particles were labeled as PSL-3.

2.3.3. Method III

The dried silica particles were subjected to ultrasonication by adding five volumes of methanol. About 50 gm of silica particles were added to 250 ml of methanol. The beaker containing the mixture was ultrasonicated for 60 minutes at 30°C. The obtained particles were labeled as PSL-4.

2.3.4. Method IV

A combination of methanol reflux and ultrasonication was tried in this method. Three volumes of methanol solvent were added to the dried silica particles and subjected to methanol reflux and ultrasonication. About 50 gm of dried silica particles were taken, and 150 ml of methanol was added. The mixture was subjected to reflux for three hrs at 60°C. Later, the mixture was collected in a beaker and ultrasonicated for 30 minutes at 30°C. The solution was finally filtered under vacuum and vacuum dried at 80^0C to obtain dried mesoporous silica particles labeled as PSL-5.

2.4. Characterization of MSN

The systematic characterization of all the mesoporous materials obtained by different methods was carried out using FTIR, SEM, XRD, and Nanozetasizer.

2.4.1. FTIR

The Mesoporous Silica nanoparticles were characterized for the presence of functional groups by infrared spectroscopy (FT-IR-RUKER Germany) using the KBr pellet method (1:100 w/w of the sample was taken concerning KBr) in the scan range of 400–4000 cm^{-1} at a resolution of 4 cm^{-1}.

2.4.2. XRD

X-ray diffractometer (Bruker AXS) operated at a voltage of 40 kV and a current of 30 mA with Cu-Kα radiation (λ=0.15418nm). The scanning was done in the region of 2θ from 0° to 80° for high angle and 0^0 to 10^0 for low angle XRD.

2.4.3. SEM

Scanning electron microscopy analysis was carried out using SEM- HITACHI S-3700 at an accelerated voltage of 15 KV, which helps visualize the surface morphology and arrangement of the synthesized nanoparticles.

2.4.4. Zetapotential

The zeta potential of the mesoporous silica nanomaterial and carbon nanospheres was determined using Zetasizer nanoS (Malvern Instrument, Malvern, UK). The sample was analyzed at 25^0C using PBS as a dispersion medium. About 1ml of sample was filled in the cuvette for analysis.

The applicability of these mesoporous materials was tested by developing a mosquito-repellent formulation.

2.5. Preparation of Mosquito repellant cream

The ingredients for preparation of cream formulation were selected based on different batches of creams prepared by various oil phase ingredients. During the preparation, the oil phase and aqueous phase ingredients were separated. All the oil phase ingredients except citronellol (CO) were heated to about 65°C. The aqueous phase was prepared by adding all the aqueous soluble ingredients and gently stirring them in a separate container. The temperature of the aqueous phase was raised to about 65^0 C. Citronellol was added to the oil phase, maintained at about 50^0C to prepare F1 and F8 formulations. All the other formulations (**Table 1**) were prepared by incorporating the essential oil in SBA 15 via solvent evaporation.

Table 1. Formulation of mosquito repellant cream**.**

No.	Ingredients	F1%	F2%	F3%	F4%	F5%	F6%	F7%	F8%
	Oil phase								
1	Stearic acid	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
	Cetyl alcohol	-	-	-	1	2	-	-	1
	Stearyl alcohol	-	-	-	1	2	-	-	1
	Citronellol	5	5	5	5	5	5	5	5
	Aqueous phase								
2	Glycerine	2.5	2.5	2.5	7.5	7.5	2.5	2.5	7.5
	Propylene glycol	1.25	1.25	1.25	2.5	2.5	2.5	1.25	2.5
	Potassium hydroxide	0.45	0.45	0.45	0.9	0.9	0.45	0.45	0.9
	Distilled water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
	Preservatives								
3	Methyl paraben	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
	Propyl paraben	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
4	Silica nanoparticles	-	0.1	0.15	0.05	0.1	0.2	0.25	-

Then the Mesoporous particles loaded with citronellol were added to the oil phase. O/W emulsion was prepared by slowly adding the aqueous phase to the oil phase through the walls of the container. The stirring rate was maintained at about 700 rpm for about 25 minutes. The prepared emulsion was cooled. The cream was subjected to sonication for about 5 minutes to remove trapped air at room temperature. The prepared formulations are preserved at room temperature until further evaluation. Among different batches of cream formulations, the formulation with good physical properties like pH, consistency, and lack of phase separation was selected to test the repellency effect.

2.6. Evaluation of cream formulation

All the formulations of repellent cream were optimized based on pH, gritty consistency, and stability. Ten volunteers tested organoleptic evaluation based on sensory observation to check the consistency [28].

2.6.1. pH

About 100 mg of each formulation was diluted with distilled water and mixed well. The pH was recorded using a digital pH meter. All the measurements were carried out in triplicate.

2.6.2. Grittiness

About 100 mg of cream was placed on a glass slide. Another slide was placed on the first slide and slowly moved to leave a thin film of cream. The thin film was observed against the light for the appearance of any grit.

2.6.3. Consistency

About 50 mg of each formulation was tested and examined for softness, stickiness, and greasiness by applying stress using a finger; the formulation with good consistency spreads easily and must be nongreasy and non-sticky.

2.6.4. Stability

The formulated cream preparations were allowed to stand at room temperature for about 45 days to check phase separation.

Based on the results of the above tests (**Table 2**), formulation F4, which showed the best results, was selected to evaluate mosquito repellent activity along with the best formulation without carrier.

Table 2. Evaluation of cream formulation**.**

S. No	Formulation	pH	Grittiness	Consistency	Stability
1	F1	6.3	No	Poor	Phase separation
2	F2	6.4	No	Good	Phase separation
3	F3	6.6	Yes	Poor	No Phase separation
4	F4	6.7	No	Excellent	No Phase separation
5	F5	6.5	Yes	Good	Phase separation
6	F6	6.6	Yes	Poor	Phase separation
7	F7	6.2	Yes	Poor	Phase separation
8	F8	6.4	No	Good	No phase separation

2.7. Evaluation of mosquito repellency

Formulations F8 and F4 and citronellol alone were tested for mosquito-repellent efficacy. The test was carried out using diurnal mosquitos by arm cage method [29-30] on three volunteers. About 1 g/600 cm^2 of skin was applied by rubbing the cream on the arms. The treated forearm was exposed to 10 mosquitos inside the cage. The evaluation was conducted for 30 minutes and one-hour intervals until the first mosquito bite was observed. Each of the tests ends with the first bite.

3. Results and Discussion

3.1. Characterization of SBA 15 FTIR

The SBA-15 synthesized without template removal shows the IR spectrum as depicted in **Figure 1** (PSL-1). The appearance of peaks at 2883 cm^{-1} indicates the C-H stretching vibration, and peaks at 1459 cm^{-1} and 1378 cm^{-1} indicate C-H deformations. The appearance of the peaks complies with the presence of the Template.

In **Figure 2** (PSL-2), the characteristic peak at 3425 cm^{-1} depicts the -OH of the silanol group. The characteristic sharp peak at 1077cm-1 shows the asymmetric stretching vibration of siloxane [31- 32]. The peaks at 969 cm^{-1} and 801 cm^{-1} show stretching vibration of the silanol group. The characteristic peak around 580 shows angular deformation of Si-O-Si.

The peak at 3372 cm^{-1} depicts the -OH of the silanol group of PSL-3 (**Figure 3**). The characteristic sharp peak at 1071 cm^{-1} shows the asymmetric stretching vibration of siloxane [31-32]. The peaks at 964 cm^{-1} and 799 cm^{-1} show stretching vibration of the silanol group. The characteristic peak around 556 cm^{-1} shows angular deformation of Si-O-Si.

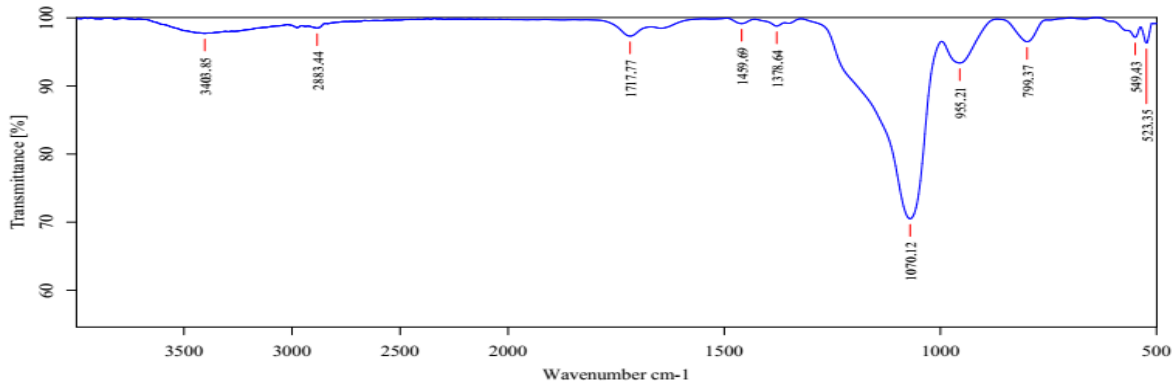


Figure 1. FTIR of Synthesized SBA-15 (PSL-1).

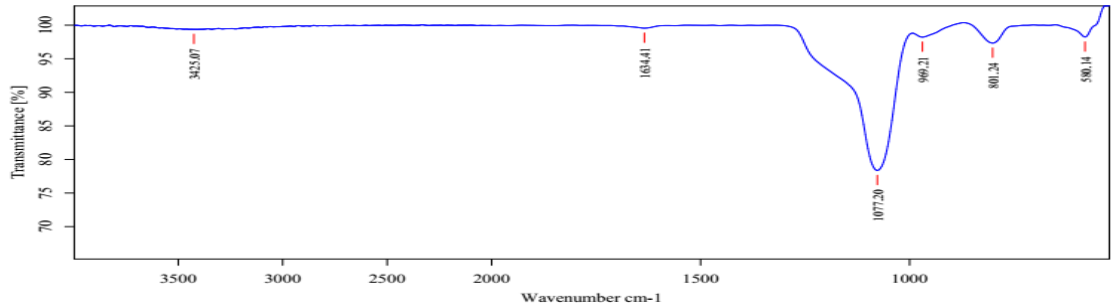


Figure 2. FTIR of Calcined Silica (PSL-2).

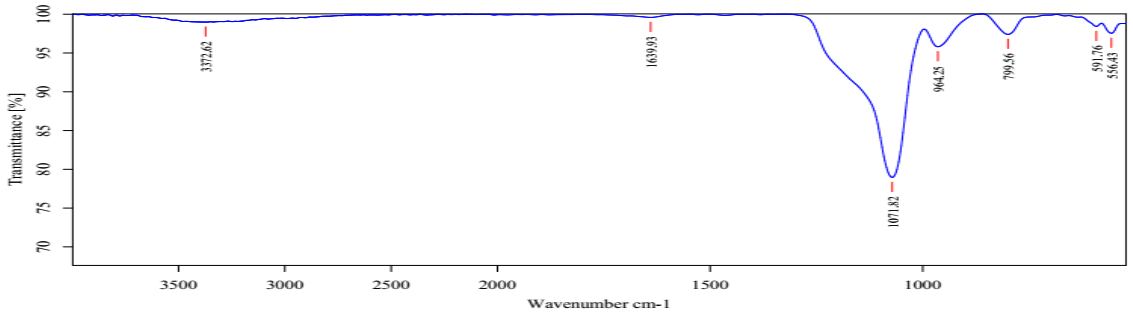


Figure 3. FTIR of Methanol refluxed silica material (PSL-3).

In **Figure 4** (PSL-4), the peak at 3329 cm^{-1} depicts the -OH of the silanol group. The characteristic sharp peak at 1070cm-1 shows the asymmetric stretching vibration of siloxane [29- 30]. The peaks at 958 cm^{-1} and 800 cm^{-1} show stretching vibration of the silanol group. The characteristic peak around 552 cm^{-1} shows angular deformation of Si-O-Si. Using only ultrasonic waves in method III for template removal is inefficient in removing templates [33]. The solvent extraction method was more efficient than method III, but the volume of solvent employed was high.

The peak at 3312 cm^{-1} depicts the -OH of the silanol group of PSL-5 (**Figure 5**).

The characteristic sharp peak at 1073cm-1 shows the asymmetric stretching vibration of siloxane [31-32]. The peaks at 961 cm^{-1} and 801 cm^{-1} show stretching vibration of the silanol group. The characteristic peak around 560 cm^{-1} shows angular deformation of Si-O-Si.

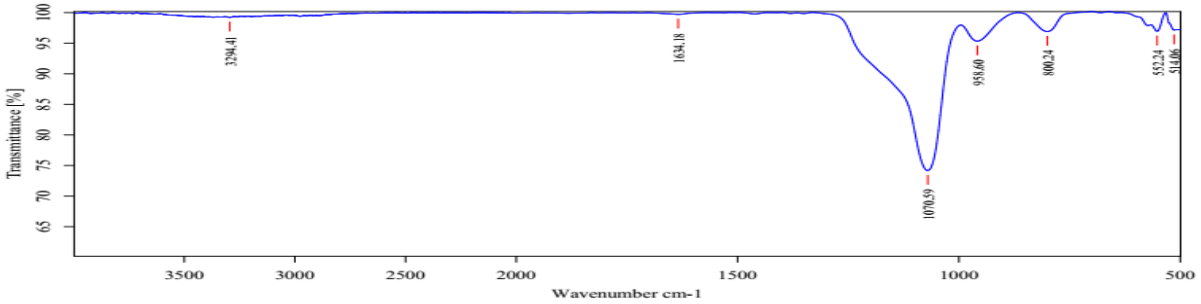


Figure 4. FTIR of Ultrasonicated silica material (PSL-4).

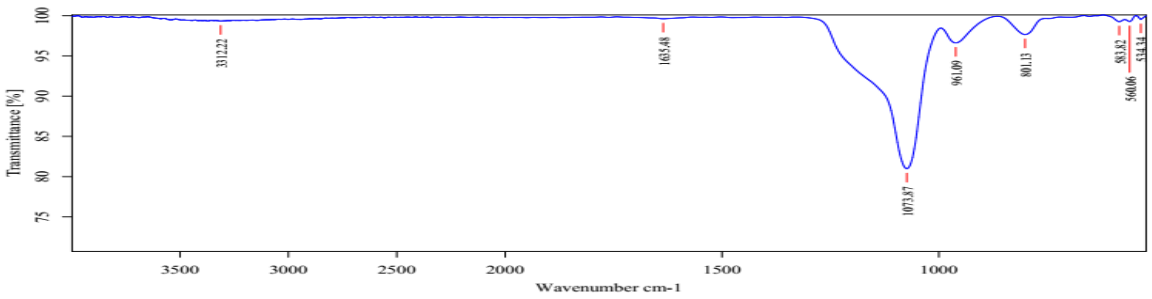


Figure 5. FTIR of silica material obtained by hybrid method (PSL-5).

In all the spectra, the peaks in the 1634-1639cm^{-1} range indicate the -OH angular deformation of water molecules that are adsorbed onto the surface of silica nanoparticles. A comparison of all the methods for template removal is depicted in **Table 3**.

The presence of a template after the sol-gel synthesis is evident from FTIR Spectra of PSL-1. All four template removal methods effectively expose the functional groups as evidenced by respective FTIR Spectra. Method IV involved solvent reflux and ultrasonication to impart porosity in silica particles and was more efficient than the other three methods regarding time consumed, amount of solvent used, and no liberation of obnoxious gases. Different methods employed in the template removal process have shown great efficiency in generating pores among silica particles. The silica material processed via conventional methods is compromised in retaining the properties of a mesoporous nature-like tendency to undergo modification for multi-functionalization and surface area. Thus, there are certain disadvantages associated with the method I of template removal, like structural deformity of the silanol group impeding the advantage of mesoporous material release of obnoxious gases that result in pollution [27]. Although the conventional method of calcination and solvent extraction generates good porosity, certain pitfalls like an intense process, longer time, consumption of more solvent, and environmental impact during synthesis are observed. Method IV, involving mild conditions, is equally effective in imparting porosity. From the FTIR spectra, the sample PSL-5 was chosen for further characterization.

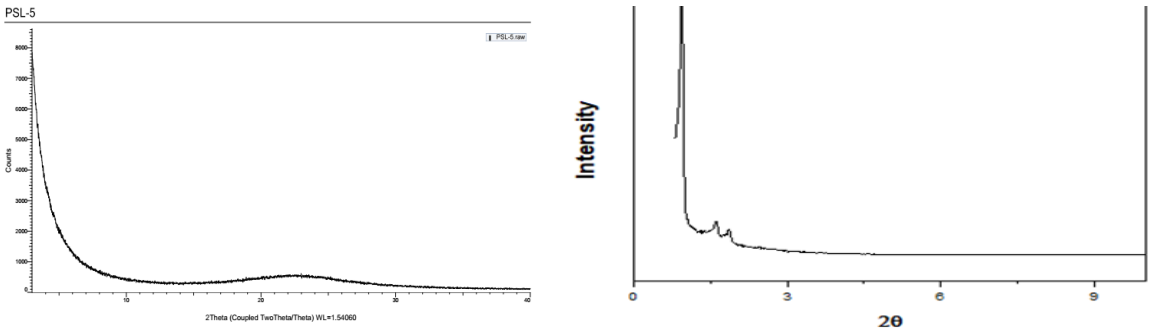
3.1.1. XRD of PSL-5

The high angle XRD in the scan range of 10^0-80^0 shows the amorphous nature. The hexagonal crystalline structure of SBA-15 is clear with peaks at 2 θ 0.94^0, 1.40^0, and 1.70^0 in low-angle XRD**.** The spectrum showed a porous hexagonal structure, as shown in **Figure 6**. Even after a long time after synthesis, the low-angle XRD Pattern shows stability by retaining crystalline structure. The obtained mesoporous material retained a hexagonal structure even after one year, which can be used for diverse applications.

Table 3. Comparison of all four template removal procedures**.**

S. No	Characteristic	Method			
		I	II	III	IV
1	Time	+++*	+++	+	++
2	Solvent Ratio	1:5	1:5	1:5	1:3
3	Temperature	400^{0}C	60^{0}C	30^{0}C	30^0-60^{0}C
4	Pollution	+++	-*	-	-
5	Characteristic siloxane peak in FTIR	1077 cm^{-1}	1071 cm^{-1}	1070 cm^{-1}	1073 cm^{-1}

+++* indicates more intense; -* indicates null



High angle XRD Low angle XRD

Figure 6. XRD of PSL-5 (Left: High angle XRD, Right: Low angle XRD).

3.1.2. SEM of PSL-5

The uniform particle size distribution is evident from the SEM image of PSL-5, as seen in **Figure 7**. No evidence of agglomerates shows the suitability of PSL-5 as the carrier for various applications.

3.1.3. ZETA POTENTIAL of PSL-5

The Zetapotential of SBA-15 determined by the Zeta sizer was found to be 16.8 mv **(Figure 8**). The Zetapotential indicates repulsion among particles that contributes to the stability of the mesoporous material.

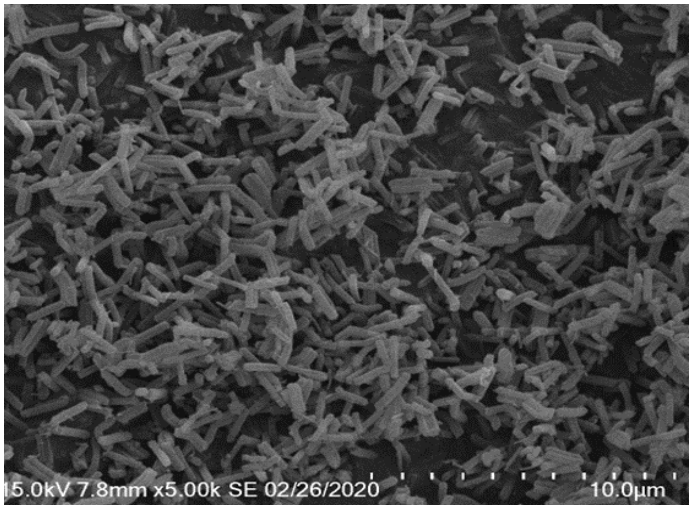


Figure 7. SEM image of PSL-5.

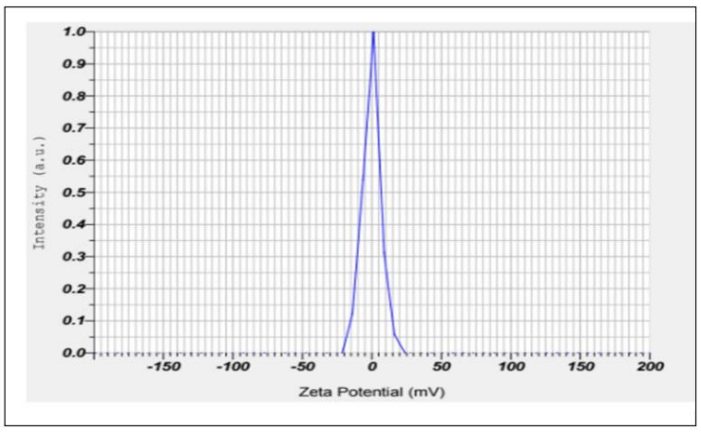


Figure 8. Zeta potential of PSL5 sample.

3.1.4. FTIR of PSL-5 and Citronellol admixture (1:1)

The FTIR of the physical admixture of Mesoporous material (**Figure 9**) and citronellol depicts the presence of both the functional groups of Mesoporous silica as well as Citronellol. More intense peaks are observed in the admixture, indicating the incorporation of citronellol in the mesoporous material. The peak appearance at 2962cm-^{1} and 2918cm-^{1} shows C-H stretching vibration. The peak at 1378 cm^{-1} indicated C-O-H deformation. There is a shift in the vibrational peak of siloxane from 1070 cm^{-1} to 1060 cm$^{-1,}$ indicating the incorporation of citronellol into the porous structure. The appearance of major peaks of citronellol and PSL-5 and the shifting of some peaks in the FTIR spectrum show the carrier's compatibility and successful incorporation of citronellol in the mesopores of PSL-5, respectively.

3.2 Applicability of SBA 15 (PSL-5) as a slow-release carrier in mosquito repellent cream

The formulation F4 deterred the mosquitoes for a prolonged period compared to F8 formulation in which mesoporous carrier SBA 15 was not used (**Table 4**). The repellency effect was prolonged for more than 3 hrs with the carrier. When citronellol was applied alone on the skin, it could repel mosquitoes for about 30 minutes. This shows that using a simple carrier like SBA -15 could effectively repel mosquitoes for a prolonged period.

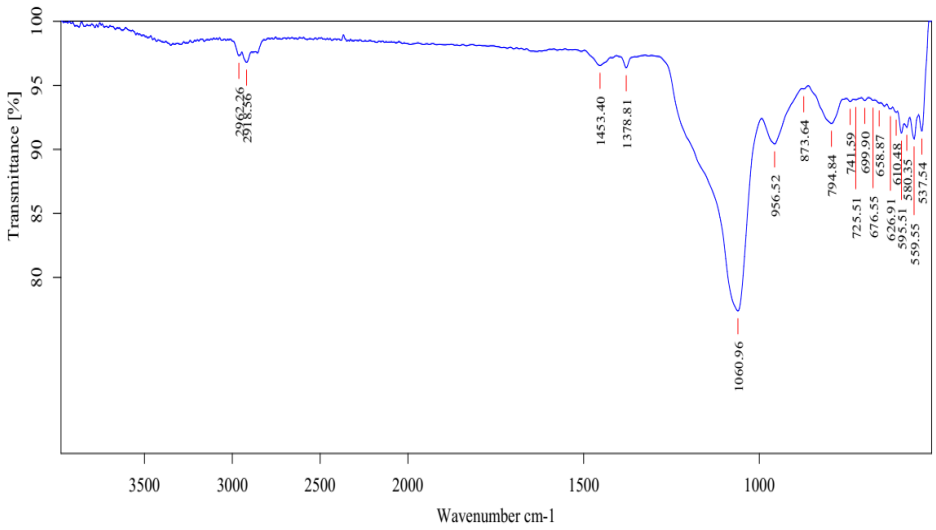


Figure 9. FTIR of PSL-5: Citronellol (1:1 weight ratio).

Table 4. Mosquito Repellency-Efficacy of SBA 15**.**

No	Formulation	Repellency time (Minutes)
1	CO	30 ± 05
2	F8	40 ± 05
3	F4	210 ± 05

4. Conclusion

There is always a demand to develop economical methods of industrial importance. The current low-cost method was developed to impart porosity in SBA 15 with the advantage of stability for long-term use that makes these materials feasible for application in varied fields as carriers. The mosquito repellent cream formulation F4 developed by incorporating the carrier obtained via an economical route has shown better repellency than the cream without the carrier. Thus, the novel template removal method developed is economical and environmentally friendly. Further studies can be carried out using mesoporous material as a slow-release carrier to optimize different formulations that demand more action duration.

Acknowledgments

The authors express their gratitude to ATGC Biotech. Hyderabad responsible for providing analytical facilities to carry out research. The authors thank Dr. Ravindra Babu Peram for his technical support in the study.

Conflict of interest

The authors declare to have no conflict of interest.

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