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Nanosilica for Sustained Release of Quercetin and its Antioxidant Activity

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Abstract:- This study was carried out to synthesize silica nanoparticles for Sustained drug release. Synthesis of nanosilica was carried out from Rice husk ash by sol-gel method and the size distribution was controlled by using different surfactants like, a cationic (CTAB) and anionic (SDS) surfactant. The quercetin – a flavonoid was successfully incorporated in nanosilica synthesized using 2% SDS surfactant and was grafted with PEG 4000. The quercetin loading capacity into nanosilica was determined depending on different concentrations used for loading. The release of this loaded quercetin was traced using UV spectrophotometer for sustained release in Ethyl acetate. The % release profile was also determined. The Antioxidant activity of the quercetin incorporated nanosilica was checked using a DPPH antioxidant assay. The successful nanosilica synthesis and drug loading and grafting by PEG 4000, all were confirmed by using characterization techniques like Dynamic light scattering for particle size analysis, Scanning electron microscopy (SEM) and IR spectroscopy.

Keywords:- *Silica nanoparticles, Rice husk ash, sol-gel method, Surfactants, CTAB, SDS, Quercetin, PEG 4000, Sustained release, Antioxidant activity, 2,2-diphenyl-1-picrylhydrazyl(DPPH), UV spectrophotometer, Particle size analysis, SEM and IR spectroscopy.*

I. INTRODUCTION

A. Synthesis of Nanosilica:

Manipulation of matter on a 'nano' scale, is considered to be a key enabling technology. It is commonly known as nanomedicine, Medical applications of nanomaterials are expected to significantly improve disease diagnostic, therapeutic modalities and subsequently reduce health care costs [1].

The nano silica powder is generally prepared by using sol–gel method. In most of these methods, nano silica powder is synthesized using chemicals as a raw material. In chemical methods, it is easy to control size, shape and purity of the material but the starting reagents are costly. In industrial applications, low costs and large quantities of initial precursor are needed. Rice husk ash is one of the most abundant by-products produced in the paddy field. Rice husk is a form of waste from the rice milling industries and is produced in abundance in around the country. All riceproducing countries have abundant quantity of rice husk. India alone produces 12 million tons of rice husks every year. Thus worldwide annual husk output is estimated is 80 million tons. So it is an eco-friendly process as it minimizes the paddy husk ash waste. Rice husk are often left to rot in field or burnt in open. Rice husk contains silica in range of 20- 25wt%. The silica in rice husk exists in the hydrated amorphous form like silica gel. The amorphous nature of silica in rice husk makes it extractable. Thermal degradation and pyrolysis of rice husk followed by the combustion of the char results in a highly porous and amorphous silica with a varying percentage of unburnt carbon. Combusted at moderate temperature, the white ash obtained from rice husk contains approximately 92-97% amorphous silica [2].

Highly pure, small particle-size nano silica powder with high-surface area from agricultural by-product, such as rice husk ash, by using a simple user-friendly, alkali extraction followed by an acid precipitation method. The method is simple, cost-effective, reliable and reproducible. The purity obtained by this method is enhanced to conventional methods [3].

B. Drug Loading and PEG Grafting:

Flavonoids are a large group of phenolic compounds that are widely spread in different plant foods. Quercetin (3,3′,4′,5,7-pentahydroxyflavone) is a common dietary flavonol with a wide range of pharmacological activities including antioxidant, antiplatelet, anti-inflammatory, antimutagenic, anticarcinogenic, antiangiogenic, antibacterial, antitumor, antiviral, and hepatoprotective. The beneficial biological properties of quercetin make it a promising therapeutic agent. A possible approach to overcome this problem is loading of quercetin in appropriate drug delivery systems [4]. The possibility of a combination of controlled drug delivery and biocompatible properties of mesoporous silica has great advantages once silica can induce bioactivity through its extrinsic properties. Silica has a porous network with different diameters and extensions that provide the possibility of hosting different molecules. The wall structures of silica pores are formed by a disordered network of free silanol groups and silane bonds that act as reactive nuclei and can be hosts for chemical species [5-8].

This paper to contribute to the development of drug controlled release systems for the treatment of diseases like cancer. Thus, mesoporous silica matrix were synthesized and characterized the flavonoid quercetin ($C_{15}H_{10}O_7$) was incorporated to the particles.

In this field drug delivery system utilizing polymeric carrier, which covalently conjugates molecule of interest, plays an important role in modern therapeutics. Such polymer-based drug entities are called as "polymer therapeutics" The objectives for designing polymer therapeutics are primarily to improve the potential of the respective drug by enhancing water solubility, particularly relevant for drugs with low aqueous solubility, targeted delivery of drugs to specific site of action in the body and Stability against degrading enzymes or reduced uptake by endothelial system. The smart drug delivery systems should possess some important feature such as pre-scheduled rate, self-controlled, targeted, predetermined time and monitor the delivery [9]. PEG pro-drugs have been designed mostly for the delivery of anticancer agents due to its overall implications in the treatment. However it should be noted that PEG-antitumor pro-drug is expected to be stable during circulation and degrade or hydrolyze only on reaching the targeted site [10]. The coating or encapsulation of nanoparticles has been found to be of particular interest in sustained drug delivery. A polyethylene Glycol as a coating steric stabilizer is covalently bound to the particle at the one end Thus, in an aqueous suspension, the aggregation among the nanoparticles is prevented by the repulsion force of the PEG surface moiety. Some of the advantages are PEG is nontoxic, and its attachment to silica nanoparticles provides a biocompatible and protective surface. Due to high aqueous solubility, PEG polymer is considered as a versatile candidate for drug conjugation [11].

C. Sustained Release:

Much attention has been devoted to the development of suitable apparatus to assess *in vitro* release from nanoparticulates. In contrast to oral dosage forms where release media typically mimics pH of the gastrointestinal tract, selection of release media for nano-sized dosage forms will vary depending on the site of administration as well as the site of action of the formulation. In general, selection of release media for nanoparticulate preparation is generally based on drug solubility and stability, assay sensitivity, and the method used. Drug releases from nanoparticle by three categories, such as sample and separate (SS), continuous flow (CF), and dialysis membrane (DM) methods [12].

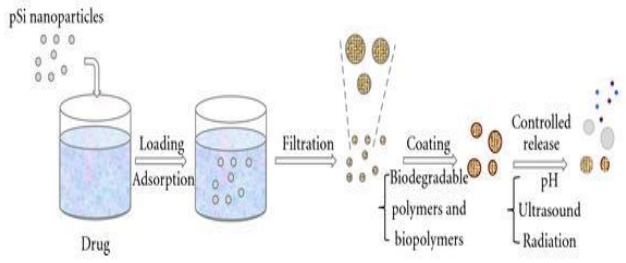

Fig 1:- Schematic for sustained drug release from nanosilica

In the sample and separate method, the dosage form is introduced into the release media that is maintained at a constant temperature, after which drug release is assessed by sampling of the release media (filtrate or supernatant) or the nanoparticles [13]. The use of syringe filters to achieve physical separation between the release media and nanoparticles, the small size of nanoparticles has separated by use of high energy separation techniques like centrifugation, ultracentrifugation, and ultrafiltration. Generally, this method provides a direct approach to monitor drug release [14]. In continuous flow drug release occurs as a result of buffer or media constantly circulating through a column containing the immobilized dosage form and is monitored by collecting the eluent at periodic intervals. Most used method is sample and separate, only a few examples of the continuous flow have been reported for nano-sized dosage forms. Flow rates used in this method depend on the type of pump as well as the filters used. This method suffer from several disadvantages including difficulty in set-up, instrument costs, filter clogging, adsorption to the filter and glass beads, and difficult to maintain the constant flow rate lead to variables in results. Low flow rates have been known to be a key factor causing slow or incomplete release from dosage forms [15]. This is the most versatile and popular method, in this method, physical separation of the dosage forms is achieved by usage of a dialysis membrane which allows for ease of sampling at periodic intervals. In general, the volume enclosed in a dialysis bag (inner media) is significantly smaller than the outer media. Thus, container size will depend on the total volume of release media required for the *in vitro* release study. In the regular dialysis technique, drug released from the nanoparticles diffuses through the dialysis membrane to the outer compartment from where the samples analysed [16].

D. Determination of Antioxidant activity from nanosilica

To determine the antioxidant activity in a like manner by using a stable free radical α, α-diphenyl-β-picrylhydrazyl (DPPH; $C_{18}H_{12}N_5O_6$, M = 394.33). The assay is based on the measurement of the scavenging capacity of antioxidants towards it. The odd electron of nitrogen atom in DPPH is reduced by receiving a hydrogen atom from antioxidants to the corresponding hydrazine. DPPH can accept an electron or hydrogen radical to become a stable, diamagnetic molecule; it can be oxidized only with difficulty, and then irreversibly. DPPH shows a strong absorption band at 517 nm due to its odd electron and solution appears a deep violet colour, the absorption vanishes as the electron pairs off. The resulting decolourization is stoichiometric with respect to the number of electrons taken up.

It is a rapid, simple, inexpensive and widely used method to measure the ability of compounds to act as free radical scavengers or hydrogen donors, and to evaluate antioxidant activity of foods. It can also be used to quantify antioxidants in complex biological systems, for solid or liquid samples. DPPH method may be utilized in aqueous and non-polar organic solvents and can be used to examine both hydrophilic and lipophilic antioxidants. Ascorbic acid is used here as a standard antioxidant.

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II. EXPERIMENTAL SECTION

A. Materials:

Rice Husk Ash (obtained from Ahmedabad, India), Sodium hydroxide (Merck grade), Surfactants CTAB (Cetyltrimethylammonium Bromide and SDS (Sodium dodecyl sulfate) (S.D.Fine Chem), Sulphuric Acid (Merck grade), Quercetin (Sigma Aldrich), Polyethylene Glycol molecular weight 4000 (PEG 4000), Whatman Filter paper, L-Ascorbic acid stock, Ethyl Acetate (Merck Grade), and DPPH (2,2-diphenyl-1-picrylhydrazyl). (Sigma Aldrich).

B. Methods:

➢ *Extraction of Silica from Rice Husk Ash (RHA):*

2.5 N NaOH solution was added in to 25 gm of RHA, mixed using a clean glass road and the beaker was kept for boiling for 90 minutes continuous stirring was carried out during boiling. After 90 minutes, content was allowed to cool down and the solution was filtered using a whatman filter paper, obtained filtrate was sodium silicate and residue above the filter paper is carbon. The residual carbon was washed using distilled water and then dried in a hot air oven.

$$2NaOH\ (aq.) + RHA\ (s) \longrightarrow Na2SiO3\ (aq.) + H2O\ (g)$$

Sodium Hydroxide Sodium silicate

➢ *Preparation of mesoporus Nanosilica:*

Sodium silicate solution was split up into two beaker and adds 2% Cetyl trimethylammonium Bromide (CTAB) cationic surfactant in one beaker and 2% Sodium dodecyl sulfate (SDS) anionic surfactant was added into another beaker. 5 M H_2SO_4 was added drop wise using separating funnel till neutral pH was achieved, after achieving neutral pH the mixture was stirred for extra half hour. The mixture was centrifuged at 500 rpm for 6 minutes, the supernatant obtained was discard and warm distilled water was added, this step repeated till all the un reacted surfactant was removed. Residue was dried in hot air oven at 90 °C around 8 hrs. Dried residue was grounded as fine as possible using mortar and pestle.

$$Na2SiO3\ (aq.) + H2SO4\ (aq.) \xrightarrow{\text{Surfactant}} SiO2(s) + Na2SO4\ (aq.) + H2O$$

Sodium silicate Sulphuric acid Silica oxide NP

➢ *Incorporation of quercetin in Silica Nanoparticles:*

Quercetin was incorporated into silica nanoparticles synthesized using 2% SDS surfactant. Quercetin stock of 10µg/ml was prepared in ethanol. The stock was properly stirred by using Sonicator for 15 minutes. The absorbance of this mixture (at 375 nm) was then taken using an UV spectrophotometer and noted down, 100 mg of silica nanoparticles synthesized using 2% SDS surfactant was weighed and added into the vial. The assembly was stirred for around 27 hours using a magnetic stirrer.

➢ *PEG grafting of Quercetin loaded Silica nanoparticles:*

The absorbance of stirred sample was taken (at 375 nm) using UV spectrophotometer, samples showed increase in absorbance reading compared to the absorbance taken for quercetin stock before loading. 100 mg of Polyethylene Glycol molecular weight 4000 (PEG 4000) was weighed and added to reaction mixture in and the assembly was then kept on stirring for 24 hours using a magnetic stirrer. After stirring, the mixture was filtered out using a Whatman Filter paper. The absorbance of filtrate (at 375 nm) was taken using an UV spectrophotometer and noted down. The PEG coated Quercetin loaded nano-silica which was retained on filter paper was allowed to air dry and then stored properly in sample vial and kept in dark.

➢ *Sustained release of Quercetin from PEG coated Quercetin loaded nanosilica:*

5 mg of PEG coated quercetin loaded nano-silica was weighed and added to 10 ml Ethyl acetate in a glass vial. Immediately after the addition, 2 ml aliquot was taken and absorbance was checked at 375 nm (0 minute reading). The same aliquot was added back to vial and then assembly was kept undisturbed throughout experimentation time, absorbance readings (at 375 nm) were taken using an UV spectrophotometer after some definite time intervals in a fashion similar to 0 minute reading. The process was repeated till a constant absorbance reading was obtained. This reading indicates the maximum release of the quercetin from nanosilica.

➢ *Determination of Antioxidant activity using DPPH:*

10 µg/ml L-Ascorbic acid stock was prepared in distilled water and kept for sonication for 15 minutes prior to use and 2 µM DPPH stock was prepared in Ethanol. The stock was prepared and stored in amber coloured bottle and at cold temperature (4 °C). Based on controlled release calculations, stock of 1 µg/ml quercetin in Ethyl acetate was prepared, dilutions of this stock served as positive control for released quercetin, 400 µl aliquot of released quercetin was taken from PEG coated quercetin loaded nano-silica sample added in Ethyl acetate after constant absorbance reading at 375 nm taken using an UV spectrophotometer.

The dilutions of L-Ascorbic acid stock were made as per the table 1.

Concentration of Ascorbic acid (µg/ml)	Volume of Ascorbic acid stock (µl)	Diluent/ distilled water (µl)	Total volume (µl)
0	--	400	400
0.3	12	388	400
0.3	13	384	400
0.6	24	376	400
0.8	32	368	400
1.0	40	360	400

Table 1:- DPPH Assay dilutions for 10 µg/ml L-Ascorbic acid

Sample Concentration (µg/ml)	**Volume of sample stock (µl)**	**Diluent/ Ethyl acetate (µl)**	**Total volume (µl)**
0.2 Quercetin	80	320	400
0.4 Quercetin	160	240	400
0.6 Quercetin	240	160	400
0.8 Quercetin	320	80	400
Released Quersetin.	400	--	400

Table 2:- DPPH Assay dilutions for PEG coated Quercetin loaded nanosilica and Positive controls.

All the dilutions were made 3600 µl of DPPH was added to each tube, all the tubes were kept on sonicator for half a minute. This was done to mix all the contents well. The tubes were incubated in dark at room temperature for 30 minutes. The absorbance was taken at 515 nm using an UV Spectrophotometer. Based on the results, % Scavenging activity of released quercetin was calculated with following formula.

$$\%\,\text{Scavenging activity} = \left(1 - \frac{\text{Absorbance of Sample (515 nm)}}{\text{Absorbance of Control (515 nm)}}\right) * 100$$

III. RESULTS AND DISCUSSION

A. Nanosilica Extracted from RHA:

The concentration of sodium hydroxide (2.5 N) used for extraction of silica from Rice husk ash plays significant role in obtaining the pure quality of silica. The silica obtained is in form of sodium silicate (solution), after addition of surfactants (2 % CTAB and 2% SDS) and treatment with sulphuric acid the sodium silicate gets converted to gel. Thus, the process is sol-gel. The obtained gel is filtered and dried, SiO_2 in powder form.

RHA (gm)	**Silica synthesized (gm)**	**% Silica yield**
25	20.4	81.60%

Table 3:- The % yield of synthesized silica

B. Characterization of Nanosilica:

➢ *Particle Size Analysis:*

Particle size analysis was carried out, for nanosilica made using 2% CTAB and 2% SDS surfactant.

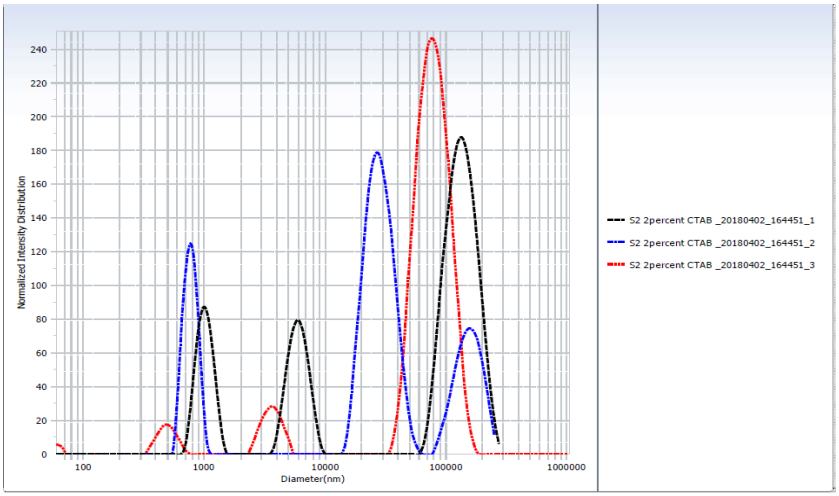

Fig 2:- Particle size distribution for silica made using 2% CTAB.

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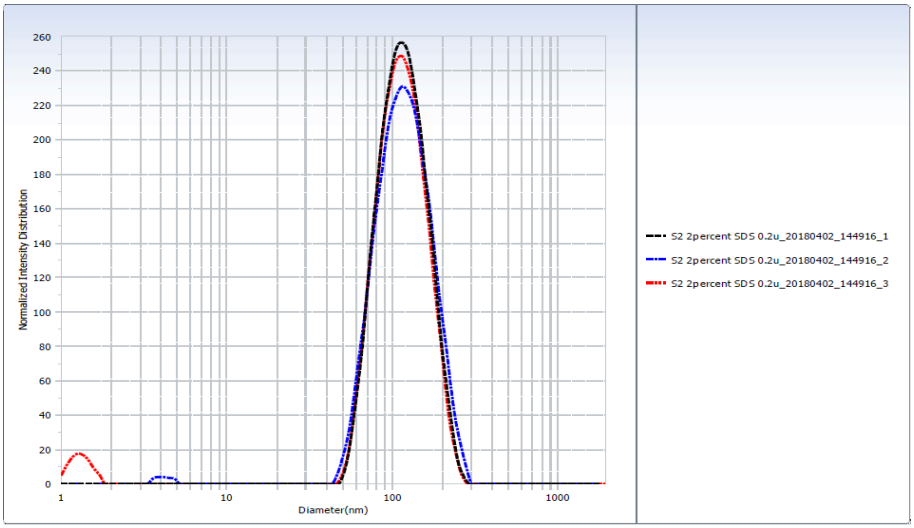

Fig 3:- Particle size distribution for nanosilica made using 2% SDS.

The distribution obtained in silica made using 2% CTAB is not an ideal one. The particle sizes (diameters) obtained in three iterations was 5638.5 nm, 4915.7 nm and 13213.4 nm. These are in micrometer ranges and thus, the silica powder synthesized cannot be considered as nanosilica. This could have been happened due to agglomeration. The huge variations during 3 iterations also shows that small sized particles might be present in solution, but presence of large particles are hiding them from DLS laser source. This silica sample was not used for any further experimentation.

The particle size distribution obtained for nanosilica sample made using 2% SDS surfactant showed an ideal result. The particle sizes obtained during 3 iterations were 142.4 nm, 140.2 nm and 159.9 with average particle diameter of 147.5 nm. It was also found that in the dispersion 10% of scanned particles were having diameter less than 68.8 nm while 90% of scanned particles were having diameter less than 172.3 nm. Thus, the width of the graph tells us that the particle falls in range of around 70 – 170 nm. Thus, nanosilica with quite low polydispersibility index (0.109) was obtained using 2% SDS surfactant. Same sample was used for further experimentation.

The SEM was carried out only on nanosilica made using 2% SDS surfactant.

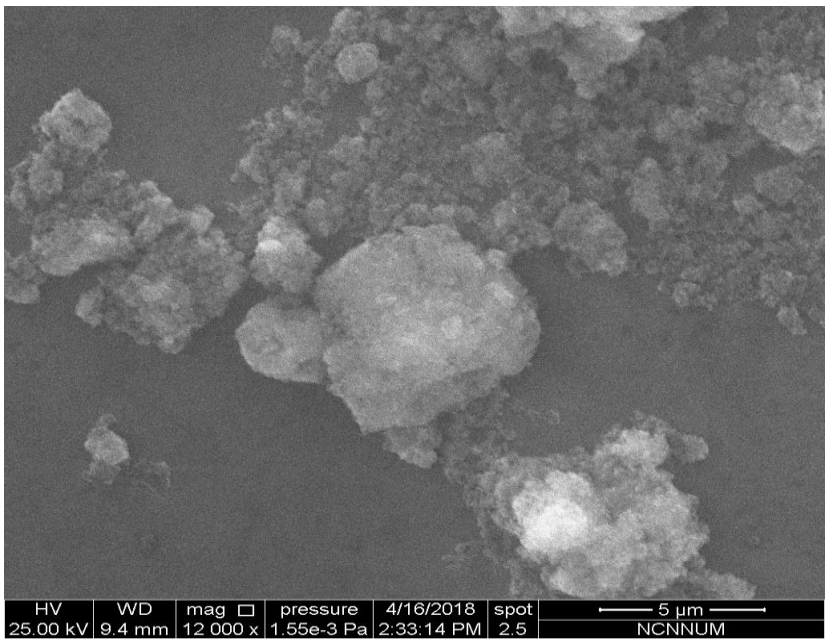

Fig 4:- The SEM result for nanosilica made using 2% SDS from 5 µm

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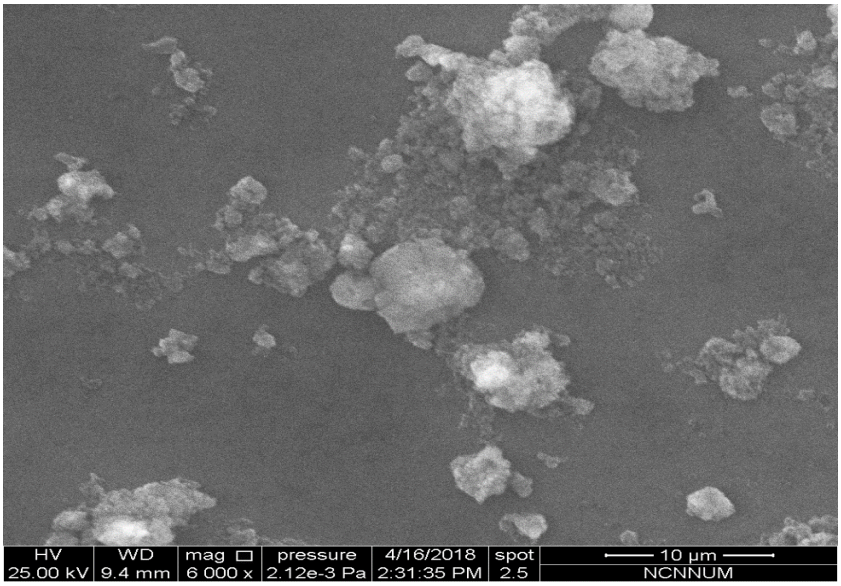

Fig 5:- The SEM result for nanosilica made using 2% SDS from 10 µm.

The data was collected over a selected area of 5 µm and 10 µm surface of the sample. The difference between two images is clear, as smaller distance (5 µm) shows less particles but high focus, while larger distance (10 µm) shows more particles. The results indicate that, agglomeration of nanosilica is present. This was very well expected as no functionalization of nanosilica or polymer coating was carried out at this stage. The nanoparticles obtained are irregularly shaped and thus have many cavities over its surface. Such topography is suitable for loading a drug moiety in it by simple physical attachment or adsorption [17]. Thus, the nanosilica can be used for loading of quercetin**.**

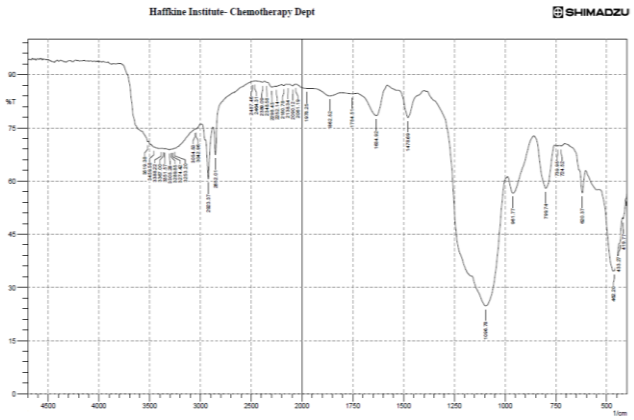

Fig 6:- IR results for silica made using 2% CTAB.

Infra Red (IR) gives idea about the molecules (functional groups) present in the given sample.

Broad peak at 3200 cm^{-1} indicates presence of OH groups. The CH_2 stretching at 2852.01 cm^{-1} and Si-O-Si stretching at 1096.78 cm^{-1}, confirms the silica particles controlled by CTAB surfactant.

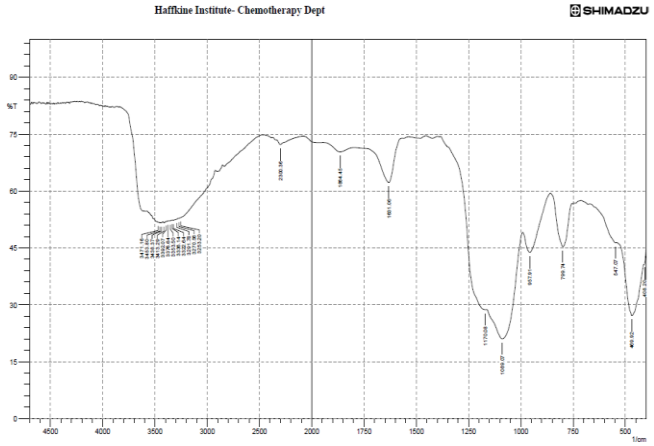

Fig 7:- IR results for nanosilica made using % SDS.

The CH_2 bending at 1631.06 cm^{-1} and Si-O-Si stretching at 1089.07 cm^{-1}, confirms the silica particles controlled by SDS surfactant. The shift seen in CH_3 asymmetric stretching and CH_2 bending (includes scissoring and wagging) band pattern reconfirms the same.

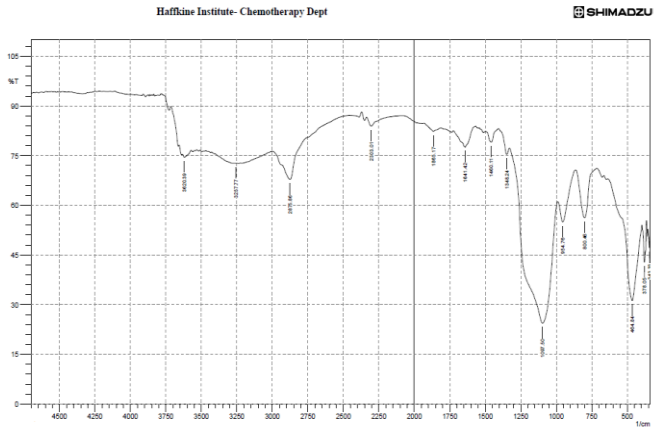

Fig 8:- IR results for nanosilica made using 2% SDS and PEG coating.

The intensity of peak at 1641.42 cm^{-1} which corresponds to peak at 1631.06 cm^{-1} in figure 4.2.5 is much smaller. This indicates the successful grafting by Poly ethylene glycol (PEG), as it hides the exposed groups of silica and SDS surfactant.

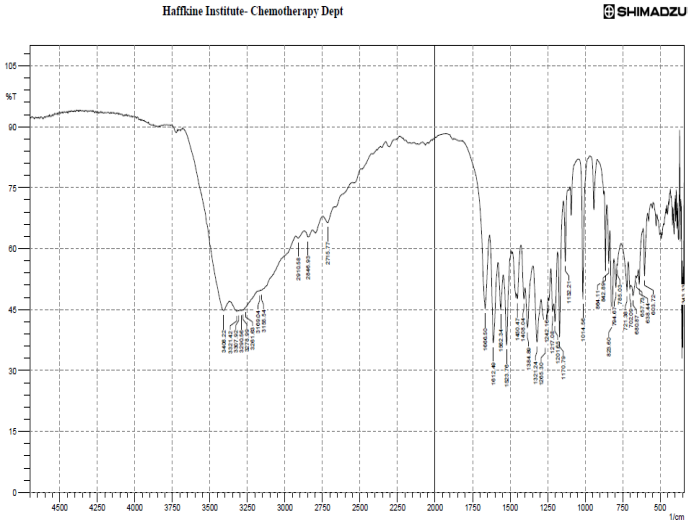

Fig 9:- IR results for Standard Quercetin.

Broad peak at 3200 cm^{-1} indicates presence of OH groups which are largely present in quercetin structure itself. The C=O stretching at 1666.50 cm^{-1} is a strong indicator of quercetin. The expected frequencies with respect to quercetin in presence of silica have been considered from the literature [18].

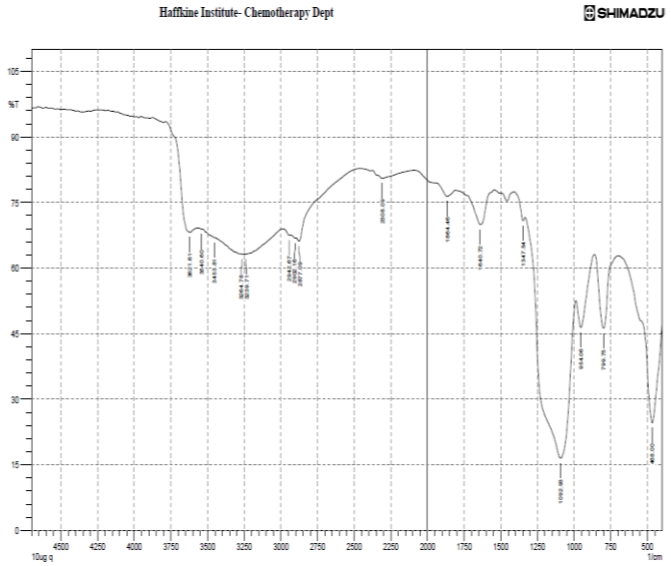

Fig 10:- The IR results for PEG coated 0.01% Quercetin loaded nanosilica made using 2% SDS.

Broad peak at 3200 cm^{-1} indicates presence of OH groups of quercetin. The slight shift of C-H stretching bands of quercetin at 1648.20 cm^{-1} and 1640.72 cm^{-1} in respective loaded nanosilica are indication of successful loading. Also, the slight shifts in Si-O-Si stretching at 1092.93 cm^{-1} of silica and CH_2 wagging at 1347.54 cm^{-1} of SDS surfactant reconfirm the same, as addition of quercetin has changed their interaction environment.

IV. LOADING AND RELEASE PROFILE

A. Standard graph for Quercetin loading:

In order to obtain concentration of quercetin that has been loaded in nanosilica, it is important to first plot a standard graph for a range of quercetin concentrations. The slope of this graph will be used to determine the concentration based on the absorbance obtained by UV-spectrophotometer. For 0.01% quercetin loading, a stock of 10µg/ml in ethanol was directly used, while for 10% loading, a stock of 10 mg/ml was used. But 10 mg/ml is very high range of concentration for spectrophotometric analysis and hence, was diluted 1000 times.

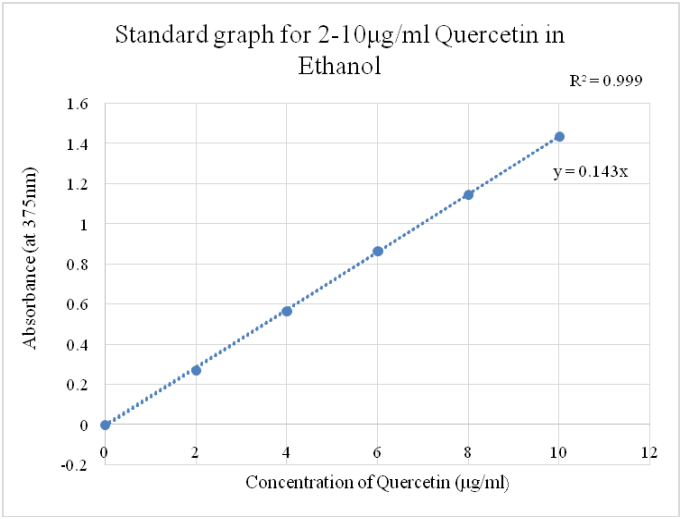

Fig 11:- Standard graph for loading 2-10 µg/ml Quercetin in Ethanol.

B. Standard graph for Quercetin release:

In order to obtain concentration of quercetin that has been released from nanosilica, it is important to first plot a standard graph for a range of quercetin concentrations. The slope of this graph will be used to determine the concentration based on the absorbance obtained by UV-spectrophotometer. For 0.01% quercetin loading, a stock of 10µg/ml in ethyl acetate was used.

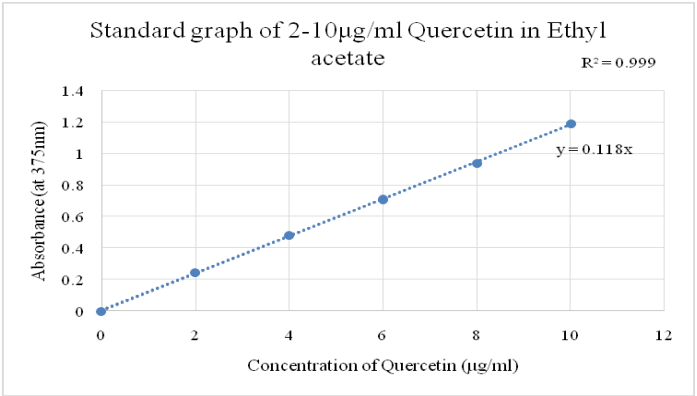

Fig 12:- Standard graph for release 2-10 µg/ml Quercetin in Ethyl acetate.

C. Sustained release of Quercetin from nanosilica:

Sr. No.	Time (mins)	Absorbance (at 375 nm)	Sr. No.	Time (mins)	Absorbance (at 375 nm)
1.	0	0.0227	9.	90	0.1259
2.	10	0.0447	10.	100	0.1402
3.	20	0.0559	11.	110	0.1460
4.	30	0.0832	12.	120	0.1526
5.	50	0.1028	13.	150	0.1400
6.	60	0.1063	14.	180	0.1467
7.	70	0.1114	15.	210	0.1344
8.	80	0.1111			

Table 3:- Absorbance of released quercetin from 0.01% Quercetin loaded nanosilica in Ethyl acetate

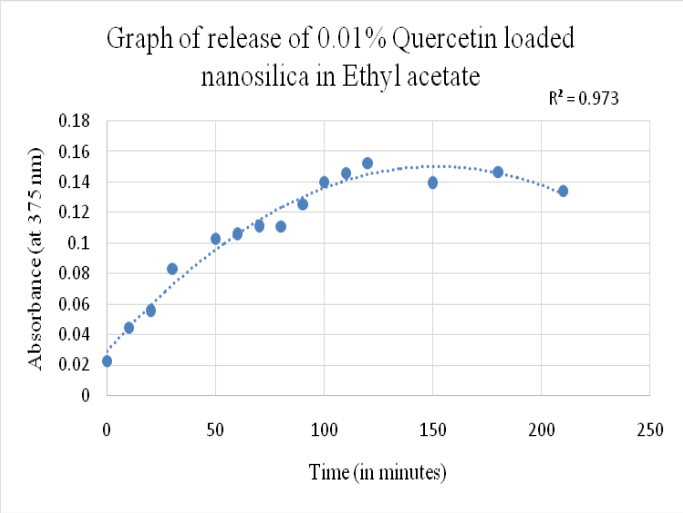

Fig 13:- Graph of sustained release from PEG coated 0.01% Quercetin loaded nanosilica.

5 mg of PEG coated 0.01% Quercetin loaded nanosilica particles were tested for release profile in 10 ml of Ethyl acetate. It can be seen that sustained release of quercetin is seen till 120 minutes as the absorbance readings at this point are maximum and stable.

D. Amount Quercetin loaded and released:

10 ml of 10 µg/ml Quercetin stock prepared in ethanol was taken and 100 mg nanosilica was used for drug incorporation. For obtaining the absorbance of the same the values were extrapolated on graph obtained in figure 13.

Sr. No.	Sample	Absorbance (at 375 nm)
1.	Before loading	1.4363
2.	Residual filtrate post PEG coating	0.2532

Table 4:- Absorbance of quercetin for 0.01% loading nanosilica in Ethanol

Based on slope value obtained from graph 11, the unloaded quercetin was 1.77µg and hence loaded amount of quercetin was found to be 8.23 µg for 100 mg nanosilica. The release study, 5 mg loaded nanosilica sample was taken and it thus contains 0.4115µg of Quercetin. This is the highest amount of quercetin that can be released. The % loading was found to be 82.30%.

5 mg of sample was suspended in 10 ml of Ethyl acetate. The absorbance obtained after 120 minutes was 0.0459. Based on slope value obtained from graph 12, the released quercetin was 0.389 µg for 5 mg nanosilica. The highest amount of quercetin that can be released is 0.4115 µg. Thus, % release was found to be 94.53%.

E. Scavenging Property of Quercetin incorporated nanosilica:

➢ *Standard graph for DPPH activity:*

In order to obtain % scavenging activity quercetin that has been released from nanosilica, it is important to first plot a standard graph for a range of L-ascorbic acid concentrations for DPPH scavenging. The slope of this graph will be used to determine the concentration based on the absorbance obtained by UV- spectrophotometer. For 0.01% quercetin nanosilica, a stock of 10 µg/ml L-Ascorbic acid in distilled water was used. L-Ascorbic acid is a standard antioxidant used for DPPH assay, and the respective samples.

Concentration of L-Ascorbic acid (µg/ml)	Absorbance (at 515 nm)
0	0.0153
0.3	0.0111
0.4	0.0083
0.6	0.0065
0.8	0.0042
1.0	0.0016

Table 5:- DPPH assay of 0.3-1.0 µg/ml L-ascorbic acid stock.

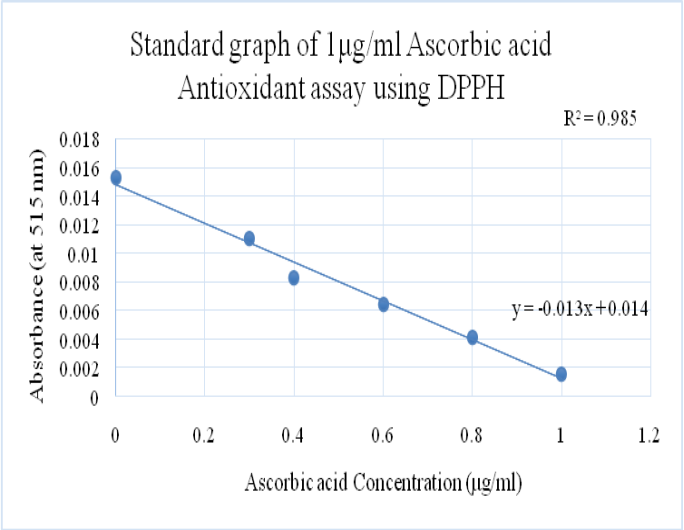

Fig 14:- Standard graph of 0.3 -1 µg/ml L-ascorbic acid antioxidant assay using DPPH.

The equation of the graph was found to be y=-0.013x + 0.014. The y in line equation indicates absorbance reading while x represents corresponding concentration.

Sample concentration (µg/ml)	Absorbance (at 515 nm)
0.2 Quercetin	0.0122
0.4 Quercetin	0.0076
0.6 Quercetin	0.0058
0.8 Quercetin	0.0031
Released Q. 0.01%	0.0097

Table 6:- DPPH Assay for PEG coated Quercetin loaded nanosilica and Positive controls

Based on equation obtained from graph 4.5.1, the released quercetin from 0.01% nanosilica was found to be 0.37 µg after 120 minutes; the expected amount was 0.31 µg and % scavenging property was found to be 36.60%. IC_{50} value for the assay was found to be 0.53µg/ml AAE.

V. CONCLUSION

In summary, we have developed a simple approach to prepare an intelligent drug controlled delivery system. Nanosilica particles with irregular shape and amorphous nature were synthesized from Rice husk ash. The synthesis was based on sol-gel method cationic surfactant (CTAB) and SDS anionic surfactant was used in order to guide the nanoparticle production. It was found that, the use of CTAB surfactant gave more yield by weight but the size of these particles was in micrometer range. Whereas, SDS yield was comparatively less than CTAB, but was in nanometer range (70-170 nm). This suggests a possibility that CTAB surfactant has less control in silica particle size than SDS surfactant. Scanning electron microscope (SEM) analysis on nanosilica made using SDS surfactant showed irregularity of surface, this indicates that the adsorption of quercetin on such surface is possible, thus making it a suitable candidate for quercetin as drug loading. The quercetin is known to have antioxidant properties and hence, both nanosilica samples (after 120 minutes release) were used in antioxidant assay using DPPH. Batch-1 particles showed 63.39% scavenging activity while Batch-2 showed 36.60%. The IC_{50} value for the given assay concentration was found to be 0.53 µg/ml AAE.

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