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Development, Preparation of Berberine Loaded Magnetic Nanoparticles by Modified Co-Precipitation Method and Characterization for Enhanced Dissolution and Stability Studies

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Abstract

The main goal of this present study was to prepare berberine loaded magnetic nanoparticles and to study some characters like bioavailability, stability, and dissolution. Berberine is an isoquinoline alkaloid naturally-derived from *Berberis aristata* additionally called Indian barberry, "chutro" or tree turmeric, is a shrub belonging to the family Berberidaceae and the genus Berberis comprising about 450-500 species of deciduous evergreen shrubs which well-known shows an extensive spectrum of pharmacological benefits, consisting of antiviral and anticancer houses etc. The Magnetic Nanoparticles was prepared with Iron salts by encapsulating a herbal drug BBR into the prepared magnetic nanoparticles which was characterized by FTIR, XRD, SEM, TGA, Drug loading Efficiency, zeta potential, VSM and Stability Studies. The data obtained from the XRD, FTIR and TGA studies states that formed BBR/MNPs was present in the structure with iron, silanol groups and berberine moieties. The average particle size after loading with berberine of MNPs 100 to 250 nm shown a regular spherical shape which was shown by results of HRSEM. The zeta potential value was found to be -9 mv and 15 mv at p^H 6 respectively. The VSM results shown that value of Fe-MCM-41 MNP is (81.76emu/g). The *in-vitro* dissolution studies at a three different P^H 5.5, 6.5, 7.4 were 86%, 84% and 82%, of four BBR/MNPs was stated. Loading efficiency and stability were good. All four prepared types of magnetic nanoparticles are good in structurally arranged, sufficient percentage of elements on their particle surface along with good size range, which possess high surface area and high pore volume, show magnetic response sufficient for drug targeting in the presence of an external magnetic field. Dissolution study of Berberine loaded MNP of Fe-MCM-41 shown maximum drug release at P^H 5.5.

Keywords: Co-precipitation Method, FTIR, HRSEM, VSM, Loading efficiency, Stability, Dissolution study.

Introduction

Natural herbal medicines have a multifaceted role in the prevention, diagnosis and treatment of ailments. During use, natural medicines show low side effects, low toxicity and more compatibility with all polymers used in the preparations. But it has some problems with low stability and low bioavailability. Here in this work has selected the drug called berberine. In Figure 1 Berberine (BBR) belongs to isoquinoline alkaloids, extracted from various parts like root, rhizome, stem and bark of herbs such as *Berberis aristata* and *Berberis vulgaris*. Active berberine components have shown diversified pharmacological uses, including antilipidemic,

anti-depressant and anti-inflammatory effects, treatment of diabetics, and control of cardiovascular diseases, anticancer and antimicrobial properties (1-3). It is discovered with inside the temperate and sub-tropical areas of Asia, Europe, and America. Magnetic nanoparticles are a category of nanoparticle which may be organized the usage of magnetic fields. It generally encompass components, a magnetic material, (iron, nickel and cobalt) and a chemical factor that has functionality.

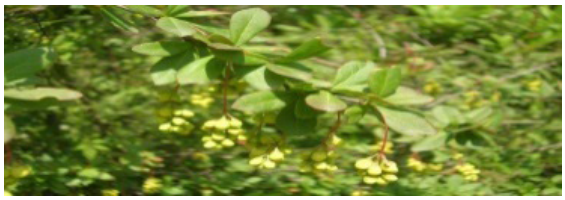


Figure 1: *Berberis aristata* plant

They are composed of some magnetic nanoparticles called magnetic Nano beads with a diameter of 50–200 nm [4-5]. The current improvement of nanomedicine is an artwork of turning in capsules to the target-site with the aid of using enhancing their protection and efficacy. Among them, Magnetic nanoparticles play a key position to expose their centered drug transport the usage of a magnetic field. The magnetic nanoparticles had been the point of interest of a lot studies currently due to the fact they own appealing houses that could see capability use in catalysis consisting of nanomaterial-primarily based totally catalysts,[6] biomedicine[7] and tissue unique targeting,[8] magnetically tunable colloidal photonic crystals,[9] microfluidics,[10] magnetic resonance imaging,[11] magnetic particle imaging,[9] facts storage,[12] environmental remediation,[13] Nano fluids,[14-15] optical filters,[16] illness sensor,[17] magnetic cooling[18-19] and cation sensors.[20]

Materials and Methods

The pure form of berberine powder was received as a compliment from Himalayan Herbaria Inc., Uttar Pradesh, India. The other chemicals such as Pluronic P123 ($EO_{20}PO_{70}EO_{20}$), Tetra ethyl ortho silicate (TEOS, 98%), Conc. HCl (48%), Ethyl alcohol (>99.9%), Hexane and Butanol were procured from Merck labs. Iron Acetyl acetone, Cetyl trimethyl ammonium bromide (CTAB) and ammonium hydroxide (NH_4OH) was obtained from Sigma-Aldrich.

Method of Preparation:

In this present study, we fabricated four Berberine-loaded magnetic nanoparticles using a modified co-precipitation method with calcination. The four types of magnetic nanoparticles were prepared using ingredients and quantity of ingredients mentioned in Table 1. The weighed amounts of all ingredients of step 1 are taken and the mixture was stirred over night at 32°C. It was transferred to a Teflon bottle and heated and refluxed for 48 hr at 100°C. The resultant precipitate was filtered, washed with Double-deionized (DD) H_2O and then dried. The intact surfactant layer was removed by calcinating at about 500°C for 8 hr. Then 0.3153 g of Iron (III) acetyl acetone dissolved in 3.0 ml of acetone with 0.3 ml of HNO_3 and stirred for 4 hr at 80° C. 0.25 g of formed nanoparticles were suspended in Fe $(AcetylAc)_3$ solution overnight and the solvent removed by stirring for 4 hr at 25°C. Then powder heated up to 500° C in a furnace for 2 hr with increasing temperature of 2°C per minute. [21-23]

Encapsulation of drug into magnetic nanoparticles:

0.4 g of the prepared mesoporous Fe-SiO2, Fe-MCM-41, Fe-KIT-6 and Fe-SBA-15 samples were taken individually and added to 20 ml of a 1.4 g berberine-hexane solution and macerated for 3 days with stirring. Then the berberine-loaded magnetic nanoparticles were obtained by centrifugation, collecting the product by filtration using hexane washing. Then the materials were dried at 60°C for 10 hours under vacuum. Figure 2 expressed graphical picture of methodology.

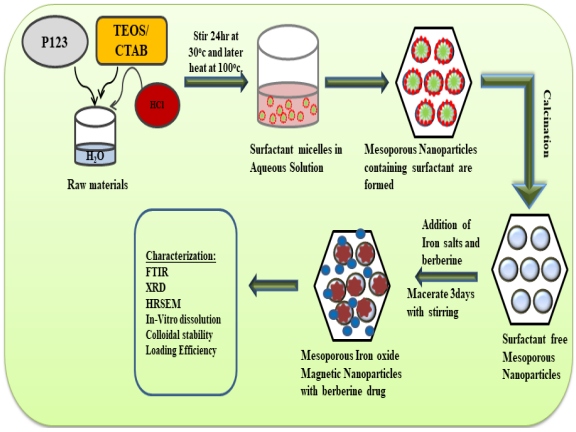


Figure 2: Graphical Abstract of Berberine loaded Magnetic Nanoparticles

Characterization of berberine loaded magnetic nanoparticles:

Drug Response Study:

UV-Vis spectroscopy (UV-Vis) is facile and low-price characterization technique this is regularly used for the study of nanoscale substances. NPs have optical properties which can be sensitive to size, shape, concentration, agglomeration state and refractive index close to the NP floor, which makes UV-Vis spectroscopy a vital device to identify, signify and check out those substances, and compare the steadiness of NP colloidal solutions. Usually, UV−Visible spectrophotometer is an essential for analyzing the formation of MNPs in aqueous suspension [24]. The UV−Vis spectrum of BBR and synthesized BBR-MNPs discovered absorption peak at 403 nm.

FTIR:

FTIR is extensively used for the evaluation of each organic and inorganic compound. It can affirm the composition of each solids, liquids, and gases. It is specially used for the identity of unknown compounds which allows the in-situ evaluation of interfaces to research the surface adsorption of purposeful organizations on nanoparticles. A benefit is that it permits users to investigate a layer of nanoparticles covered at the ATR element, even as additionally changing the overlying segment. It is hired to observe the chemical composition of magnetic nanoparticles [25]. These pellets have been analyzed in FTIR (prolific inst. Ltd, Mumbai, India). Then Data have been gathered at a wave wide variety of 400–4000 cm^{-1}.

X-ray diffraction (XRD):

X-ray diffraction (XRD) is one of the maximum considerably used strategies for the characterization of NPs. Typically; XRD affords facts concerning the crystalline shape, nature of the segment, lattice parameters and crystalline grain size. A gain of the XRD strategies, usually accomplished in samples of powder form, commonly after drying their corresponding colloidal solutions, is that it effects in statistically representative, volume-averaged values. It is used for the segment identity of crystalline substances because it affords facts approximately common dimensions of nanocrystals. XRD (X-Ray Diffractometer) (shimadzu analytical Ltd, Maharashtra, India) turned into accomplished for apprehend the conduct of crystal shape of the synthesized Magnetic nanoparticles.

Thermal gravimetric analysis (tga):

TGA affords facts regarding the mass and composition of the stabilizers. With this technique, a nanomaterial pattern is heated and an additive with distinctive degradation temperatures decompose and vaporize, and extrude of mass is recorded. The temperature and the lack of mass are recorded with the aid of using the TGA tool and, thinking of the beginning pattern mass, the sort and amount of NP natural ligands are determined. The pattern turned into positioned in an aluminum pan and heated from room temperature (25°C) to 250°C at a heating fee of 10°C/min.

High resolution scanning electron microscopy (hrsem):

HRSEM is specially used for the take a

look at of Morphology, dispersion of NPs in cells and different matrices/supports, precision in lateral dimensions of NPs, short examination–elemental composition. Measurement of common diameter of nanoparticles turned into accomplished in de-ionized water with the aid of using the dynamic mild scattering technology [26] at room temperature (25˚C) and morphology functions of polymeric nanoparticles have been studied the usage of a scanning electron microscopy (SEM tool S-4800).

Elemental mapping:

Elemental mapping exhibits the distribution of elements in the pattern. It is to verify the adsorption at the surface of MNP; Energy Dispersive X-Ray Analysis (EDX), known as EDS or EDAX, is an x-ray method used to discover the fundamental composition of substances. Applications encompass substances and product research, troubleshooting, deformulation for elemental evaluation became employed and became detected the use of EDX spectrum Analyzer (Redlands pvt Ltd, Kerala, India). Energy dispersive X-ray spectroscopy (EDS) is a well-known technique for figuring out and quantifying elemental compositions in a totally small pattern of material (even some cubic micrometers). It offers a spectrum that shows the peaks correlated to the fundamental composition of the investigated pattern.

Loading efficiency:

Drug loading performance is the ratio of the quantity of drug with inside the nanoparticle to the entire quantity of drug implemented in formula of the nanoparticles. One of the maximum crucial parameters in growing nanoparticle transport structures is the encapsulation performance that is the indicator of loading performance of the drug. UV–Visible spectroscopy is used to estimate the content material of Berberine (Drug) at a wavelength of 403 nm. It is used to calculate the drug loading. Where, W_0, W_1 and W_{NP} represent the preliminary weight of Berberine, the burden of the detected Berberine with inside the solution, and weight of the BBR-MNPs respectively [27].

Zeta potential (ζ):

Zeta potential (electro kinetic potential) is a degree of the “effective” electric powered charge at the nanoparticle surface, and quantifies the fee balance of colloidal nanoparticles. When a nanoparticle has a net floor charge, the charge is “screened” through an elevated attention of ions of opposite charge close to the nanoparticle surface. This layer of oppositely charged ions movements with the nanoparticle, and collectively the layer of surface charge and oppositely charged ions are known as the electric double layer. The Zeta Potential is a degree of the distinction in ability among the majority fluid wherein a particle is dispersed and the layer of fluid containing the oppositely charged ions this is related to the nanoparticle surface. Particles with a positive Zeta Potential will bind to negatively charged surfaces, and vice versa. The significance of the Zeta Potential presents data approximately particle balance, with better significance potentials displaying multiplied electrostatic repulsion and consequently multiplied balance. Measurement of Zeta potential became diagnosed via way of means of Zetameter. Generally, a best zeta potential with small particle size decides the stability.

Vibrating sample magnetometer analysis:

A vibrating-sample magnetometer is a systematic device that measures magnetic properties primarily based totally on Faraday’s Law of Induction. VSM is a flexible method for measuring the magnetic second of a pattern while it is vibrated perpendicularly to a uniform magnetizing area. Minor changes are like 10^{-5} to 10^{-6}emu may be detected with this technique. The VSM method may be used to acquire the magnetic second data of samples. Vibrating Sample Magnetometer (VSM model) device used to estimate the magnetic properties of Fe-MCM-41Magnetic Nanoparticles. The hysteresis curve acquired among implemented

magnetic area from -20000 to 20000 on X-axis and Magnetization (emu/g) on Y-axis.

Colloidal stability of berberine magnetic nano particles:

The berberine loaded magnetic nanoparticles prepared with deionized water with an adjusted concentration at 1mg/ml used to determine stability was conducted for seven days using DLS at 37°C which was determined by analysis of analysis. Where, colloidal stability of the particles in each day (t_n) is equaled to the nanoparticle size of each day (t_n) to the initial size of the nanoparticle at the first test (t_0).

In-vitro dissolution study:

The *In-Vitro* dissolution study was carried by preparing three different dissolution media such as phosphate buffer solutions (PBS) pH 5.5, pH 6.5 and pH 7.4 were selected. Method II (the paddle method), according to the USP, the bath volume for each medium is 900ml at 37°C±0.5°C and its rotational speed is 100 rpm [27]. The 100 mg of crude BBR and prepared BBR loaded MNPs was placed in to 5 ml of sample aliquot was removed at predetermined time intervals (i.e. 2 hr, 4 hr, 8 hr, etc. up to 36 hr) and filtered using Whatman filter paper No. 1. The filtered samples were diluted and absorbance was measured using a dual-beam spectrophotometer (Lab India UV/ Visible Spectrophotometer, India) at a maximum wavelength of 403 nm. The test data were tabulated clearly.

Results and Discussion

A broad peak was observed at 210-607 nm by the overlap of the Fe_2O_3 and BBR absorption bands. By the drug response study, the results was confirmed that the surface interaction of iron nanoparticles and the drug on the surface of the silica materials. The spectrum was shown in Figure3.

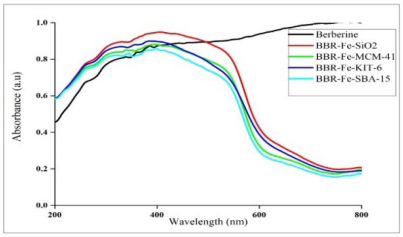


Figure 3: DRS UV-VIS Spectra BBR MNPs

In FTIR study, the BBR drug shown a significant bands located at 3410 cm^{-1} (O−H stretching vibrations) indicates the presence of water molecules, 2922 and 2853 cm^{-1} indicates C−H stretches (alkanes), and peaks at 1646, 1140, and 1157 cm^{-1} indicates C=C vibrations(aromatic group), C-H bending in-plane and C−H vibrations respectively. The results were shown in Figure 4.

Figure 4: FTIR curves of BBR MNPs

In the XRD study, the peaks observed at 14.9 °, 18.2 °, 41.0 ° are due to characteristic peaks of drug berberine present in all materials (Figure 5). These results were consistent with previously reported results. These results indicated the successful loading of the drug on all the materials (Fe-SiO_2, Fe-MCM-41, Fe-KIT-6 and Fe-SBA-15 and 750°C is due to dehydroxylation from the surface silanol group (Si-OH) Weight loss appears to be less with SBA-15 compared to all materials.

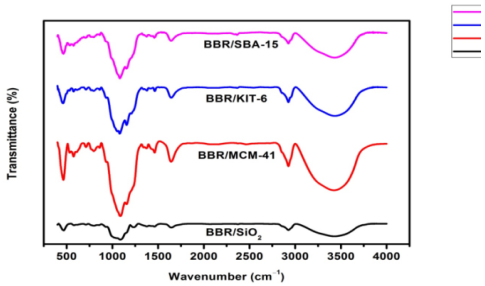


Figure 4: FTIR curves of BBR MNPs

Table 1: Preparation of Four Magnetic Nanoparticles

BBR/SiO_2				BBR/MCM-41				BBR/KIT-6				BBR/SBA-15			
STEP 1				STEP 1				STEP 1				STEP 1			
Name of Ingredients	Quantity of Ingredients	Name of Ingredients	Quantity of Ingredients	Name of Ingredients	Quantity of Ingredients	Name of Ingredients	Quantity of Ingredients	Name of Ingredients	Quantity of Ingredients	Name of Ingredients	Quantity of Ingredients	Name of Ingredients	Quantity of Ingredients	Name of Ingredients	Quantity of Ingredients
Pluronic $_{(123)}$	1.4g	CTAB	2.4g	Pluronic $_{(123)}$	1.23g	Pluronic $_{(123)}$	1.23g	Pluronic $_{(123)}$	1.23g	Pluronic $_{(123)}$	1.23g	Pluronic $_{(123)}$	0.17g	Pluronic $_{(123)}$	0.17g
TEOS	5.2g	Deionised water	120 ml	TEOS	44g	water	44g	TEOS	44g	water	44g	TEOS	1.09g	TEOS	1.09g
Ethanol	6.0ml	Ammonium hydroxide	8 ml	Ethanol	2.25g	Con HCl	2.25g	Ethanol	2.25g	Con HCl	2.25g	Con HCl	2.9 ml	Con HCl	2.9 ml
Con HCl	2.7ml	TEOS	10ml	Con HCl	98%	TEOS	98%	Con HCl	98%	TEOS	98%	Water	202.6g	Water	202.6g
STEP 2		STEP 2		STEP 2		STEP 2		STEP 2		STEP 2		STEP 2		STEP 2	
Iron	0.153g	Iron	0.3153g	Iron	0.3153 g	Iron	0.3153 g	Iron	0.3153 g	Iron	0.3153 g	Iron	0.3153 g	Iron	0.3153 g
Acetyl acetone	3.0ml	Acetone	3.0 ml	Acetone	3.0ml	Acetone	3.0ml	Acetone	3.0ml	Acetone	3.0ml	Acetone	3.0 ml	Acetone	3.0 ml
Nitric acid	0.3ml	HNO_3	0.3 ml	Nitric acid	0.3ml	Nitric acid	0.3ml	Nitric acid	0.3ml	Nitric acid	0.3ml	Nitric acid	0.3 ml	Nitric acid	0.3 ml
SiO_2	0.25g	MCM-14	0.25	KIT 6	0.25g	KIT 6	0.25g	SBA-15	0.25g	SBA-15	0.25g	SBA-15	0.25g	SBA-15	0.25g

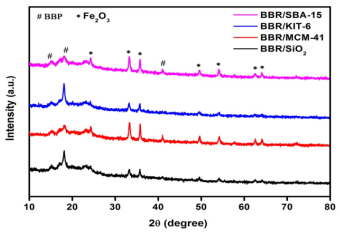


Figure 5: XRD graphs of BBR MNPs

By TGA study two stages of weight loss observed below 200 and 750 ° C at different temperatures, due to dehydroxylation from the surface silanol group (Si-OH), the removal of absorbed water from the material and decomposition of drug from the material. Figure 6

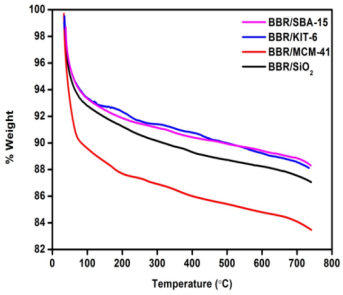


Figure 6: TGA graphs of BBR MNPs

In the Scanning Electron Microscopy (HRSEM) study states that the materials possess irregular shape, spherical like morphology due to loading of drug on the nanoparticles containing silica materials. The results were represented in SEM graphs of all MNPs before and after indicate the size range from 100nm – 250nm that possess optimum size range with good in appearance. The HRSEM images were shown in Figure 7a-7d.

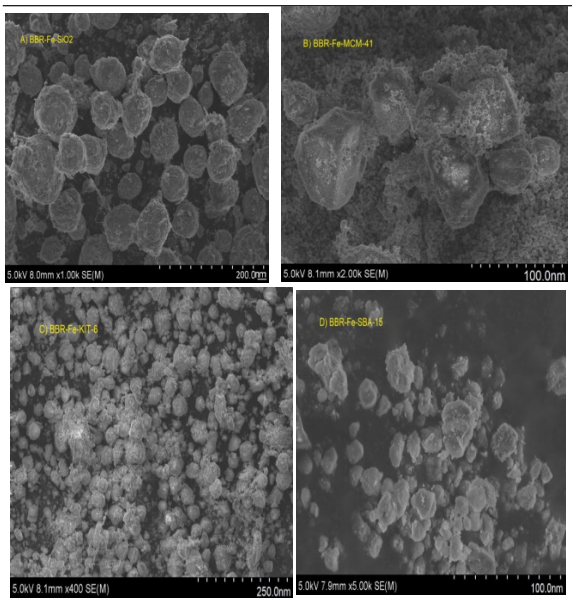


Figure 7 (a) BBR/Fe SiO_2, (b) BBR/Fe MCM-41, (c) BBR/ Fe KIT-6 and (d) BBR/ Fe SBA-15

The elemental mapping study used to confirm the presence of C, Fe, Si, F, Cl and O on the surface of the samples. EDX analysis was carried out in a micrometer range scanning and atomic percentages of all the catalysts were shown in the figure 8. The presence of C, Fe, Si, F, Cl and O on the surface of the samples was detected clearly observed in Figure 8.The elemental percentage was shown in Table 2.

Table 2: Elemental Mapping of MNPs

MNP	Elemental (%)					
	C	O	F	Si	Cl	Fe
Fe-SiO_2	21.98	35.63	18.44	16.54	0	7.41
Fe-MCM-41	29.25	40.23	4.42	14.13	0.92	11.06
Fe-KIT-6	23.31	30.55	29.30	11.52	0	5.31
Fe-SBA-15	30.18	42.31	10.0	11.17	0.22	6.12

The results obtained by loading efficiency of four berberine loaded MNPs were calculated, and it was shown in Figure 9, indicates high percentage for BBR/MCM-41 with 98% than other. The loading efficiency percentage and colloidal stability percentage reports were shown in Table 3.

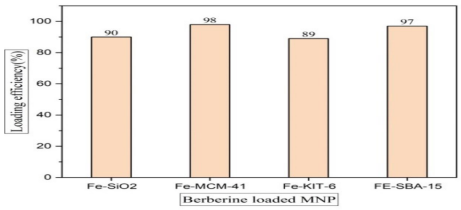


Figure 9: Loading efficiency BBR loaded MNPs

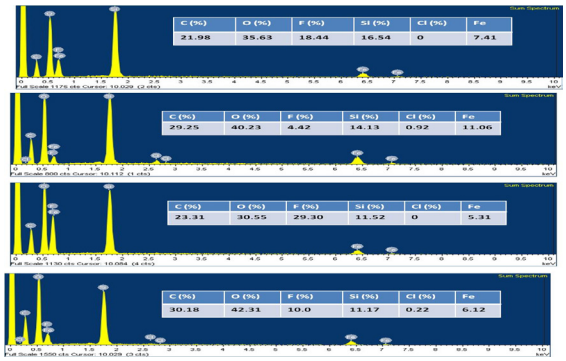


Figure 8: Elemental mapping of prepared MNPs

The zeta potential values at a P^H 3 to 11 for the electrostatic stabilization was estimated for nanoparticles indicates negative charge of Fe-MCM-41 MNP due to presence of iron molecules, in Figure 10 the final product of BBR/MCM-41 nanoparticles, shows a positive charge due to its presence of Drug Berberine which was stabilized.

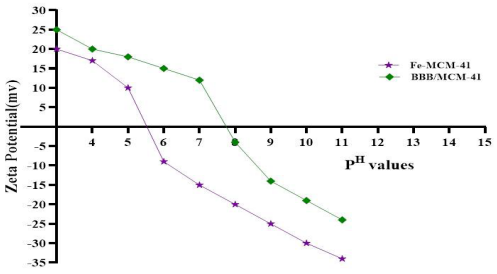


Figure 10: Zeta potential of Fe MCM-41 and BBR/Fe MCM-41

The hysteresis curve of magnetic nanoparticles was given by VSM. In Figure 11,

The synthesized Fe-MCM-41MNP possess optimum particle size of 50 nm which shows Zero remanence and coercivity, indicating super para magnetic activity, that can easily magnetized while exposing to magnetic field was stabilized and used for diagnosis, imaging.

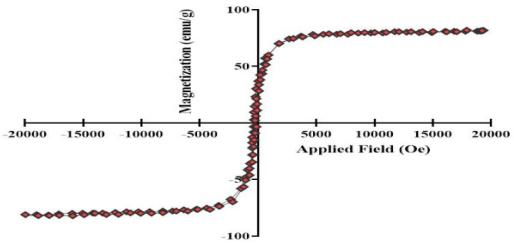


Figure 11- Vibrating Sample Magnetism of Fe-MCM-41 MNP

The results of colloidal stability studies was shown by using Dynamic Light Scattering instrument for seven days at 37°C, the % stability of berberine loaded was determined and shown in the Figure 12.

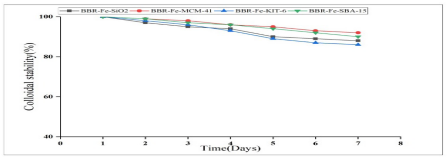


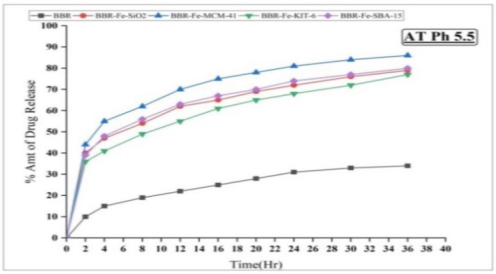
Figure 12 Colloidal Stability of formed BBR MNPs

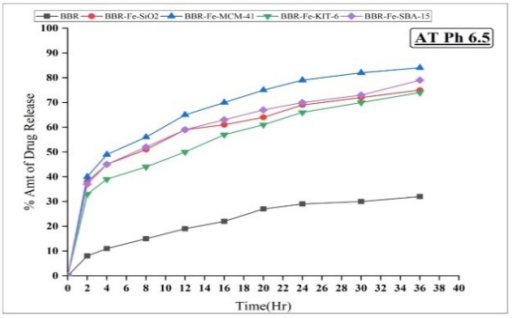
Table 3: Loading Efficiency and Colloidal Stability of BBR loaded MNPs

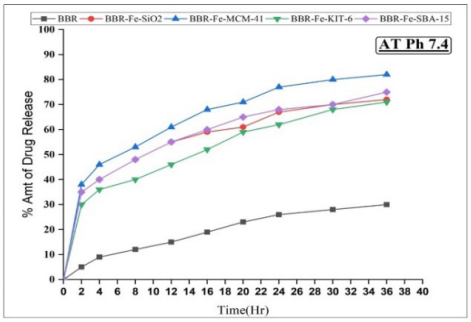
MNP	Loading Efficiency (%)[a,b]	Colloidal Stability(%) 1st day	Colloidal Stability (%) 7th day
BBR/Fe-SiO_2	90±1.2	100	88±2.0
BBR/Fe-MCM-41	98±0.9	100	92±1.1
BBR/Fe-KIT-6	89±2.1	100	86±2.3
BBR/Fe-SBA-15	97±1.7	100	90±0.9

a Loading Efficiency(%) = drug loading efficiency (%) and b(Mean ± SD; n = 3)

The results of *In-Vitro* Dissolution studies of MNPs at a three different P^H 5.5, 6.5, 7.4 were reported in Table 4 and Figure 13(a-c). The % drug release was found to be 34 ± 0.71, 32 ± 1.03, 30 ± 1.31 respectively, which indicates the greater drug release for BBR loaded MNPs than the pure BBR with more surface area, which leads to more bioavailability. The P^H decreases the % of Drug release increases. By using 3 different ranges of P^H (5.5, 6.5, 7.4), the basic P^H (7.4) obtained lesser bioavailability than P^H 6.5, And this acidic P^H 6.5 obtained lesser bioavailability than P^H 5.5 , then this acidic P^H 5.5 has higher bio-availability. So, acidic P^H conditions are favorable[26][27].







Figures 13(a-c): Invitro Dissolution Study at P^H 5.5, P^H 6.5 and P^H 7.4

Conclusion

Four different mesoporous Magnetic Nanoparticles were prepared using the Pluronic block co-polymer P123 as a surfactant template, then inserted an iron oxides using co-precipitation with a calcination steps. Then, the study continued to final characterization tests like Drug Response Study, FTIR, X-Ray Diffraction (XRD), TGA, Scanning Electron Microscopy (HRSEM), Loading Efficiency, Colloidal Stability, *in-vitro* Drug release studies. Drug Response Study resulted that Berberine exhibited maximum absorbance at 403nm, The resulted X-ray diffraction (XRD) were shown that the formed composites conserved ordered mesoporous structure after the formation of Iron oxide nanoparticles in the pores, FTIR indicated that the surface contains silanol group and Fe–O on the surface of the materials at 1093 cm-1 and 1020 cm^{-1} peaks respectively, TGA indicated that Fe-KIT-6 MNPs were stable due to less loss of its weight at various temperature, Scanning electron microscopy (SEM) resulted that all mesoporous magnetic nanoparticles are within the range of size from 50nm-100nm before loading and 100-250nm after berberine loading also possessed a regular spherical shape, All types of MNPs has good loading efficiency and colloidal stability, Dissolution study of all four types of MNPs at three different P^H 5.5, 6.5, 7.4 were reported, among all Fe-MCM-41 MNP at three different P^H 5.5, 6.5, 7.4 exhibits 86%, 84%, 82%. We concluded that all four types of magnetic nanoparticles are good in structurally arranged, sufficient percentage of elements on their particle surface along with good size range, which possess high surface area and high pore volume, show magnetic response sufficient for drug targeting in the presence of an external magnetic field. Dissolution study of Berberine loaded MNP of Fe-MCM-41 shown maximum drug release at P^H 5.5.

Conflict of Interest

The researchers hereby express no degree of conflict of interest with respect to this investigation.

Acknowledgments

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Abbreviations

MNP: Magnetic Nanoparticle; **TEOS:** Tetra ethyl ortho silicate; **CTAB:** Cetyl Trimethyl Ammonium Bromide; **SEM:** Scanning Electron Microscope; **mL:** Milli Liter; **°C:** Degree Centigrade; µg: Microgram; **rpm:** Revolutions per minute; µm: Micrometer; **nm:** Nanometer; **MCM-41:** Mobil Composition of Matter No. 4; **KIT-6:** Mobil Composition of Matter; **SBA-15:** Santa Barbara Amorphous; **SiO_2**: Silicon Oxide. **BBR**: Berberine

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Table 4: *In-vitro* Dissolution Study of BBR and all four BBR loaded MNPs at P^H 5.5, 6.5 and 7.4

	At P^H 5.5						At P^H 6.5						At P^H 7.4					
	% Amount of Drug release						% Amount of Drug release						% Amount of Drug release					
Time (hr)	BBR	BBR-Fe-SiO_2	BBR-Fe-MCM-41	BBR-Fe-KIT-6	BBR-Fe-SBA-15	BBR	BBR	BBR-Fe-SiO_2	BBR-Fe-MCM-41	BBR-Fe-KIT-6	BBR-Fe-SBA-15	BBR	BBR	BBR-Fe-SiO_2	BBR-Fe-MCM-41	BBR-Fe-KIT-6	BBR-Fe-SBA-15	
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	10±3.2	40±2.4	44±1.4	36±2.2	39±5.5	8±2.8	38±2.8	40±3.3	33±2.8	37±1.9	5±3.8	35±2.6	38±4.5	30±2.5	35±2.4			
4	15±4.4	47±3.5	55±2.3	41±3.4	48±4.2	11±2.2	45±3.4	49±4.6	39±3.9	45±0.9	9±5.1	40±3.4	46±3.0	36±3.6	40±5.5			
8	19±2.8	54±4.5	62±1.9	49±1.7	56±3.2	15±3.5	51±3.2	56±2.3	44±2.6	52±2.4	12±2.8	48±3.2	53±2.6	40±4.4	48±3.2			
12	22±1.8	62±5.1	70±3.2	55±4.5	63±1.7	19±4.4	59±1.9	65±1.7	50±5.1	59±4.9	15±4.7	55±4.1	61±1.7	46±5.2	55±4.4			
16	25±2.3	65±1.9	75±4.1	61±3.2	67±4.7	22±5.1	61±1.8	70±1.1	57±2.5	63±5.3	19±3.6	59±1.7	68±2.3	52±2.8	60±1.8			
20	28±3.5	69±2.8	78±3.6	65±2.6	70±3.8	27±2.3	64±2.4	75±2.4	61±3.2	67±2.3	23±2.3	61±4.4	71±2.8	59±1.6	65±5.0			
24	31±1.2	72±3.2	81±1.8	68±5.1	74±2.8	29±2.9	69±2.8	79±3.4	66±4.4	70±1.5	26±2.5	67±5.0	77±3.5	62±3.2	68±4.4			
30	33±0.9	76±2.6	84±2.8	72±2.9	77±2.0	30±1.6	72±3.9	82±4.1	70±1.9	73±2.7	28±1.2	70±2.4	80±4.9	68±0.8	70±2.3			
36	34±4.0	79±1.5	86±0.8	77±3.2	80±1.9	32±2.7	75±4.0	84±1.8	74±2.6	79±3.9	30±0.9	72±1.6	82±5.1	71±1.7	75±2.8			

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