ORIGINAL ARTICLE

Microwave-generated Bionanocomposites for Solubility Enhancement of Nifedipine

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Abstract

Aim: Oral dosage form of drug mainly depends on its absorption, dissolution, and diffusion through gastrointestinal membrane is promising approach/mechanism. The major challenge in case of most of the drugs is aqueous solubility. This work focusing on preparation of bionanocomposites (BNCs) of such poorly water-soluble drug by microwave induced diffusion (MIND) technique to enhance drug solubility in aqueous medium and increase its rate of dissolution. Considering to this the drug was selected from Biopharmaceutical Classification System class-II drug. **Materials and Methods:** Nifedipine and newer natural carriers such as *Moringa oleifera* Gum and *Aegle marmelos* (L.) were selected and used for BNCs preparation which was based on their wetting and surface active agent property. BNCs were prepared by most convenient and cost-effective MIND technique. The enhanced solubility and dissolution of BNCs were assessed by *in vitro* solubility and dissolution studies. **Results and Discussion:** It was demonstrated that the dissolution of nifedipine enhanced with an increase in polymer concentration. Mostly, the optimized ratio of drug and polymer from the entire composite was found Nifedipine Moringa Oleifera Bionanocomposite (NIMONC) 1:2 and Nifedipine Aegle Marmelos Bionanocomposite (NIAMNC) 1:3, BNCs with natural carriers which shown significant enhancement in solubility. Characterizations of prepared BNCs have been done by Fourier transform infrared spectroscopy, differential scanning calorimetry, X-ray diffraction studies, and scanning electron microscopy. **Conclusion:** Enhancement in the solubility might be because of formation of drug dispersion at micro and nanoscale level. Hence, the development of BNCs is a promising approach to increase solubility and rate of dissolution of poorly water-soluble drug.

Key words: Bionanocomposites, microwave induced diffusion technique, natural carriers and solubility enhancement, nifedipine

INTRODUCTION

Most of the active pharmaceutical ingredients have poor solubility profile and which is challenging to formulate and development into its dosage form.[1] Effectiveness of drug and its efficacy can be severely limited by poor aqueous solubility and most of the drug also show side effect because of poor aqueous solubility. Increasing drug solubility shows a considerable increase in efficiency and minimizes side effects of certain drugs.[2-7] Drugs with poor water solubility are associated with the slow drug absorption and finally inadequate or diverse bioavailability. From the literature survey, it was found that near about 40% of newly synthesized drugs has difficulty in water solubility. The poor aqueous solubility of drug in the gastrointestinal fluid often causes inadequate bioavailability. To achieve therapeutic plasma concentration requires high drug dose. The designed and developed celecoxib with acacia (1:4) BNCs shown acceptable solubility, i.e., 0.0113 mg/ml and its percentage of drug release was found to be 91.58%.[10]

The Biopharmaceutical Classification System (BCS) of drugs comprises into four categories according to their solubility and permeability. BCS class-II drugs exhibit high permeability

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and low solubility.[7,10-12] The selected nifedipine chemically it is 3, 5-dimethyl 2, 6-dimethyl-4-(2-nitrophenyl)-1-4-dihydropyridine-3,5-dicarboxylate with chemical formula: $C_{17}H_{18}N_2O_6$. Further, nifedipine has high permeable through biological membrane but have limitation of poor aqueous solubility. Drug absorption rate and bioavailability of such poorly water-soluble drugs are controlled by rate of dissolution in gastrointestinal fluids. This problem has been tried to solve by many researchers by various methods in the past to enhance solubility and dissolution ultimately bioavailability.[8,9,13] As nifedipine is poorly aqueous soluble results in poor dissolution rate and decrease in its gastrointestinal absorption. Hence, nifedipine drug has been selected and which is belongs to BCS class-II drug.

Nifedipine is yellow powder, affected by exposure to light. Nifedipine is practically insoluble in water; freely soluble in acetone (USP, Pharmacist Pharmacopeia, 2008-2009). Nifedipine is an oral calcium-channel blocking agent, usually used in the treatment of angina pectoris and hypertension. Nifedipine is a poorly water-soluble drug and its oral bioavailability is very low. Diseases - such as angina, asthma, and epilepsy - require immediate drug response to manage the disease condition. Improvement of the aqueous solubility of poorly water-soluble drugs is one of the important factors for the enhancement of absorption and required oral bioavailability (Ohshima *et al.*, 2009).[14]

They are highly permeable through biological membrane but have limitation of poor aqueous solubility. Drug absorption rate and bioavailability of such poorly water-soluble drugs are controlled by rate of dissolution in gastrointestinal fluids. This problem has been tried to solve by many researchers by various methods in the past to enhance solubility and dissolution ultimately bioavailability.[15] As nifedipine is poorly aqueous soluble results in poor dissolution rate and decrease in its gastrointestinal absorption.

Oral route is the most common way of drug delivery system for drug administration. The majority of sold pharmaceutical products (drugs) are given orally and BNCs produce increased saturation solubility, and therefore, shows increased dissolution velocity.[16] The increase in surface area by particle size reduction increases dissolution property. Nanosize means the particle size between 100 nm and 1000 nm.[15,17,18] Continuous advancement in the other drug delivery system leads to pay attention toward oral drug delivery system to increase clinical efficiency and patient compliance. From pharmaceutical point of view, a numerous type of polymer is used to control drug release from dosage form. The use of natural polymer rather than synthetic polymer is more preferred. Natural polymers are mainly used because they are readily available, inexpensive, nonreactive, capable of chemical modification and potentially compatible and degradable.[19] Due to the development of polymer based BNCs, these are extensively used in the pharmaceutical industry. Polymer BNCs are the polymer that has been reinforced with small quantities of nanosize particles having high aspect ratio.[20]

In this study, a novel technique used called microwave induced diffusion (MIND) which is green and cost-effective for the production of BNCs. Microwave heating starts from the direct interaction of electromagnetic energy with the material.[25-28,30] The extent to which the material is heated by microwave energy is reliant on the range of parameters, but particularly dielectric properties are more important.[21] Polar liquids like water are very readily heated. Microwave heating can confer several benefits over conventional heating which includes rapid heating and cooling, reduced temperature gradients across the sample, lower energy usage, and enhanced reaction rates.[22] BNC is the process of complex formation between drug and natural polymers [(*Moringa oleifera* Gum and *Aegle marmelos* (L.)] where microwave energy plays a significant role in reducing particle size of materials. It breaks intermolecular bonding and reduces the particle size. Nowadays microwave also applied for reducing particle size of drug material up to nanometer (nm). Reduction in particle size increases effective surface area of the drug and thereby enhances solubility and dissolution rate. In this study, nifedipine BNCs formation enhance solubility ultimately leads to increase in bioavailability of the drug. Microwave heating is a well-established method for processing and drying.[23,24]

The newer natural polymer *M. oleifera* Gum and *A. marmelos* (L.) is used for the formation of BNCs. *M. oleifera* Gum is naturally occurring, water soluble, complex polysaccharides obtained from the incision area on bark tree of *M. oleifera* and *A. marmelos* Gum was found in beal fruit, i.e., *A. marmelos* (L.). These are selected on the basis of their good surfactant and wetting property which are associated with increase in the solubility and dissolution.[20] Nifedipine with its high permeability property through biological membrane but it shows low aqueous solubility. Thus, it is needed to enhance the solubility and dissolution ultimately bioavailability of nifedipine.

MATERIALS AND METHODS

Materials

Nifedipine was obtained as a generous gift from Alkem Lab (Mumbai, India). The drug was stored in an amber glass container wrapped with aluminum foil and kept in a refrigerator at 5-7°C. The isolation and collection of *M. oleifera* Gum were done by making an incision at different places on stem parts of tress of *M. oleifera* and gum was collected in suitable air tight container after air drying. Further, isolation and collection of *A. marmelos* (L.) corr., i.e., (beal fruit) gum: Fruit contain a large amount of gum, and after breaking beal fruit gum was air dried and neatly collected in suitable air tight container.

Extraction and purification of natural gums

Collected both the gum, *viz.*, *M. oleifera* and *A. marmelos* Gum, respectively, were dried on ground under sunlight. Dried gum was passed through Sieve No. 80. Dried gum (10 g) was stirred in distilled water (250 ml) for 6-8 h at room temperature. By centrifugation method supernatant was obtained, and residue was washed with water and the washing was added to supernatant. The procedure was repeated four times.

Finally, the supernatant was made up to 500 ml and treated with twice the volume of acetone by continuous stirring. The precipitated material then washed with distilled water and same was dried at 50°C-60°C under vacuum.

Characterization of pure nifedipine

Solubility determination

The solubility of nifedipine drug was determined by taking excess amount of drug into 150 ml of distilled water and kept for 24 h on orbital shaker incubator at room temperature 25°C.[23] The obtained solution was filtered through Whatman filter paper no. 1 and the drug concentrations were determined by taking ultraviolet (UV) absorbance using UV-visible spectrophotometer (UV-Carry 60, Agilent) at 238 nm wavelength.

Fourier transform infrared (FT-IR) spectrophotometric studies

The identification of nifedipine was done by FT-IR spectroscopy. The FT-IR spectrum was obtained using FT-IR spectrophotometer (Agilent Corp., Germany). The wavelength of rang from 400 to 4000/cm with a resolution of 4/cm was used. Characteristic peaks of the drug, *M. oliefera* and *A. marmelos* Gum were compared with the formulated BNCs to check the compatibility of drug-polymer.

Characterization of polymers

Swelling index (SI)

SI of gums was calculated to check the swelling power. Accurately weighed 10 g of *M. oleifera* and A. *marmelos* Gum were transferred into 100 ml measuring cylinder. The initial volume occupied by gum was noted. Distilled water was added in the cylinder up to 100 ml and the open end of cylinder was sealed with an aluminum foil. Measuring cylinder was kept aside for 24 h and volume of swelled gum was noted. The SI of gum was calculated by the following formula;

$$\% \text{ Swelling} = \frac{X_t - X_0}{X_0} \times 100 \quad (1)$$

Where, X_0 is the initial height of the powder in the graduated cylinder and X_t denotes the height occupied by swollen gum after 24 h.

Viscosity determination

Viscosity of gum was determined by taking 1 g of each of *M. oleifera* and *A. marmelos* Gum, respectively, and dispersed in 100 ml distilled water (1% w/v). The viscosity of resultant dispersion was measured by viscometer (Brookfield DV-E, Brookfield Engineering Laboratories, Inc., Middleboro, MA, USA) using spindle 3 at 100 rpm.[29]

Foaming index

The foaming index was calculated to check the surfactant property of *M. oleifera* and *A. marmelos* Gum. Accurately, weighed 1 g of gum was transferred in 250 ml measuring cylinder containing 100 ml distilled water to make dispersion. Resultant dispersion was vigorously shaken for 2 min. The foaming index of gum was calculated by the following equation,

$$\text{Foaming index} = V_f - V_i \quad (2)$$

Where, V_f is the volume of 1% w/v solution of carrier after shaking and V_i is the volume of 1% w/v solution of gum carrier before shaking.[29]

Preparation of bionanocomposites (BNCs)

The BNCs were prepared by adding accurately weighed quantity of drug nifedipine and natural carrier such as *M. oleifera* and *A. marmelos* Gum were taken in 1:1 to 1:9 w/w proportions as shown in Table 1. Homogeneous physical mixture of drug and carrier was prepared using mortar and pestle. Slurry was prepared by adding 5 ml of distilled water in each gram of drug-carrier physical mixture. A fixed amount of slurry (6 g) was placed in a glass beaker and irradiated with microwave radiations at power 700 W (IFB Microwave Oven, Model 17PM-MEC1, Kolkata, India) with continuous stirring.[16]

The temperature was noted using inbuilt temperature measurement probe at the end of the treatment. BNCs were

Table 1: Formulation design for BNCs batches

Sample	Drug+Gum carrier	Proportionate ratio (w/w)								
NIMO	NI - *M. oleifera*	1:1	1:2	1:3	1:4	1:5	1:6	1:7	1:8	1:9
NIAM	NI - *A. marmelos*	1:1	1:2	1:3	1:4	1:5	1:6	1:7	1:8	1:9

NIMO: Nifedipine with *Moringa oleifera*, NIAM: Nifedipine with *A. marmelos* Gum, BNCs: Bionanocomposites

grounded using mortar and pestle to obtain required size of 80-250 µm.[15] The formulated BNCs of nifedipine drug with natural carrier (*M. oleifera* and *A. marmelos* Gum) were denoted by and respective process variables for the preparation of NIMONC and NIAMNC are given in Table 2.

Solubility study

Pure nifedipine drug is practically insoluble in water. The solubility study of BNCs (NIMONC and NIAMNC) was carried out by adding excess amount of pure nifedipine drug (equivalent to 30 mg) and BNCs to 150 ml distilled water in a separate flask. The resultant mixture was stirred for 24 h at 25°C temperature using orbital shaker incubator. The supernatant liquid was collected and filtered through 0.2 µ membrane filter and analyzed by UV-visible spectrophotometer at 238 nm wavelength.

Drug content (entrapment) analysis of BNCs

The incorporated nifedipine drug into the BNCs, i.e., nifedipine + *M. oleifera* (NIMO) and nifedipine + *A. marmelos* (NIAM) was calculated by dissolving BNCs mixture in the 25 ml methanol. The resulting solution was filtered by 0.2 µ membrane filter and analyzed by UV-visible spectrophotometer (UV - Carry 60, Agilent) at the wavelength of 238 nm against the methanol as a blank.

Stability study

Stability testing is performed to ensure that drug products retain their fitness for use until the end of their expiration dates. Evidence on how the quality of drug varies with time under the influence of temperature, humidity, and light is the purpose of this study. The stability study was performed on optimized BNCs at 4°, 30±2°/65±% relative humidity (RH) and 40±2°/65±5% RH. Percent drug content and *in vitro* release studies were performed.

Characterization of BNCs

Characterizations of BNCs were carried out by FT-IR, differential scanning calorimetry (DSC), X-ray diffraction (XRD), scanning electron microscopy (SEM), and transmission electron microscopy to ensure the compatibility of drug and polymer.

FT-IR spectroscopy

FT-IR spectra of pure drug (nifedipine), pure polymers (*M. oleifera* and *A. marmelos* Gum), and BNCs of drug with individual polymers were carried out to check compatibility of drug with polymer. BNCs of drug with each polymer Nifedipine Moringa Oleifera Mixture (NIMOM) and Nifedipine Aegle Marmelos Mixture (NIAMM) were mixed with potassium bromide (KBr) of IR grade in the ratio of 1:100. The pellets were scanned using FT-IR spectrophotometer (Agilent Corp., Germany). Infrared spectrum of material gives the information regarding drug-polymer interactions. The materials were scanned through a range from 400 to 4000/cm with a resolution of 4/cm. Characteristic peaks of the pure drug, *M. oleifera* and *A. marmelos* Gum were compared with the formulated BNCs to check the compatibility of drug-polymer.

Table 2: Process variables for preparation of NIMONC and NIAMNC

Sample	Ratio (w/w)	Time (min)
NIMONC	1:1 to 1:9	7
NIAMNC	1:1 to 1:9	7

DSC

DSC studies of pure drug (nifedipine), pure polymer (*M. oleifera* and *A. marmelos* Gum), and BNCs of drug with individual polymer were performed to access the enhanced solubility of drugs. DSC thermos-gram was obtained using differential scanning calorimeter (DSC 60; Shimadzu) at heating rate of 11°C/min from temperature 0°C to 250°C. The DSC gives the information related to melting point, type of heating reaction (either endothermic or exothermic) and physical, chemical interaction between drug and polymer.

XRD studies

XRD study of drug (nifedipine), pure polymers (*M. oleifera* and *A. marmelos* Gum), and BNCs of nifedipine drug with individual polymers were determined to evaluate the changes in the crystallinity made when drug was mixed with gums. The crystallinity property is associated with physicochemical properties of material. The XRD patterns of the drug, polymers, and BNCs were recorded using (Bruker, D8) and Cu-kα radiation. The scanning angle ranged from 1 to 42 of 3θ.

SEM

The surface morphology of nifedipine BNCs was observed by SEM. The samples were mounted directly onto the SEM sample holder using double-sided sticking tape and images were recorded at the required magnification at acceleration voltage 15 kV and working distance of 8 mm on XL30-SFEG Philips (Lab exchange, Burladingen, Germany). The mean particle size, standard deviation, and 95% confidence interval were calculated by a written program which randomly selects 100 particles of the SEM images.

RESULTS AND DISCUSSION

Physical characterization of carriers

By using rheometer R/S-CPS+rheometer (7030107) with the measuring system: C75-2 the viscosity and thixotropic analysis ere carried out, and from the study, it was found that less % sewlling index the lesser viscosity and for *A. marmelos*

and *M. oleifera* Gum . Hence, both the gum (polymer) revels the stability and helps in enhancement of solubility for optimization of BCS class-II drug, i.e., poorly water-soluble drugs by preparing its BNC and can withstand in microwave radiation.

The % swelling and foaming index were represented in Table 3. The swelling property and viscosity of *M. oleifera* and *A. marmelos* Gum was low. Due to the less viscosity of *M. oleifera* and *A. marmelos* Gum, they were considered for solubility and dissolution enhancement of selected BCS class-II drug. Hence, both the gums were more suitable and conveniently useful for the enhancement of solubility and dissolution rate of poorly water-soluble drug.

Solubility studies of pure, physical mixture, and BNCS of nifedipine

The solubility study mainly focused that use of *M. oleifera* and *A. marmelos* Gum utilized to enhances solubility of poorly water-soluble drug.[30-32] The solubility study performed in mg/ml for of physical mixture of selected BCS class-II drugs and from Figure 1 and it was observed that the solubility of physical mixture low as that of pure form of nifedipine drug.

The solubility study for nifedipine drug was performed by comparing them such as their physical mixture and prepared BNCs and it was observed that there was significant increase in solubility as the drug polymer ratio increased. After NIMONC ratio of 1:02 and for NIAMNC of ration 1:03, there is no any significant enhancement of solubility as shown in Figure 2.

Table 3: Organoleptic and physical characterization of natural gum

Parameters	M. *oleifera* L.	*A. marmelos*
Colour	Brownish black	Yellowish white
Odour	Characteristic	Characteristic
Taste	mucilaginous	Mucilaginous
Swelling index	19.7±2.21	20.3±1.01
Foaming index	17±0.92	16±0.65

*All values are represented as means±SD, *n*=2.21 for Moringa Oleifera and *n*=1.01. for Aegle Marmelos

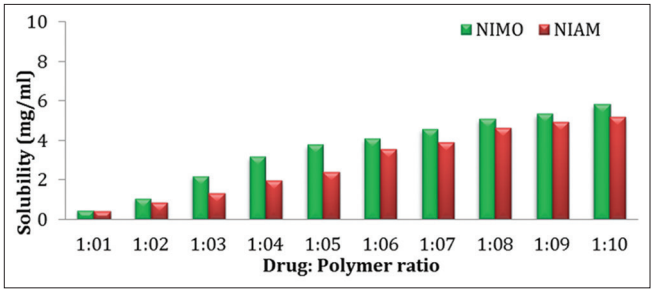

Figure 1: Solubility study of Nifedipine with *Moringa oleifera* and Nifedipine with *A. marmelos* Gum physical mixture

The solubility (mg/ml) of prepared BNCS of nifedipine with *M. oleifera* and *A. marmelos,* respectively, as shown in Figure 3. It was found that the optimized ratio for NIMONC (1:02) and NIAMNC (1:03) was selected after their solubility study performed. This optimized ratio was then confirmed with powder dissolution and found to be increased in solubility.

Enhancement of solubility with for NIMONC (1:02) and NIAMNC (1:03) was found more and this is due to less foaming index and viscosity profile of *M. oleifera* and *A. marmelos* Gum, drug diffused in the gum in the form of its BNC with structural modification, i.e., it was made to hydrophilic form of drugs which get enriched with possible hydrogen bonding and this hydrogen bonding helps the molecule to go underdispersion and ring opening for the drugs by reveling molar volume without affecting its potential parent activity of drugs. This hydrophilic nature obviously utilized for solubility enhancement of poorly water-soluble.

Powder dissolution test nifedipine BNCs

The powder dissolution test was carried out to check solubility enhancing properties of the materials.[33] The dissolution profile of physical mixture showed remarkable improvement in the dissolution rate when compared with the pure, nifedipine and their physical mixture with natural carriers.

Physical mixture and nifedipine with both the gum demonstrated result as shown in Figure 4; the cumulative drug release in % for pure drug of nifedipine was found 5.5 ± 1.9. The cumulative drug release of physical mixture of Nifedipine Moringa Oleifera Physical Mixture (NIMOPM) was 64.99 ± 4.5 and Nifedipine Aegle Marmelos Physical Mixture (NIAMPM) 56.22 ± 4.5 after 60 min.

BNC of nifedipine with both the gum demonstrated good result. As shown in Figure 5, the cumulative drug release in % for pure drug nifedipine was found 5.5 ± 1.9. The cumulative drug release of BNCS such as NIMONC was 92.11 ± 1.1 and NIAMNC 64.99 ± 1.1 after 60 min.

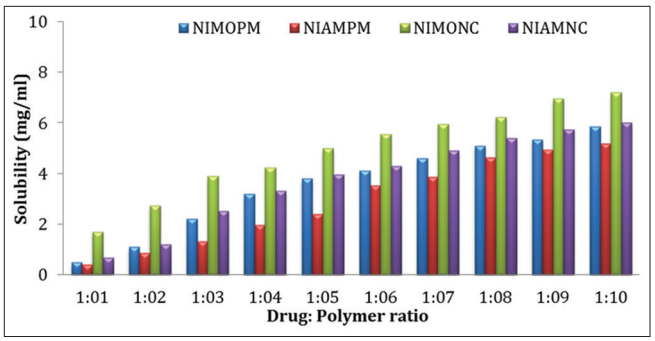

Figure 2: Comparative solubility study of Nifedipine with *Moringa oleifera*, Nifedipine with *A. marmelos* Gum physical mixture and their bionanocomposites

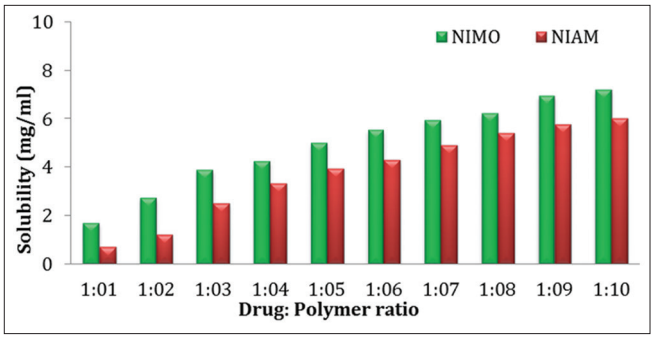

Figure 3: Solubility of bionanocomposite of nifedipine with *Moringa* oleifera and *Aegle marmelos*

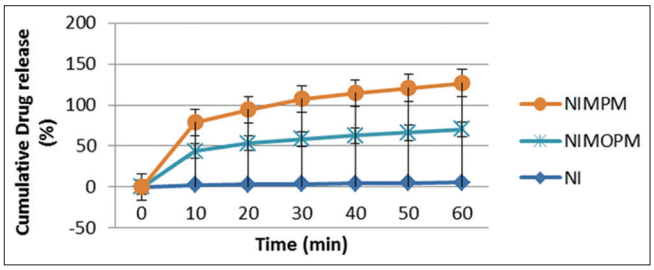

Figure 4: Powder dissolution study of physical mixture of nifedipine with *Moringa oleifera* and *Aegle marmelos*

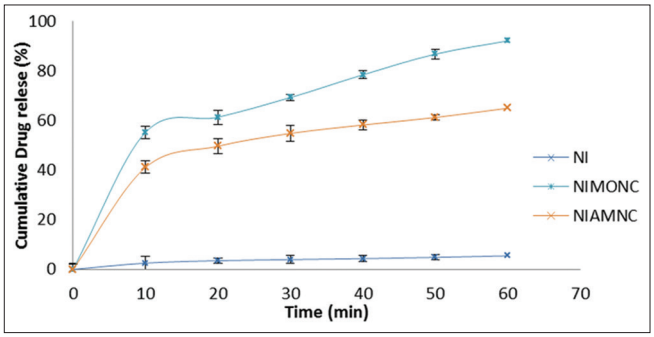

Figure 5: Powder dissolution study of prepared Nifedipine with *Moringa oleifera* and Nifedipine with *A. marmelos* Gum bionanocomposites

Drug content (entrapment) analysis of BNC

Uniform dispersion of drug in the BNCs was determined by drug content analysis. It was found that 95-98% drug was entrapped in the BNCs showing uniform dispersion of drug for both the drugs.

Stability study

The study was performed for BNCs prepared by storing BNCs F1 at 4°C in refrigerator, at 30 ± 2°C, 65% ± 5% RH and at 40°C ± 2°C/65% ± 5% RH in humidity control oven for 30 days. Two parameters namely residual percent drug content and *in vitro* release studies were carried out. The results of drug content after 30 days of stability testing at different storage conditions are shown in Table 4. By comparing this data with the previous release data of BNCs, it was found that there is slight decrease in the drug release. These results may be due to oxidation of nifedipine formulation to some extent during storage.

Characterization by FT-IR studies

The various functional groups include in the nifedipine drug, which were analyzed using FT-IR spectroscopy. The assignment of bands observed in the vibration spectra was essential step for solving structural and chemical overwhelm. The recorded spectra are shown in Figure 6. The broadband at 3285.991/cm corresponds to the amine and hydroxyl groups, the peak at 2926/cm was caused by OH stretching. A sharp band at 1614/cm was assigned to C=O stretching of the secondary amide secondary.

The peak at 1444/cm and 1300/cm belong to aromatic N-O stretching and ether bonds and NH stretching amide tertiary band, respectively. The peaks observed at 1090/cm and 1031/cm were the secondary hydroxyl group (characteristic peak of −CH-OH in cyclic alcohols, C-O stretch) and the primary hydroxyl group (characteristic peak of $-CH_2OH$ in primary alcohols C-O stretch). The bands around 1031/cm were indicated to C-O-C stretching. Pure nifedipine displays a peak characteristic of the N-H stretching vibration at 3285/cm and a band with main peak at 1614/cm indicative of the C-O stretching of the ester group as shown in Figure 7**.**

DSC studies

DSC thermograms of pure nifedipine DSC exhibited sharp endothermic peak at 98°C indicating melting of nifedipine. DSC of NIMONC and NIAMNC shown same endothermic peak as that of pure drug but with reduced intensity which might be due to decrease in the crystalline nature of drug. Slight shift in the melting point indicated reduction of the drug to nanocrystalline form. Broadening of peak indicated that most of the drug converted into nanocrystalline form. No chemical interaction between drug and polymer was observed. Physical interaction was the mechanism by which drug bound to the polymer. These studies confirmed that as the crystal size of crystalline nanoparticle reduces and its melting point reduces minutely (Figure 8).

XRD studies

XRD was performed to check the physical state of drug and its BNCs. The XRD pattern of pure nifedipine observed crystalline peak between 100 and 600. It demonstrated characteristic diffraction peaks at 6, 23, 19, 23.50, 29, 33, 35.50 37 and 39 with intense peak at 23 and 24 indicating crystalline nature of nifedipine. XRD pattern of NIMONC and NIAMNC indicate reduced peak intensity due to decreased crystallinity. Reduced peak intensity of BNCs might be due to a reduction in the drug size to the nano level (Figure 9).

Table 4: Drug content after 30 days storage of optimized BNCs

BNCs nifedipine	Percentage of drug content at 4°C	Percentage of drug content at 30°C±2°C/65%±5% RH	Percentage of drug content at 40±2°C/65%±5% RH
NIMONC	86.46	86.32	80.94
NIAMNC	86.12	86.03	80.77

BNCs: bionanocomposites, RH: Relative humidity

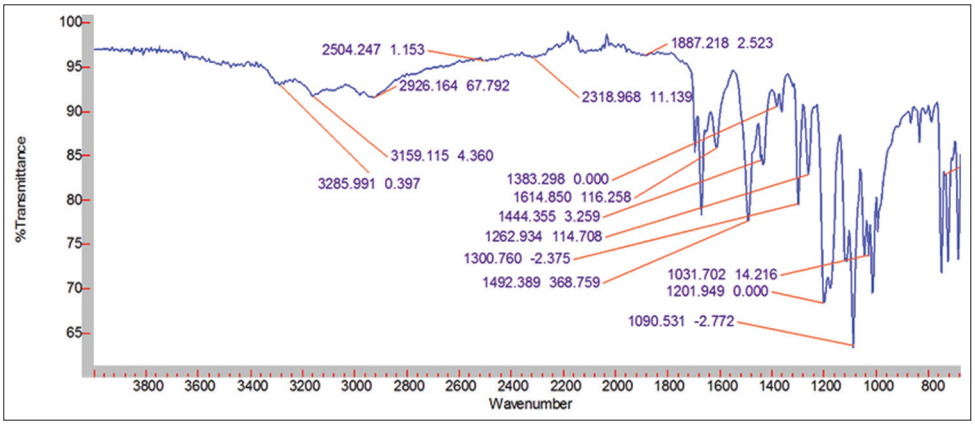

Figure 6: Fourier transform infrared of pure nifedipine

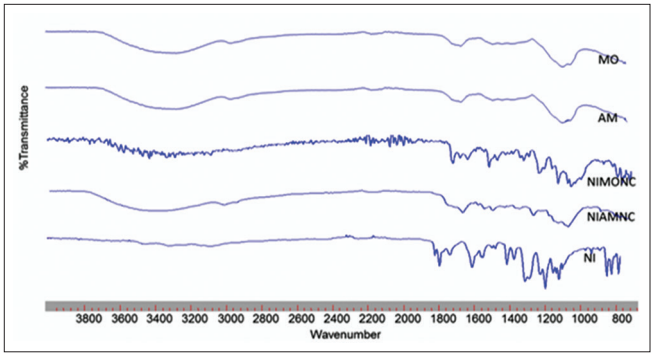

Figure 7: Fourier transform infrared studies of pure nifedipine, *Moringa oleifera*, *Aegle marmelos*, and NIMONC and NIAMNC

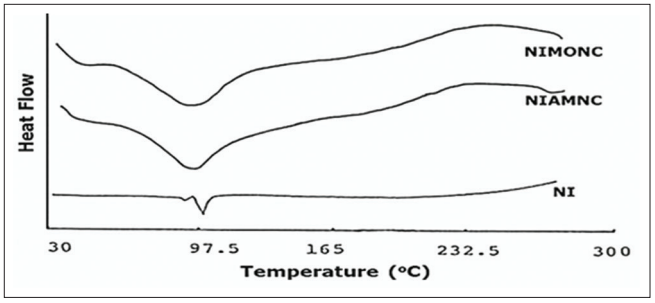

Figure 8: Differential scanning calorimetry studies of nifedipine, NIMONC and NIAMNC

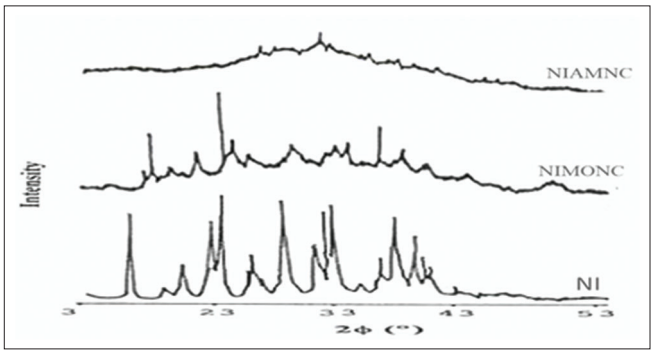

Figure 9: X-ray diffraction studies of nifedipine, NIMONC and NIAMNC

SEM

The SEM study was done to check surface morphology of the drug particles. Nifedipine particles were variable shaped with a rough surface, while NIMO and NIAM particles were of irregular shape and size Figure 10, clearly, demonstrate crystal shape of nifedipine was completely changed in NIMONC and NIAMNC shown embedded nifedipine crystals in the matrix.

CONCLUSION

From the result obtained by performing experiments as stated in material methods, the use of newer natural carriers such as *M. oleifera* and *A. marmelos* for the conversion of nifedipine into its BNCs by simple, convenient and cost-effective method employed, i.e., MIND technique which was shown promising approach to enhance the solubility and dissolution rate of prepared BNCs. The result of FT-IR, XRD, DSC, and SEM shows that nifedipine generated into the BNCs is significantly responsible for the enhancement of solubility and dissolution rate. It also shows that there is no significant interaction between drug and polymer. *In vitro* evaluation of optimized formulation confirms the use of BNCs for increasing solubility and dissolution rate of drug. On the basis

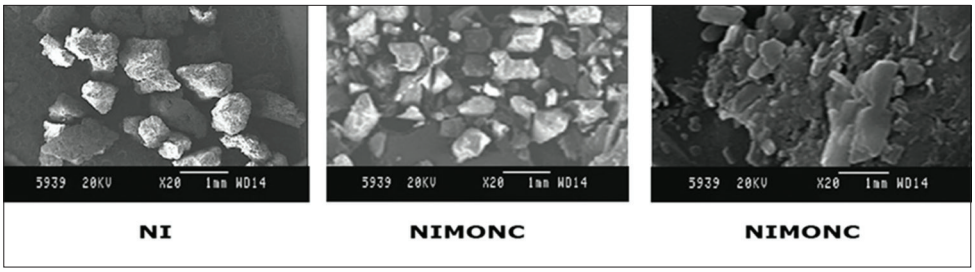

Figure 10: Scanning electron microscopy images of nifedipine, NIMONC and NIAMNC

of present research study, it was concluded that microwave generated BNCs is one of the potential approaches to enhance solubility, dissolution rate, and ultimately bioavailability of BCS class-II drug.

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