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Preparation and Characterization of Orlistat Bionanocomposites Using Natural Carriers

Running Title: Composite of Orlistat Bionanocomposites Using Natural Carriers

Santosh Payghan[1]*, VAISHALI PAYGHAN[1], Kavita Nangare[1], Lalita Dahiwade[1], Karna Khavane[2], Ram Ram[3]
[1]Vasantidevi Patil Institute of Pharmacy, Kodoli, Tal. Panhala, Dist. Kolhapur- 416 114, India.
[2]Gurunanak Institute of Pharmacy, Majlgaon, Beed
[3]Dept. of Pharmaceutics, College of Pharmacy, Warananagar

Corresponding Author Information
Santosh Payghan
sapayghan.tkcp@gmail.com
9096202858
https://orcid.org/0000-0002-0653-6784
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Abstract:
Bionanocomposites are biopolymers or a natural polymer embedded in a combination of two or more different chemicals using natural carriers or bio. Bionanocomposite is widely used in drug formulation and in the development of new drugs for various therapeutic drugs, new dosage forms and in pharmacological medicine. Useful and improved melting was achieved by converting selected BCS Class II drug into bionanocomposites (BNCs) using natural carriers such as the gums of MoringaOleifera (MO) and AegleMarmelos (AM) respectively. The current work focuses on the enhancement of the novel natural polymer such as MoringaOliefera and AegleMarmelos used to prepare bionanocomposite for BCS class II orlistat using a microwave system designed for distribution method (MIND). The natural polymer helps to improve the melting of the dispersion when it converts them into Bionanocomposite. Definitions of orlistat, natural carriers and prepared BNCs were developed and studied comparatively. The FTIR, DSC study revealed that there was no communication between drug associations and environmental carriers. Crowd reduction studies were conducted to investigate the material that enhances the melting of BNC compound dissolving and in vitro disposal of BNCs prepared by DSC, SEM XRD and FTIR. BNCs have an effect between orlistat: MO (OSMO-BNC-1: 3), orlistat: AO (OSAM-BNC- 1: 4) is well developed. Ornat BNCs formulated with MO and AO provide significant improvements in dissolving and highlight their use in reducing fortification. In addition, land melting limits were applied and determined the melting of BNCs prepared using the Hansen Solubility parameters in particular, Hoy's, Fedor and Van Krevelen System and it was found that from this report there was a significant increase in melting of batches prepared for BNCs.
Keywords: Bionanocomposite, BCS class II, Orlistat, *Moringa Oliefera, Aegle Marmelos*, microwave-assisted fusion method, Hansen solubility parameter.

INTRODUCTION

The therapeutic efficacy of a drug depends on its availability and ultimately in the formulation of chemicals hydrophilic compounds of the compound and the dissolution of drug molecules. There is a great deal of difficulty in preparing and developing the most effective form of improper water solubility of many drugs. Innocence is a parameter for achieving the desired combination of drugs in the distribution of the system so that the therapeutic response is shown. It is estimated that 40% or more of the drug molecules identified during the experiment of compounds do not dissolve well in water. There is a need for systematic and simple preparation and structural methods to make less-soluble drugs available. Making these drugs unavailable means that they show enough absorption after oral administration or they may be injected with 3-4 injections.

The main purpose of this work is to prepare, mark the structural requirements of the hydrophilic environment, to construct and test the bionanocomposite of Orlistat with its low water content reducing its drug absorption which reflects the BCS class-II drug profile. Current work is being done to provide alternative drug delivery with improved solubility and a level of detoxification in the form of nanocrystal drugs that will overcome the problems that exist in existing dosage form. Many methods have been used to stabilize moisture such as salt formation, co-crystallization, co-solvency, hydrotropic, solvating agent and nanotechnology by chemical modification. Under body modification to reduce particle size, crystal behavior modification, gravity, mixing with surfactants and drug distribution to carriers.

Nanocomposite is a combination of two or more different chemicals that have different properties and blends, in an effort to combine these two beautiful structures. The combination has two elements of different textures and the combination of those displays is enhanced in its larger structures. The body composition of the drug and its natural or bio-carrier compounds are nanotechnology and their experimental parameters such as in-vivo and in-vitro profile and biological detection are therefore called bionanocomposite.

Bionanocomposite for microwave irradiation can be used in a variety of ways such as improved melting, melting and the availability of drug-soluble drugs. Microwave radiation contains frequent frequencies between infrared and radio waves, in the range of 0.3-300 GHz. It passes through objects and causes their molecules to glide, releasing heat. Microwaves, which have the ability to penetrate into anything, allow heat to be produced at any time in the sample at a specific time.

Orlistat is a lipase inhibitor for the management of obesity, which works by inhibiting the absorption of saturated fats. Orlistat is a modified inhibitor of gastric and pancreatic lipase. The Orlistat falls under category II according to BCS which means it exhibits poor oral discretion due to low melting. In this study, the MIND process was used to increase the melting and oral availability of Orlistat using MoringaOleifera and Aegle Marmelos gum as the lead. Performance tests of the method, physicochemical composition and in vitro dissolution were presented in this report. The promotion and use of new polymer such as MoringaOleifera and Aegle Marmelos gum to improve the melting of Orlistat and its converted form through its combination of Nano-composition using a microwave-assisted process and the drug spread into a natural gum carrier. Gum carriers, Orlistat and integrated bionanocomposite were tested for solubility, drug content, solubility, in vitro and spectral readings, thermal and Nano scale temperatures for BNCs prepared by FTIR, DSC and SEM. The rate of melting of the drug and the reduction of the drug for the desired liquid soluble drug does not only reflect the availability of the drug. In addition, melting was determined using the parameters of Hansen Solubility and Hildebrand Solubility by bringing them closer to various systems such as Hoy's System, Fedor's Constant, Van Krevelen Equation. The use of this method in determining the melting of bionanocomposite prepared in pharmaceuticals

highlights the best systematic approach to obtaining the need for the study reported here to ensure the melting of prepared BNCs.

Hansen Solubility Parameters:

Hildebrand and Scott introduced the concept of solubility parameter (δ), which suggested that objects with similar values could be felt (Hildebrand and Scott, 1964) Hansen solubility parameter model (HSP) model 1967 Predicting liquid reactions, incompatibility of polymer mixtures, soil moisture and pigmentation on HSPs surface. After predicting the ineffectiveness of active substances / carriers in strong distribution of HSPs in medical science. Guessing the compatibility of pharmaceutical materials, and their use is recommended as a tool in pre-construction and tablet development is recommended by HSPs. The study found that drug and substance abuse disorders, as predicted by deceptive tools that could be used, could be used to predict co-crystal formation, Orlistat was selected as an active drug ingredient (API). The group donation methods used to calculate HofPs for conformers and Orlistat were used .The three-component tools used were used to predict the Orlistat and conformer irregularities laboratory tests for co-crystals were performed using thermal and fluid-assisted (LAG) methods. In the prediction of inaccuracies. Heat exchangers and powder X-ray diffraction (PXRD) were used for co-crystal precision.

$$\Delta H = V_T \left(\sqrt{Ev1/Vm1} - \sqrt{\Delta Ev2/Vm}\right)^2 \emptyset 1.\emptyset 2 \qquad (1)$$

ΔH is the heat of mixing, V_T is the total volume, ΔE_V is the energy of vaporization, V_m is the molar volume, ϕ is the volume fraction, and 1 and 2 stands for the solute and solvent. The energy of vaporization per unit volume as the cohesion energy density (CED) explained.

$$\delta = (CED)^{0.5} = (\Delta E/V)^{0.5} \qquad (2)$$

Where, V is the molar volume.

Hansen determined that total cohesion energy is the sum of dispersion E_D, polar E_P, and hydrogen bond energy E_H.

$$E_T = E_D + E_P + E_H (3)$$

The total Hansen solubility parameter or Hildebrand solubility parameter δT by dividing both sides of the equation by molar volume V.

$$\delta^2_T = \delta^2_D + \delta^2_P + \delta^2_H$$

Where:

δ= total solubility parameter

δ = dispersion interactive (London) force

δ= permanent dipoles in interacting molecules, called dipole – dipole interactive forces

δ= hydrogen bonding force

According to equation (1) if δ_T of both solute and solvent are alike, this will allow predicting solubility. (J/m3)0.5, MPa0.5 or (cal/cm3)0.5, where one (cal/cm3)0.5 is equivalent to 2.0421 MPa0.5or (J/m3)0.5 are commonly used units for δ in literatures. δ calculation methods were different between practical and theoretical ones according to either direct/indirect measuring of essential properties of material as evaporation temperature, viscosity, solubility in preset solvents, etc.

Orlistat testing / prediction for co-crystallization:

Group donation methods are applied to the limits of melting of soluble solvents using Hoys molar attraction constants, Fedor's substants, and Van Kreevalen which are currently used methods. In the present study, these methods were used to reach the melting point parameters. The resulting structure has an open combination of chains and open rings are the basic steps of Fedor's method. Then using the potential possible lumps. This is summarized and the melting point is calculated as the square root of the total energy mixing of the variable elements separated by the number of times the volume of molar substituent constants. The rate of constant molar attraction to the molar volume is expressed by the Hoys

process. Drug effects and compounds are compared and its durability status is expressed. Selection of drug-related conformer, group donation method is used in the calculation of the doctrine. Hansen solubility parameters determine whether the drug and conformer are compatible and form the molecular structure of the drug and the conformer. Fedor's method, Hoys' method and Van Kreevlens's method of calculation are derived of atomic or molecular attachments forms a structure. These methods are used in the calculation of melting theory.

MATERIAL AND METHODS

Orlistat was received as a gift sample at INTAS Pharmaceuticals Ltd., (Ahmadabad, and Gujarat, India). The drug was stored in an amber glass container wrapped in aluminum foil and stored in a refrigerator at 5-7 ° C. Moringa Oleifera and Aegle Marmelos gum were collected in a local garden, Waranananagar. MoringaOleifera gum was collected by making a hole in the trees (an area damaged by trees). Gum was collected in a suitable air-tight container followed by air drying. Another natural gum AegleMarmelos was collected as Beal fruit contains a lot of gum, and after breaking the Beal fruit gum was carefully collected in a suitable air container followed by sun and wind suspension.

Extraction and Purification of Natural Gums

Gum M. oleifera and A marmelos collected are dried in the ground under the sun. Dry gum was passed through Sieve No. 80. Dry gum (10 g) was stirred in distilled water (250 mLl.) for 6-8 h at room temperature. By centrifugation supernatant was obtained, and the remains were washed with distilled water. The process was repeated four times. Finally, a precipitant with strength of more than 500 ml was twice treated with acetone volume for continuous movement. The products were burned and washed with distilled water and the same was dried at 50 ° -60 ° C under a machine.

Swelling Characteristics

Measured 10 g of natural carrier is placed in a measuring cylinder of 100 ml. The first dose of powdered gums was noted, and the cylinder was filled with refined water up to 100 ml. The cylinder was kept aside for 24 h, and the volume of the swollen powder was noted. Inflammation index (SI) is expressed as a percentage and is calculated according to the following equation:

% Inflammation = (Xt-X0) / X0 × 100… (3)

There, X0 the first height of the powder on the graduated cylinder and Xt refers to the constant height of the swollen gums after 24 h.

Viscosity Determination

The viscosity of the cleaned gums was determined by taking 1 g each of MoringaOleifera and AegleMarmelos gum respectively and dispersed in 100 ml (1% w / v) water. The estimated distribution viscosity was measured by Rheometer (Spindle 3, Brookfield DV-E, Brookfield Engineering Laboratories, Inc., Middleboro, MA, USA).

Foaming Index

The dynamic index of the carrier term was measured to find their functional properties. One gram of carrier was dispensed in 100 ml of distilled water and stirred vigorously for 2 minutes. The overflow index of a network company is measured to establish their operational structures. The foam index is calculated by the following equation

Foam guide = Vf-Vi… (4)

There, Vf is a 1% w / v solution for a network company after a shake and Vi is a 1% w / v solution for a network company solution before shaking.

Ash Value

Three samples of purified gum were placed on pre-measured crucibles and measured. These are then placed in a preheated oven at 300 ° C for 3 h. The temperature of the furnace then rose to 600 ° C until the hot metal samples were white to ash. Samples were then extracted using lumps and allowed to cool in the desiccators. After cooling, crosses containing samples

were weighed again. The amount of ash obtained by subtracting the combined weight of ash samples and crosses from the combined weight of new samples and crucibles.
Total ash value: 5g of purified gums powder was ignited in an electric furnace at 600ºC in silica crucible until the sample reaches a constant weight.
Water – soluble ash value: Total ash obtained was heated up to 600ºC with addition of 25ml of water for 10 minutes. It was filtered through whatman paper No. 41 and the residue was ignited in the furnace to get a constant weight.
Acid - insoluble ash value: Total ash obtained was heated with addition of 25ml of 0.1 N HCL for 10 minutes. It was filtered through whatman paper No. 41 and the residue was ignited in the furnace to get a constant weight.

Physical Mixtures

A portable combination of drugs containing natural doses extracted from the gums was prepared in sequence with a simple drug mix with natural carriers in the required dosage (1: 1 to 1:10 drug: carriers) for 10 minutes.

Bionanocomposites by Microwave-Induced Diffusion (MIND)

The preparation of Bionanocomposite (BNCs) by two groups such as Orlistat and MoringaOleifera Gum (OSMONC) and AegleMarmelos Gum (OSAMNC) was performed. The apparent combination of the drug and the natural agent is made by mixing similar to each sample. Weight loss (w / w) dose of the drug in the manager is taken as required by the values that maintain the constant value of the combination. After that 4 ml of water was added to each gram of the drug carrier mixture to form consistent slurry (water is added to the carrier hydration). The prescribed amount of slurry (5 g) was placed on a glass board with a Teflon stirrer (exposed to microwaves) and treated with microwave radiation at various times with a power of 560 W. The temperature of the compound was recorded at the end of the treatment using a built-in temperature test. The samples were then milled in glass mortar and the same sample was filtered to obtain a particle size of 80-250 μm.
BNCs were prepared by incorporating the weight-bearing drug Orlistat and the Moringa Oleifera & Aegle Marmelos gum carrier at 1: 1 to 1:10 w / w size (Table 1). The same physical combination of OS and Network Company was prepared using mud and pestle. The slurry was prepared by adding 4 ml of distilled water to each gram of the drug-carrying compound. A limited amount of slurry (5g) was placed in a glass beaker and radiated by microwave radiation at 700 W (IFB Microwave Oven, Model 17 PM-MEC1, Kolkata, India) for continuous operation. Temperature was noted using a temperature measurement built-in within the end of treatment. BNCs were laid using mud and pestle to obtain the required size of 80-250 μm. The synthetic BNCs of natural-containing Orlistat (Moringa Oleifera and Aegle Marmelos) have been shown to vary in the appropriate process for preparing OSMONC, OSAMNC.

Evaluation of Bionanocomposite (BNC)

Solubility

The melting study of BNCs (OSMONC and OSAMNC) was performed by adding a higher dose of Orlistat (equivalent to 30 mg) and BNCs to 150 ml of distilled bottled water. The resulting mixture was stirred 24 h at a temperature of 25ºC using an orbital shaker incubator. The excess liquid was collected and filtered through 0.2 membrane filters and analyzed by a UV-Visible spectrophotometer of 203 nm wavelength at 28 sequences. The optimization ratio (drug: carrier) is done on the basis of the best melted detection.

Drug Content

The amount of Orlistat added to BNCs such as OSMONC and OSAMNC was determined by extracting 100 mg of the drug from bionanocomposite by diluting it into 25 ml enough methanol. The resulting solution was filtered through a 0.2 and membrane filter and analyzed

by a UV-Visible spectrophotometer (UV-Carry 60, Agilent) at a wavelength of 215 nm respectively against methanol as blank 8.

Powder Dissolution

Powdered extraction tests performed on BNCs followed the USP XXIV Apparatus 6 (paddle) method in 900 ml of dissolved media stored in 37 ± 0.5 ° C powder containing 5 mg API added to dehydration sources. The 1 ml sample was withdrawn periodically and the resulting solution was filtered through a 0.2 µm membrane filter and analyzed by a UV-Visible spectrophotometer (UV-Carry 60, Agilent) at wavelength 215 nm respectively against methanol as empty 8. All tests they are made in 3 steps. BNC dispersion profiles are compared with pure drug in similar experimental conditions.

Characterization of Bionanocomposites

A well-defined BNC standardization was performed by FTIR, DSC, XRD and SEM to ensure the best results of the current drug and polymer study**.**

Fourier-Transform Infrared Spectroscopy (FT-IR)

FT-IR spectra of impure drug (Orlistat), pure polymers (MoringaOleifera and AegleMarmelos gum) and BNCs of individual polymers (MoringaOleifera and AegleMarmelos gum) were developed to monitor drug compatibility polymer. Drug BNCs with each polymer (OSMOM, OSAMM, are stored directly in the sample holder and scanned using the FT-IR spectrophotometer (Cary 60, Agilent Corp., Germany). in terms of drug interactions with polymer. The materials are scanned in the range from 400 to 4000 cm with 1 by a resolution of 4 cm -1.The peak properties of Orlistat, MoringaOleifera and Aegle Marmelos were are compared to BNCs designed to test drug compatibility -polymer. IR detectors were used to determine and predict BNC melting by the Hansen solubility parameter.

Differential Scanning Calorimetry (DSC)

DSC studies of Orlistat, MoringaOleifera, Aegle Marmelos gum and BNCs of drugs with individual polymers (MoringaOleifera and AegleMarmelos gum) were conducted to detect improved drug availability. The DSC thermogram was obtained using a scanning calorimeter (DSC 60; Shimadzu) at a temperature of 11ºC / min from a temperature of 0ºC to 250ºC in an inert state and the physical, chemical interaction between the drug and the polymer that helps determine and predict the melting of BNCs with the Hansen solubility parameter.

X-Ray Diffraction Studies (XRD)

XRD studies of drugs (Orlistat), pure polymers (Moringa Oleifera and Aegle Marmelos gum), and BNCs of individual polymer drugs (Moringa Oleifera and AegleMarmelos gum) were intended to test changes in crystalinity the drug is mixed with gums. The crystalinity property is associated with the physicochemical properties of the material. XRD patterns of Orlistat, gums and BNCs were recorded using (Bruker, D8) and Cu-kcy radiation.

Scanning Electron Microscopy (SEM)

The surface morphology of Orlistat BNCs was detected by scanning electron microscopy (SEM). Samples were placed directly on a two-dimensional SEM adhesive sample and the images were recorded at the required amplification of 15 kV power and 8 mm working distance on XL30-SFEG Philips (Lab exchange, Burladingen, Germany).

Theoretical Prediction of Solubility:

Fedor's Substituent Constants:

$$\boldsymbol{\delta = \sqrt{\frac{\sum \Delta\Delta \mathbf{U}}{\sum \Delta \mathbf{V}}}} \qquad \textbf{... (4)}$$

Where,

*$\boldsymbol{\Delta\Delta}$U is constant for energy mixing

**$\boldsymbol{\Delta}$V is constant for molar volume

Hoys Method/Hoys Molar Attractions:

According to [(cal cc) 1/2 mol-1] unit

$$\delta = \frac{\sum molarattraction}{V} \quad \text{... (5)}$$

Van Kreevalen's Solubility Parameters:

The given calculation of solubility parameter and molar volume by Van Kreevalen's method is based on experimental molar volume and measured $cm^3Mol\text{-}1$.

$$\delta d = \sum Fd/V \quad \text{...(6)}$$

$$\delta p=\sqrt{\sum Fp^2}/V \quad \text{...(7)}$$

$$\delta h = \sqrt{\sum Uh/V} \quad \text{...(8)}$$

$$\delta^2 T= \sqrt{\delta d^2+\delta p^2+\delta h^2} \quad \text{...(9)}$$

RESULT AND DISCUSSION

Physical Characterization of Carriers

The inflammatory properties and viscosity of Moring Oleifera and AegleMarmelos gum were low (Table 2). Due to the low viscosity of MoringaOleifera and AegleMarmelos gum, they were considered for the melting and elimination of selected BCS class-II drugs. Both gums were therefore more efficient and easily exploited in improving the melting and degradation rate of orlistat.

Rheological Characterization of Gums:

Rheological description of MoringaOleifera L AegleMarmelos was performed using a rheometer R / S-CPS + rheometer with the calibration system: C75-2. Viscosity and thixotropic analysis was performed (Table 3), and from Fig. 1, low viscosity was obtained and from Fig. 2 thixotropic analysis obtained 13.23 Pa/s of Aegle Marmelos and 17.63 Pa/s of Moringa Oleifera Gum. Therefore, both gum exhibits stability and helps to increase the solubility of BCS class-II drugs by preparing its bionanocomposites and can withstand the microwave radiation.

Characterizations of Bionanocomposites:

Solubility

Melting is mainly focused on the use of MoringaOleifera and AegleMarmelos, which is used to stabilize the moisture content of water-soluble drugs. Melting was performed and expressed in mg / ml by the apparent combination of the selected BCS class-II drug. It was noted that, the melting of a more visible compound than that of Orlistat (Figure 3).

The Orlistat insoluble study conducted by comparisons similar to their body composition with BNCs prepared, found that, there was a significant increase in the solubility as the polymer drug dose increased. After the OSMO-BNC ratio of 1: 3 and the OSAM-BNC ratio of 1: 4 there is no apparent improvement in melting as shown in Figure 3.

The solubility (mg / ml) of the prepared BNCS of Orlistat with MoringaOleifera and AegleMarmelos was observed to be a well-developed dose of OSMO-BNC (1:03), OSAM-BNC (1:04) selected after practice melting research. This well-performed measure was then confirmed by the removal of the powder and found to be increasing in melting. Soluble reinforcement of OSMO-BNC (1:03), OSAM-BNC (1:04) is widely available and this is due to the foam index and viscosity profile of MoringaOleifera and the AegleMarmelos gum, a drug spread in gum form I. its bionanocomposite has a structural modification that is made of a type of hydrophilic drug enriched with hydrogen bonding and this hydrogen compound helps the molecule to disperse and open the ring rings by producing molar volume without affecting its parental function. This type of hydrophilic has apparently been used to stabilize improper water solubility.

Drug Content

The differential distribution of Orlistat in BNCs is determined by the drug content analysis. It was found that 95-98% of the drugs were trapped in BNCs showing the same prevalence.

Powder Dissolution

Powder dispersion tests are performed to check the stability of the enhancement components. The degradation profile of the apparent compound showed a surprising improvement in the degradation rate compared to Orlistat and their apparent combination with natural carriers. The combination of Orlistat with both gums showed good results. As reported in Figure 4, the dosage of prescription drugs in% of the pure drug Orlistat was found to be 54.69 ± 4.5. The combined drug release of OSMO-PM1 body composition was observed 70.2 ± 7.5%, of OSAM-PM 3 was 61.1 ± 7.5 after 60 min.

Bionanocomposite Orlistat with both gums showed good results. As reported, the cumulative drug release in% of Orlistat was found to be 54.69 ± 4.5. The cumulative drug release of BNCS such as OSMO-BNC observed 97.22 ± 1.1%, for OSAM-BNC was 70.21 ± 1.9% after 60 min (Figure 5). From the observed results it was clearly shown that the ornated BNCs of Orlistat (suggested batches) showed better drug release compared to their pure form and body composition form, it was concluded in the study that natural polymer was used for Microwave BNC included in the separation the dispersion rate is improved in the prepared BNCs.

Characterization of Bionanocomposites

Fourier Transform Infra-red Spectroscopy (FTIR) Analysis

FTIR spectroscopy of Orlistat shows a high value of 3301.30 (OH simple hydrogen bond), 2918.302 (simple CH alkanes group), 2853.553 (CH stretching alkanes group), 1721.653 (C = O carboxylic expansion group), 1665.0 (C = C amide extraction amide), 1201.904 (CO to dilute alcohol), 1841.144 (C = Extension of anhydrides) respectively (Figure 6).

MoringaOleifera whole-gum exudates from M. Oleiferahas was found to contain L-arabinose,-galactose, glucuronic acid, and L-rhamnose, -mannose and xylose, while a single polysaccharide, with a gum polysaccharide containing G-galactose, - glucuronic acid and iron certain metals such as sodium, potassium, calcium and magnesium and L-mannose have been found in mild hydrolysis of all acids. For the most part, the gum has frames with large branches that contain different units of sugar with many possible variations in terms of branch level, branch length and type of connection. The IR spectrum (Fig. 6) shows a height of 3301 and 3263 cm-1 due to the OH of the main alcohol extraction. The absorption height of 2928 cm-1 indicates –CH to extend the vibration of the methyl group. 1603 cm-1 bands are a C = O element of aldehyde. The height at 1310cm-1 is due to the variability of the CH2 equation with the C-OH group. Weak bond at 770 cm-1 due to the fact that r contributes to ring binding and ring flexion of α-D- (1-4) & α-D- (1-6). All of this in conjunction with the polysaccharide structure indicates that, either starch or cellulose, but there were certain peptide cross links and other amino sugars.

Active data of the AegleMarmelos group showed that the major neutral sugar is α-D-glucose, β -D-glucose, galactose shown in the composition of osazone. The IR spectrum is shown in Figure No. 8.5, rises to 3296.65 cm-1due to -OH to extend the main alcohol. The absorption height at 2977 cm-1 indicates -CH to extend the vibration of the methyl group. The absence of a large fragrant stretch in the region of 1838 cm-1 and the weakness of the fibers means that there are limited number ofcross-linked peptides. Belts at 1633 cm-1 element C = O aldehyde. The height at 1315cm-1 is due to the variability of the CH2 equation with the C-OH group. A weak bond at 821 cm-1 due to the fact that r contributes to ring binding and ring conversion of α-D- (1-4) & α-D- (1-6).

Scanning Electron Microscopy (SEM)

SEM research has been conducted to look at the surface morphology of drug particles. Orlistat particles were made of a smooth surface, while OSMO and OSAM particles had unequal shape and size. From the study and writing 7 it is clearly shown that the crystal

structure of Orlistat was completely changed in OSMO-BNC and OSAM-BNC shown Orlistat crystals embedded in the matrix.

Differential Scanning Calorimetry Analysis

Pharmaceutical DSC thermograms (OS), polymers (MO and AM) and BNCs for each drug with each polymer are shown in Figure 8. Orlistat DSC showed high endothermic intensity at 51^{o}C indicating melting of Orlistat. DSMO OSMO-BNC and OSAM-BNC have shown the same endothermic intensity as that of pure drugs but with less energy which may be due to a decrease in the crystal type of the drug. A slight change in the melting point showed a reduction of the drug into a nanocrystalline form. The high rate of exposure showed that most of the drug was converted to nanocrystalline form. No chemical interactions between the drug and the polymer were observed. Physical interaction was the way a drug is bound to a polymer. These studies have confirmed that as the crystalline nanoparticle size of the crystal decreases; its melting point decreases slightly. A slight change in the melting point showed a reduction of the drug into a nanocrystalline form. The high rate of exposure showed that most of the drug was converted to nanocrystalline form.

No chemical interactions between the drug and the polymer were observed. Physical interaction was the way a drug is bound to a polymer. These studies have confirmed that as the crystalline nanoparticle size of the crystal decreases; its melting point decreases slightly (figure 8).

X-Ray Diffraction (XRD)

XRD was performed to assess the physical condition of the body and its BNCs. XRD pattern of impure drug (OS), pure polymer (MO and AM) and its bionanocomposites are shown in Figure 9. The XRD pattern of pure Orlistat showed a high crystalline value between 100 and 600. , 14.50, 17.50, 19, 21, 24, 25.50, 28, 30, 32 and 35 with a very high value of 24 indicating the crystalline form of Orlistat. The XRD pattern of OSMONC and OSAMNC showed a significant decrease in elevation due to the decrease in crystalinity. Decreased levels of bionanocomposites may be due to a decrease in drug size to nano level.

THEORETICAL PREDICTION OF SOLUBILITY

Fedor's Method

Fedor has proposed a method for determining the melting parameter without using a compound density. The contribution of the largest number of active groups has been tested, and the method only requires knowledge of the formula formulation of the combination.

Based on Fedor's succession

$\delta = \sqrt{} (\Delta\Delta U / AV); = (32700) / 37.44) = 29.55H$

* U always meets the combination of forces

** ΔV remains the molar volume

The result obtained from the above calculation of Fedor's stable Orlistat was found to be 29.55 H. The hydrogen concentration is determined after the opening of the ring in the Orlistat structure. Total strength is required to determine the molecular weight in relation to the molar volume (Table 4).

Orlistat Bionanocomposite (OSMO-BNC)

A modified bionanocomposite i.e. OSMO-BNC (Orlistat with MoringaOleifera) where it was considered to dissolve was found at the time of cracking and in the amount observed in FTIR, there was hydrogen binding possible and the melting parameter helped determine it. Fedor's permanent effect was 11.08 H, due to the strong hydrogen bonding in the molecule and the conversion of the other two bonds into bonds that bind together Fedor's BNC Orlistat bond also increases and this number of hydrogen bonding increases eventually it leads to an increase in the melting of molecules i.e. smaring constantly in Fedor. In addition, the molar volume is less representatives of their numbers.

Orlistat Bionanocomposite (OSAM-BNC)

The bionanocomposite prepared namely OSAM-BNC (Orlistat with AegleMarmelos) when considered for its detection was found at the time of cracking and in the amount observed in FTIR, there was a high hydrogen binding and the melting was determined by a parameter, Fedor's Continuous Effect δ was 11.56 H. Due to excess hydrogen

Molecular bonding and the conversion of other double bonds to its binding bonds Fedor's constant of BNC Orlistat also increases and this increase in hydrogen bonding ultimately leads to increased molecular melting which means an increase in Fedor's consistency.

Hoy's Method

The Small scheme provided an easy way to measure the amount of SP in most solvents and polymers. However, the list of constants is not complete. Hoy has published a number of jaw-dropping features found in the pressure points of various groups.(Table 5).

According to [(cal cc) 1/2 mol-1] unit

$$\delta = \frac{\sum molarattraction}{V} = \frac{3110.4}{317.958} = 9.78\text{H}$$

By using Hoy's formula the molar attraction for pure Orlistat was calculated and it was found 9.78 H, where is the∑ F sum of the group molar attraction constants of the compound Hoftyzer and Van Krevelen published a series of group molar attraction constants similar to small and Hoy.

Orlistat Bionanocomposite (OSMO-BNC)

By using Hoy's formula the molar embrace for OSMO-BNC (orlistat with MoringaOleifera) was calculated and it was found 23.59 H and which more than that of pure Orlistat which was 9.78 H.

Orlistat Bionanocomposite (OSAMNC)

By using Hoy's formula the molar magnetism for OSAMNC (Orlistat with AegleMarmelos) was calculated and it was found 22.86 H, which more than that of pure Orlistat which was 9.78 H.

Van Kreevalen's Solubility Parameters

Van Krevelen derived Fi values for the assistances of atoms i.e. C, H, N, 0, halogens and statutory effects (such as double or tribal bonds, etc.) solubility parameter (δ) can be calculated using the following equation:

$$\boldsymbol{\delta = \frac{\sum Fi}{Vm}}$$

Where, $\sum =$ Fi is the sum of the atomic contribution and Vm is molar volume (Table 6). Calculation of solubility parameter and molar volume of pure Orlistat by Van Kreevalen's solubility parameter was obtained 7.71 H.

Orlistat Bionanocomposite (OSMO-BNC)

Calculation of solubility parameter and molar volume of OSMONC (Orlistat with MoringaOleifera) by Van Kreevalen's solubility parameter was obtained 8.02H which shows more than pure form of Orlistat i.e. 7.71 H.

Orlistat Bionanocomposite (OSAM-BNC)

The calculation of the melting point and molar volume of OSAMNC (Orlistat with AegleMarmelos) by Van Kreevalen's melting parameter was obtained at 9.9 H which indicates more than the purest form of the drug i.e., 7.71 H.
It was noted that, the combination of hydrogen with the Orlistat molecule was proposed to potentially improve solubility. As the formation of the impact on the established BNCs will be in line with the need to study. A greater number of covalent bonds and hydrogen bonds were formed when drugs were incorporated into their BNCs and natural carriers.
From the structure obtained -O-OH bond to indicate hydrogen bond and CH- OH meaning bond covalent bond and due to such an interaction between selected drugs and gums held in covalent bond and stated that hydrogen bonding between low energy is required to break such bond. In addition, the weak Vander Waals strength found in the prepared BNCs is why the molecular meltdown is enhanced in the proposed way.

CONCLUSION

Applications of natural polymer such as Moringa Oleifera and Aegle Marmelos for the generation bionanocomposite of orlistat by Microwave Induced Diffusion Technique (MIND) simple, convenient and cost effective method. Further, use of natural carriers influences physicochemicalproperties of drug. MIND shows promising approach to enhance the solubility and dissolution rate of prepared BNCs. Characterization approach using FT-IR, XRD, DSC and SEM explores that, orlistat generated into the BNCs shown significant liability to enhance the solubility and increased in dissolution rate. The application of Hansen solubility parameter and hilderbarand solubility parameter including Fedor's constant, Hoy's molar attraction and Van Kreveelen system in prediction and determination of solubility of prepared BNCs were reveled its utilisation in pharmaceutical formulation. It was found that, there was significant enhanced solubility of optimized ratios when compared with pure entities. Hence it was concluded here hansen Hansen solubility parameter providing acceptable determination of solubility in pharmaceutical science.

CONFLICT OF INTEREST

The Authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Table 1: Formulation design for Bionanocomposites batches

Drug + Carrier	**1:1**	**1:2**	**1:3**	**1:4**	**1:5**	**1:6**	**1:7**	**1:8**	**1:9**	**1:10**
OS- MO Gum	1:1	1:2	1:3	1:4	1:5	1:6	1:7	1:8	1:9	1:10
OS- AM Gum	1:1	1:2	1:3	1:4	1:5	1:6	1:7	1:8	1:9	1:10

*****OS- Orlistat, MO-*Moringa Oleifera* Gum, AM-*Aegle Marmelos* Gum

Table 2: Organoleptic and Physical Characterization of Natural Gums

Sr. No.	**Parameters/ Particulars**	**Moringa *Oleifera* L**	**Aegle Marmelos**
1	Colour	Brownish black	Yellowish white
2	Odour	Characteristic	Characteristic
3	Taste	mucilaginous	Mucilaginous
4	Swelling Index	19.7 ± 2.21	20.3 ± 1.01
5	Foaming index	17 ± 0.92	16 ± 0.65
* All values are represented as means ± SD, n = 3.			
6	Angle of Repose	33°	31°
7	Bulk density (gm/ml)	0.71gm/ml	0.67gm/ml
8	Tapped density (gm/ml)	1.23gm/ml	1.25gm/ml
9	Compressibility index (%)	47.27%	52.71%
10	Hygroscopicity	17%	16%
11	Swelling Index (ml/gm)	19.7	20.3
12	Loss on drying	11% w/w	9% w/w
13	Total Ash	2.6%	3.3%
14	Insoluble matter	0.03%w/w	0.02%w/w
15	pH	5.5	6.5

Table 3: RheologicalCharacterization of *Aegle Marmelos* and *Moringa Oleifera* Gum

Parameter	***Aegle Marmelos***	***Moringa Oleifera***
Viscosity (Pa.s)	0.5740	1.5442
Torque (mNm)	0.6772	4.1996
Speed (1/min)	16.8300	16.8302
Shear Stress (Pa)	6.1317	38.0230
Shear Rate (1/s)	50.4901	50.4907
Density (g/cm3)	1.0000	1.0000
Angular Velocity	0.0000	0.0000

Table 4: Calculation of ∂ value of Orlistat by F, G, C. method

Fragments/ groups	**No. of groups**	**ΔΔU* for each (cal.mol-1)**	**Total ΔΔU**	**ΔV** for each (m-1 mol-1)**	**Total ΔV**
$-CH_3$	4	1125	4500	33.5	134
$-CH_2$	18	1180	21240	16.1	289.8
-C	2	350	700	19.2	-38.4
-CH	3	820	2460	-1.0	-3
-NH	1	1000	1000	-9.0	-9.0
-O	2	800	1600	3.8	7.6
Ring closer	-	-	-	-	-
Conjugate bond	3	400	1200	-2.2	-6.6
			Σ=32700		Σ=37.44

Table 5: Calculation of solubility parameter of Orlistat based on Hoy's molar attractions.

Fragments/ group	**No. of groups**	**ΔΔU*for each (cal.mol-1)**	**Total ΔΔU**	**ΔV**for each (m-1 mol-1)**	**Total ΔV**
$-CH_3$	4	148.36	593.44	21.548	86.192
$-CH_2$	18	131.5	2.367	15.553	279.954
-C=O	2	262.96	525.62	17.265	34.53
-CH	1	85.99	85.99	9..557	9.557
-NH	1	180	180	8.774	8.774
-O	2	114.98	229.96	6.46	12.92
CH=O	1	117.12	117.12	13.417	13.417
Six membered Ring	1	-23.44	-23.44	0	0
Conjugated bond	3	23.26	69.78	0	0
Ortho	2	9.69	19.38	0	0
Meta	2	6.6	13.2	0	0
Base value	0	0	0	0	0
			Σ=4178		Σ=431.97

Table 6: Calculation of solubility parameter and molar volume of Orlistat by Van Kreevalen's solubility parameter.

Fragments/ Groups	**No of groups**	**Fd**	**Total Fd**	**Fp**	**Total Fp**	**Fp2**	**Uh**	**Total Uh**
-CH3	4	420	1680	0	0	0	0	0
-CH2	18	270	4860	0	0	0	0	0
-C=O	2	0	0	0	0	0	0	0
-CH2	1	80	80	0	0	0	0	0
-NH	1	280	280	610	610	372100	8400	8400
-O	2	100	200	410	820	672400	3000	3000
-CH=O	1	200	1800	0	0	0	0	0
6/5 member ring	1	190	190	0	0	0	0	0
			Σ8890		Σ=1044			Σ=14400

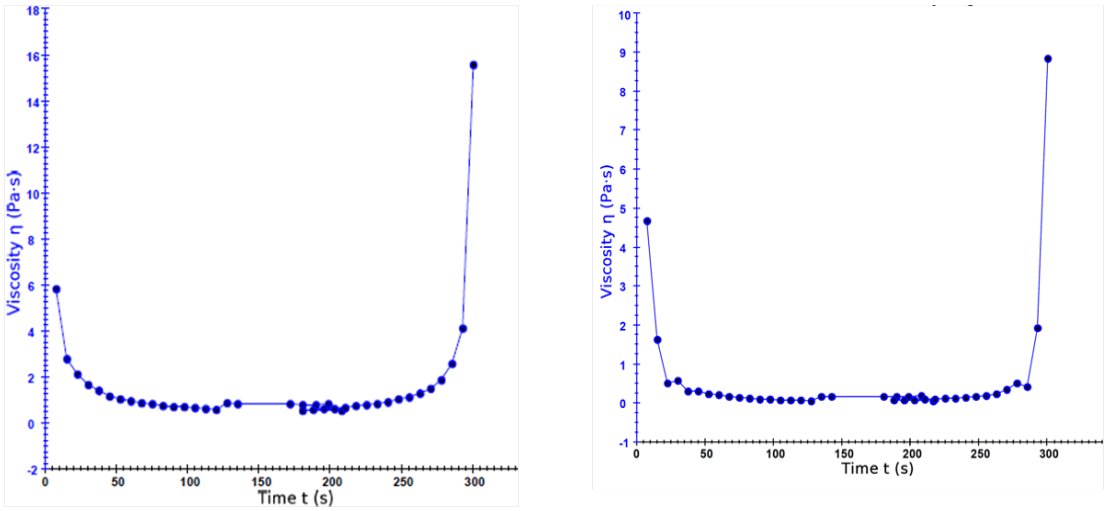

Figure 1: Viscosity Diagram of (A) Aegle Marmelos (B) Moringa Oleifera

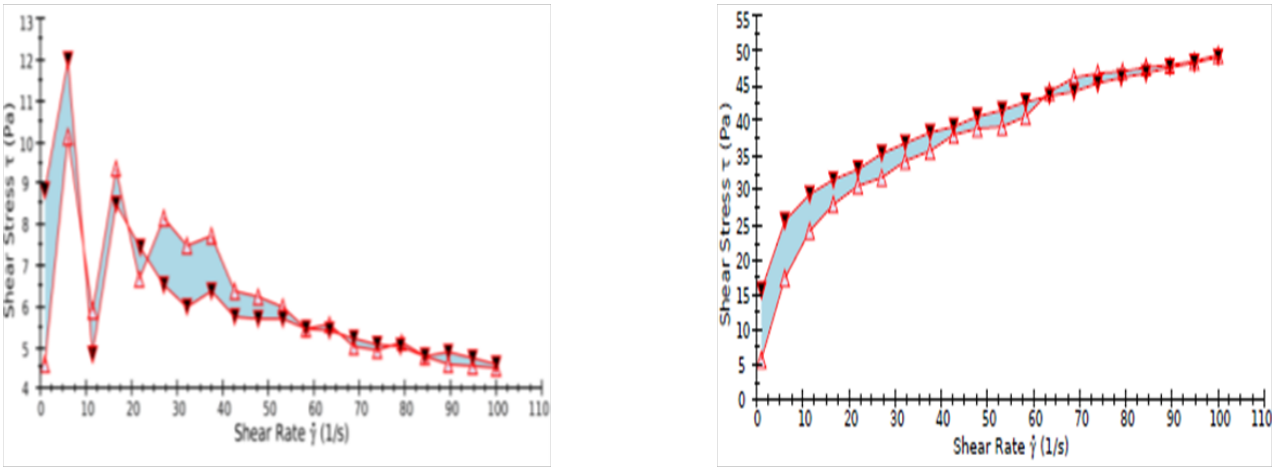

Figure 2: Thixotropic analysis of Aegle Marmelos & Moringa Oleifera

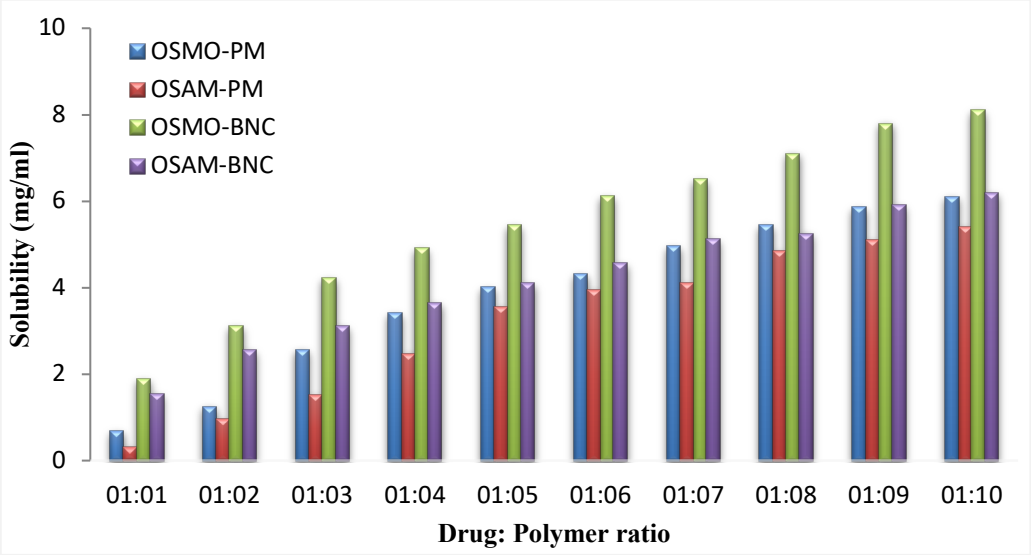

Figure 3: Solubility of orlistat in Physical Mixture and Bionanocomposite with *Moringa Oleifera* and *Aegle Marmelos (*OSMO-PM; OSAM-PM and OSMO-BNC, OSAM-BNC)

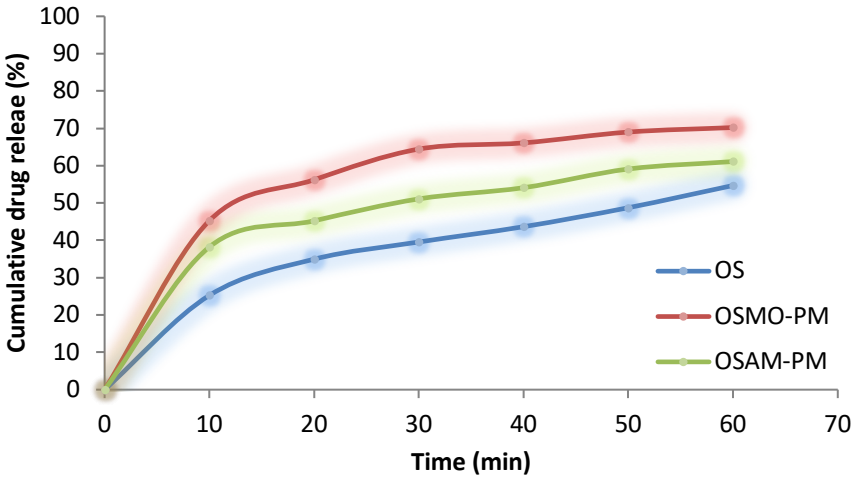

Figure 4: Powder Dissolution of Physical Mixture of orlistat with *Moringa Oleifera* and *Aegle Marmelos*.

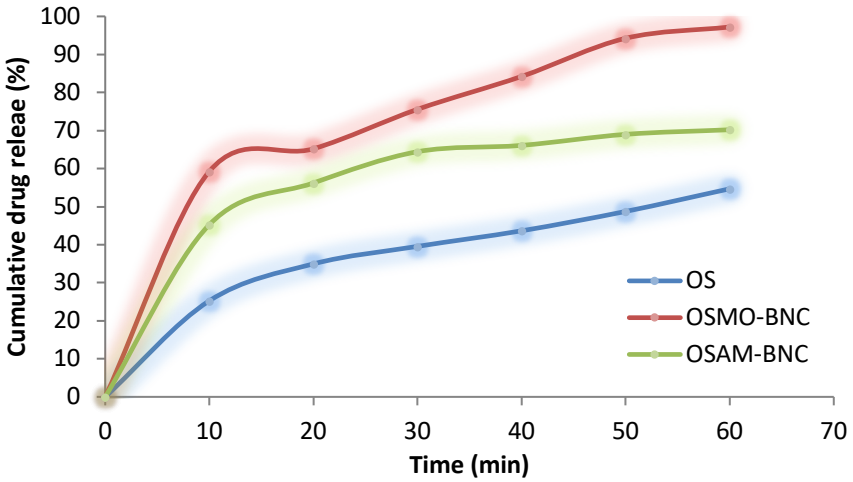

Figure 5: Powder Dissolution study of Bionanocomposite of Orlistat with *Moringa Oleifera* and *Aegle Marmelos*.

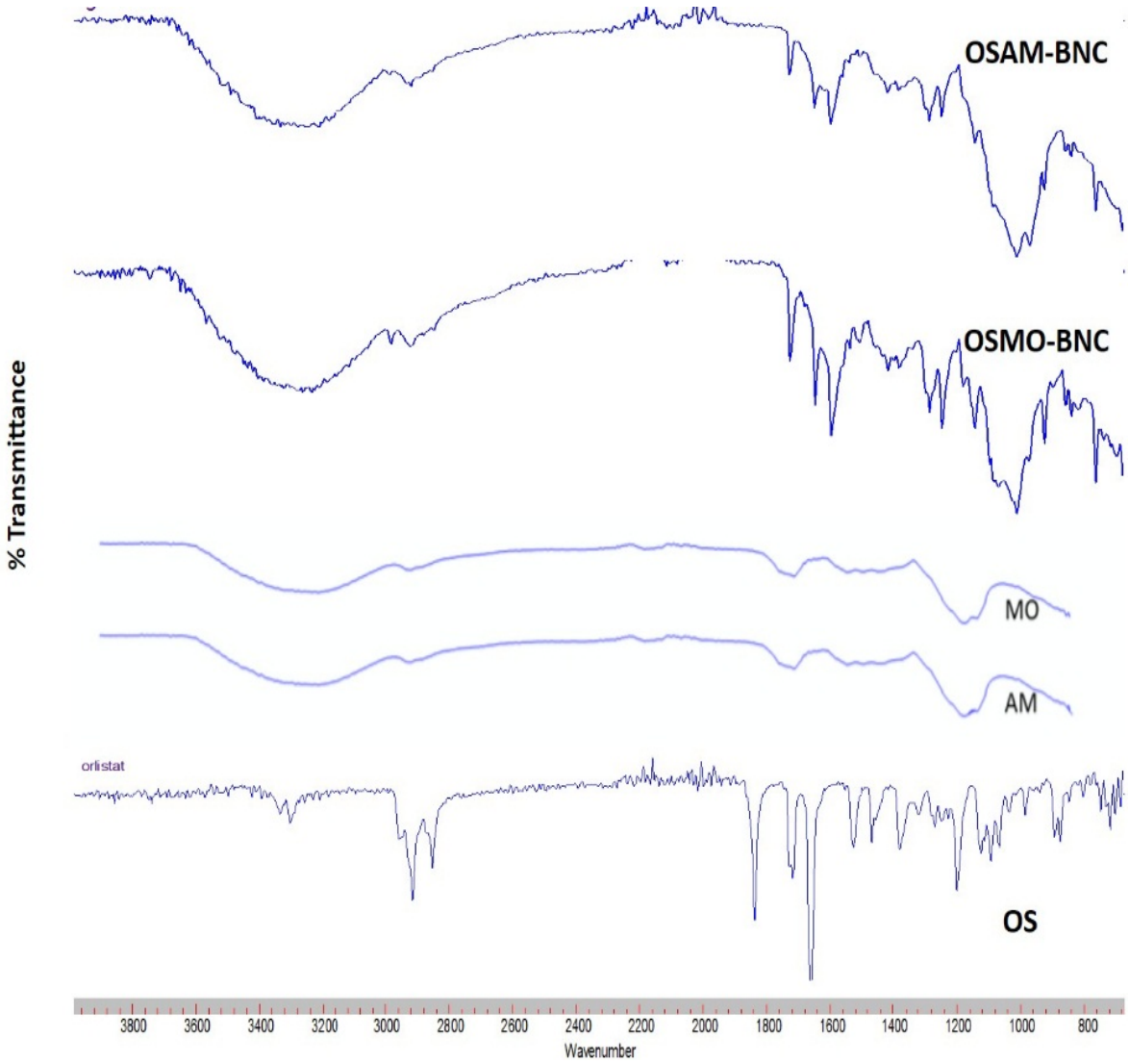

Figure 6: FT-IR studies of pure *Moringa Oleifera* (MO) *Aegle Marmelos* (AM), orlistat (OS) and BNCs such as OSMO-BNC, OSAM-BNC

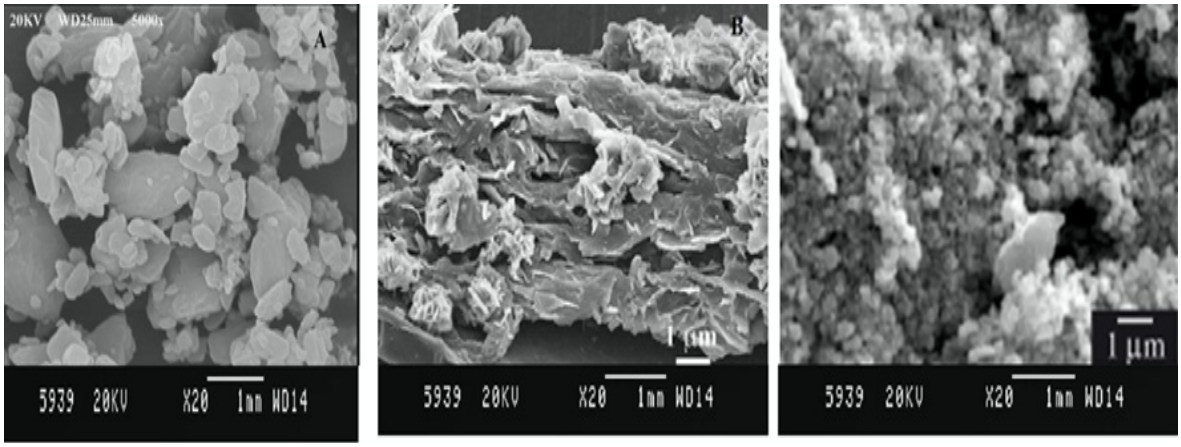

Figure 7: SEM images of Orlistat and its BNCs i.e. OSMO-BNC and OSAM-BNC with *Moringa Oleifera* and *Aegle Marmelos.*

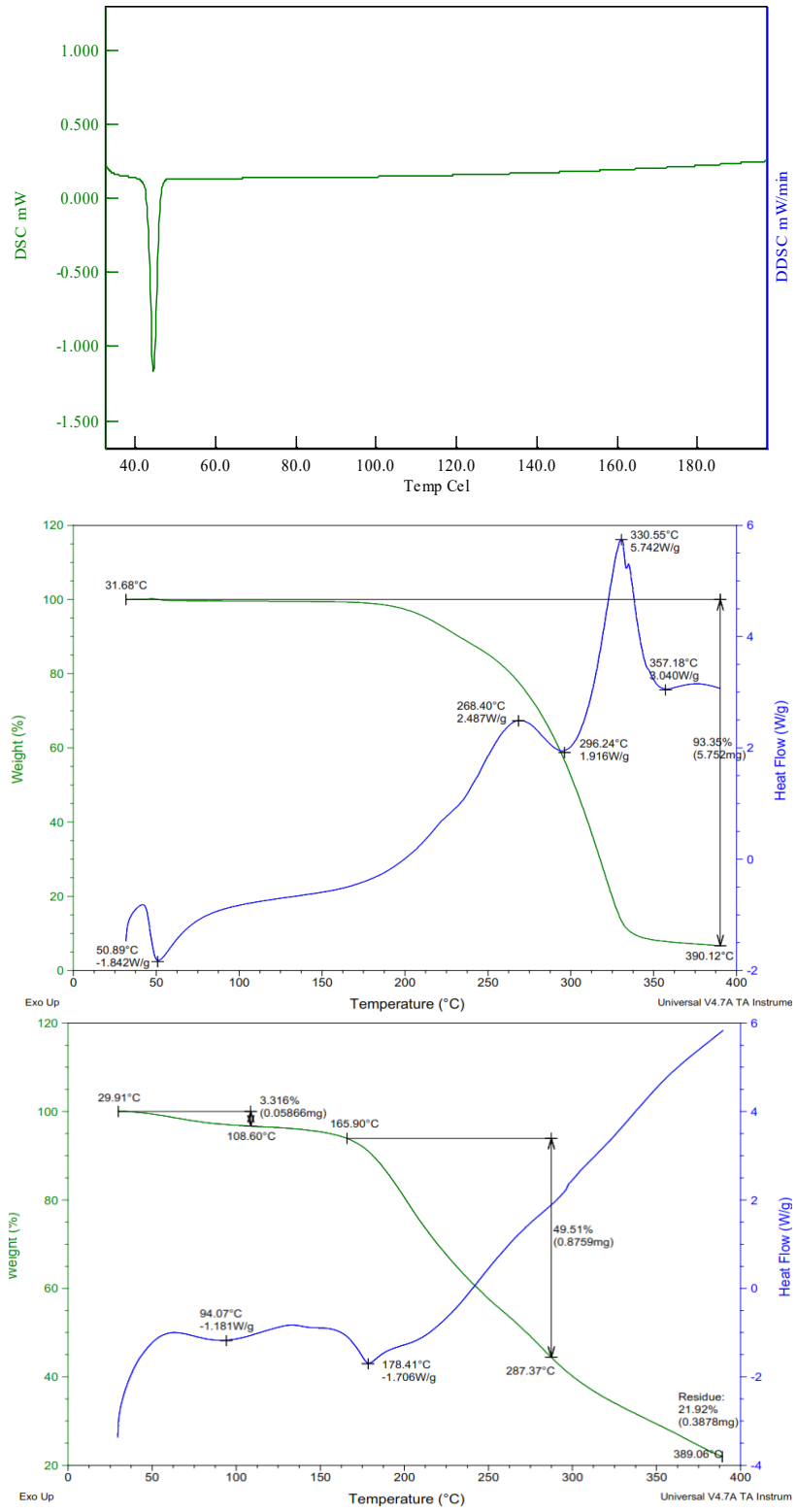

Figure 8: Differential scanning calorimetry (DSC) of (A) orlistat and its BNCs i.e. (B) OSMO-BNC (C) OSAM-BNC with *Moringa Oleifera*, and *Aegle Marmelos*.

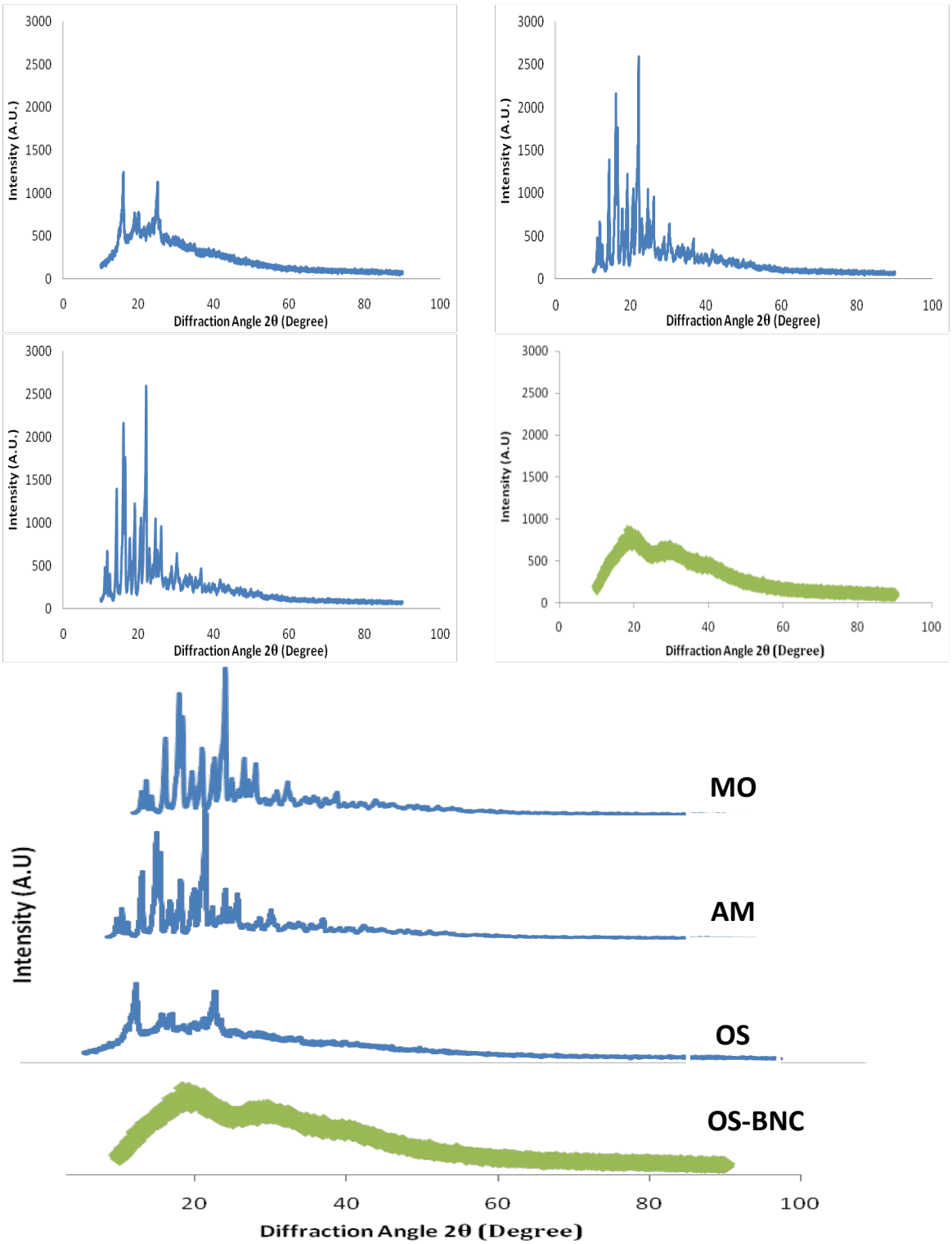

Figure 9: XRD studies of orlistat and its BNCs i.e. OSMO-BNC and OSAM-BNC with *Moringa Oleifera and Aegle Marmelos*.