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Development And Evaluation Of Microwave Generated Nanocomposites For Solubility Enhancement Of Orlistat Drug

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Abstract

The development of a technique for lowering the particle size and turning the drug into an amorphous state can increase the solubility and bioavailability of BCS Class II medications like Orlistat. A promising method for oral delivery of medications with low solubility is to create nanocomposites (NCs) utilising natural carriers. For the purpose of improving the solubility of the weakly water soluble (BCS class II) model drug Orlistat, nanocomposites were created in the current study utilising the microwave induced diffusion technique (MIDT). Due to its limited water solubility and its oral bioavailability, it is extremely low. The natural carrier's Acacia, Xanthum gum, Gelatin powder, Chitosan, and Tragacanth were used to create the nanocomposites of orlistat. With different concentrations of medication and carriers, various physical mixture and nanocomposites formulations were created. Natural carriers were chosen based on their surfactant and wetting characteristics. According to the dissolving analysis of the optimised nanocomposites IR tablet, the dissolution rates were noticeably better in NCs IR tablet as compared to the marketed tablet. Out of four tablet formulations, tablet F2 had the shortest disintegration time, so it was chosen for further examination and an in-vitro dissolving test was carried out to see whether the tablet was releasing the medicine. The amount of medication released after 30 minutes was determined to be 91.45 ± 1.2 % as opposed to the 75.65 ± 1.3 % shown on the commercial tablet. Fourier transform infrared spectroscopy, Differential scanning calorimetry, X-ray diffraction, and Scanning electron microscopy were used to characterise the optimised nanocomposites. The nanocomposites OGAN4 (Orlistat + Acacia gum powder) formulation was shown to be optimal in terms of solubility enhancement of a drug by microwave assisted synthesis based on solubility, in-vitro drug release, and physical characterization of carriers. The MID technique used in this work remains environmentally friendly, inexpensive, then a possible technique aimed at improving solubility.

Keywords: Orlistat, Nanocomposite, Microwave Induced Diffusion Technique (MIDT), Tablet, Immediate Release etc.

Introduction

It is difficult to create then establish a dosage form aimed at most of the active medicinal components due to their poor solubility profiles. Poor aqueous solubility can drastically restrict a drug's potency then effectiveness, then most drugs that remain poorly soluble in water correspondingly exhibit side effects. The effectiveness of some medications is significantly improved and their negative effects are reduced when solubility is increased. The sluggish absorption of drugs and eventual insufficient or uneven bioavailability are linked to drugs with poor water solubility. It was discovered through the literature review that water solubility is a problem for close to 40 % of recently synthesised medications. The most crucial metrics for assessing a drug's oral bioavailability in the GI tract, which has an aqueous environment, are its solubility and permeability. Pharmaceutical research faces a real difficulty in increasing the oral bioavailability of poorly water-soluble medicines in order to increase drug therapeutic effectiveness and open up new market potential [1-4].
More than 40% of the medications, according to the US Pharmacopoeia, are insoluble or only poorly soluble in aqueous conditions. The BCS class-II medicines have high membrane permeability that is solely constrained by dissolution, while being insoluble in water (solubility equal to or less than 100 g of solute per 1 ml of solvent). Crystalline solid dissolution is the process's energy-driven stage. One of the key factors in achieving the correct drug concentration in the bloodstream for pharmacological response is solubility [5]. After oral administration, poorly water-soluble medications may need high dosages to attain therapeutic plasma concentrations [6]. To combine the best qualities of both components, two or more different materials with distinct properties are fused to form a nanocomposite. A composite is made of two materials with different qualities that are combined to produce enhanced results over the individual components [7]. One of the innovative methods for increasing medication solubility is microwave (MW) irradiation [8]. Microwave irradiation with the aid of a microwave oven causes the internal structure of drug particles to be broken down, leading to the production of nanoparticles, which eventually improves solubility [9,10]. Therefore, the oral delivery of low solubility medications employing nanocomposites of poorly soluble pharmaceuticals using natural carriers can be a potential method. In the current study, poorly water soluble BCS class II model medication Orlistat was given a boost in solubility using microwave-generated nanocomposites. Tetrahydrolipstatin, the active ingredient in orlistat, is a lipase inhibitor with poor water solubility, a low melting point, poor chemical stability, a significant amount of first pass metabolism, waxy nature, and limited bioavailability (10%). Several approaches, including extrusion, spheronization, micronization, palletization, nanoemulsion, and multi-unit pellet systems (MUPS), were used to investigate orlistat. However, none of the methods are particularly helpful at improving solubility and site-specific release. So effective formulation technique is needed for orlistat. A lipase inhibitor for the treatment of obesity, orlistat works by preventing the absorption of saturated fats. A modified inhibitor of pancreatic and gastric lipase is orlistat. According to BCS, orlistat is in category II and demonstrates poor oral discretion due to low melting. Natural gums were employed as the leads in this study's microwave-induced diffusion (MID) method to boost the melting and oral availability of orlistat [11-15].

The most popular drug administration method is the oral route of administration. The bulk of pharmaceutical goods (drugs) that are sold are administered orally, and this nanocomposite tablet increases saturation solubility and, as a result, increases the rate of dissolving. Particle size decrease promotes dissolving property by increasing surface area. Nanosized refers to particles with a diameter between 100 and 1000 nm. Oral drug delivery systems are receiving attention as a result of ongoing developments in other drug delivery methods to improve clinical effectiveness and patient compliance. From a pharmacological perspective, a variety of polymers are utilised to regulate medication release from dosage forms. It is more desirable to employ natural polymers rather than synthetic ones. The primary reasons why natural polymers are employed are because they are widely accessible, affordable, nonreactive, capable of chemical modification, and perhaps compatible and degradable. These are widely used in the pharmaceutical business as a result of the invention of polymer-based orlistat nanocomposite [16,17].

Material and Methods

Materials

Orlistat obtained subsequently Zydus Cadila Healthcare Ltd., Knadaim, Goa. Acacia Gum, Gelatin Powder, then Tragacanth obtained from Loba chem. Xanthum Gum then Chitosan purchased from SDFCL, Mumbai. All other chemicals used of analytical grade.

Preformulation Study [18-21]

λ max of Olistat and construction of standard curve

To find the maximum, orlistat solution with concentrations ranging from 0.2 g/ml to 1.0 g/ml was scanned between 200 and 400 nm.

Compatibility studies by FTIR analysis

The medicine orlistat's physico-chemical compatibility with the formulation's Xanthum gum, gelatin powder, chitosan, acacia gum, and tragacanth were examined.

FORMULATION DEVELOPMENT

Preparation of Physical Mixture

Orlistat was simply blended in a 1:1 to 1:4 ratio with polymers such as tragacanth, chitosan, gum acacia, and gelatin powder to create a physical combination. Orlistat was physically combined with various polymers to create the combinations.

The physical mixture of the medication and **gum acacia** was created and designated by the abbreviations OGAP1, OGAP2, OGAP3, and OGAP4 as indicated in the Table.

As indicated in the table, the physical mixtures of the medication and **chitosan** in the ratios of 1:1, 1:2, 1:3, and 1:4 were created and designated by the letters OCP1, OCP2, OCP3, and OCP4, respectively. Similar physical mixtures of the drug with **tragacanth, Xanthum gum,** and **gelatin** powder in the ratios of 1:1, 1:2, 1:3, and 1:4 was created and designated, respectively, by the letters OXP1, OXP2, OXP3, OXP4, and OTP1, OTP2, OTP3, OTP4, and OGP1, OGP2, OGP3, OGP4 (as indicated in the table).The physical mixture created to test the physical mixture's ability to increase solubility in relation to nanocomposites.

PREPARATION OF NANOBIOCOMPOSITES

A precisely weighed amount of orlistat was thoroughly mixed with each polymer to create the nanocomposites. Drug to polymer (w/w) ratios of 1:1 to 1:4 was extracted during preparation by maintaining a steady mixture volume. Orlistat and polymer dosages at various ratios were as per the table's indication. According to the table, OGAN1, OGAN2, OGAN3, and OGAN4 represent the ratios of the drug-to-gum acacia nanocomposites that were created. The formulation of the drug-chitosan nanocomposites in the ratios of 1:1, 1:2, 1:3, and 1:4 is shown in Table and is indicated by the letters OCN1, OCN2, OCN3, and OCN4 correspondingly Like this, nanocomposites of the drug with Xanthum Gum, Tragacanth, and Gelatin Powder were created and designated by the letters OXN1, OXN2, OXN3, OXN4, and OTN1, OTN2, OTN3, OTN4 in the table, respectively. To create a consistent slurry, 4 ml of water was added for every gramme of polymer in a mixture of the medication and polymer in various ratios. A predetermined (constant) volume of slurry was placed in a beaker and microwave-irradiated at a power of 556 W while being continuously stirred for 5 minutes (CATA-2R, Catalyst System). The procedure is illustrated graphically in Figure. To obtain the appropriate particle size of 80 to 250 m, the synthesised nanocomposites were ground in a pestle and mortar and sieve.

CHARACTERIZATION OF OPTIMIZED NANOCOMPOSITES

The NCs that demonstrated positive results from dissolution experiments and solubility were examined for further characterisation.

Fourier-transform infrared spectroscopy (FTIR)

FTIR analysis was used to describe the nanocomposites' optimised ratio. In a pellet press, the mixture of these nanocomposites and (KBr) potassium bromide of IR grade was compacted at 15 tonnes of pressure. The pellets were then screened using an FTIR spectrophotometer (Shimadzu 8400S), and the acquired spectra of optimised nanocomposites were compared to those of the pure drug. The major peaks of the spectra of the optimised nanocomposites' spectra were seen to change. The FTIR ranges of nanocomposites are tabulated in the table.

Differential Scanning Calorimetry (DSC)

The ratio of optimised nanocomposites was studied using DCS. In a nitrogen environment, the sample was heated from room temperature to 200° at a rate of 10°C/min. The modifications made during the formulation

of nanocomposites and their impact on the solubility of drugs were investigated. DSC thermograms of optimised nanocomposites and pure drugs are depicted in the figures, respectively.

X-ray diffraction studies (XRD)
The crystallinity changes that occurred when orlistat was combined with polymer were measured using XRD on the optimised nanocomposites and orlistat. Then, the XRD pattern was captured using Cu-k radiation. The scanning range is therefore maintained between 10° and 80° of two degrees. The purpose of the XRD investigation was to quantify the changes in crystallinity that occurred when the medication was combined with the carriers.

Scanning electron microscopy (SEM)
Scanning electron microscopy was used to analyse the external surface morphology. SEM analysis was used to examine the precise particle structural characterizations and morphologies of pure drugs and nanocomposites. To verify the alterations integrated during the NCs creation, SEM was used to NCs that demonstrated the best results in the dissolution studies and solubility.

Transmission electron microscopy (TEM)
Transmission electron microscopy (TEM) was used on the Orlistat and optimised ratio of nanocomposites that produced the best results in solubility and dissolution testing to verify the development of embedded nanocrystals. Using TEM, the form and size of pure drug crystals dispersed in polymer were examined. With the help of a transmission electron microscope (TEM), the NCs' morphology was discovered.

In-vitro dissolution test
Orlistat and nanocomposites were subjected to an in-vitro powder dissolving test using 900 ml of pH 6.8 phosphate buffers on USP XXIV equipment II (Paddle). A precise drug dosage of powder (10 mg of orlistat) was added to the dissolving medium while the paddle was rotating at 75 rpm and the temperature was held at 37°C ± 0.5°C. A 5 ml sample was taken out every 0, 5, 10, 15, 20, 25, and 30 minutes. Approximately 5 ml of phosphate buffer solution (pH 6.8) must be replaced in the dissolution media in order to maintain the sink state. The samples were next filtered using a membrane filter before being subjected to spectrophotometric analysis at a wavelength of 205 nm. Figure and Table display the dissolving profiles of both pure drugs and nanocomposites.

Drug Content Analysis
To determine how much drug was integrated into the nanocomposites, the drug content was analysed. In 25 cc of methanol, the created nanocomposites were dissolved. The resulting solution was then filtered using a membrane filter (0.45) and subjected to UV-visible spectrophotometer analysis at wavelength 205 nm using methanol as a blank. The Table presents the results.

PREPARATION OF IMMEDIATE RELEASE TABLET

The Nanobiocomposite that exhibits the greatest increase in solubility and dissolution experiments is chosen for the creation of an immediate release tablet. For the creation of an instant release pill, a nanobiocomposite of orlistat and acacia (1:4) was chosen. The table below lists the ingredients and tablet composition. Every item is put through filter #60. The tablet was prepared using a 10 mm punch and the direct compression method.

Formulation batches
Table: Composition of IR Tablet of OGAN4

Sr.No.	Ingredient	F1	F2	F3	F4
1.	OGAN4	400	400	400	400
2.	Microcrystalline cellulose	50	50	65	65
3.	Sodium starch glycolate	30	40	30	40
4.	Magnesium stearate	3	3	3	3
5.	Talc	3	3	3	3

(All ingredients were in mg)

EVALUATION OF IMMEDIATE RELEASE TABLET

Precompression Evaluation
Angle of repose, Carr's index, and Hausner's ratio of tablet mixture were done during the precompression examination of an instant release tablet in accordance with USP 30 (2007).
Post compression Evaluation
The following test is included in the after-compression evaluation. Following USP 30 (2007), an evaluation of the product's hardness, weight fluctuation, friability, disintegration time, and drug content was conducted.

a. Weight Variation b. **Disintegration Test c.Friability d. Hardness**

ANIMAL ACTIVITY REGARDING ORLISTAT BNC's (IN-VIVO STUDIES)

Method
The rats were kept in a cage and subjected to a 12-hour light/dark cycle in a room with a temperature of 25°C and a relative humidity of 55 ± 10 %. The state of the environment and everything else was carefully observed. Four groups of six rats each were formed from the rats.

Grouping of Animal
Group I: Control (Distil Water)
Group II: Raw Orlistat API
Group III: Commercial product (Marketed Formulation)
Group IV: Selected Orlistat formulation (BNC's-OGAN4)
Rats of either sex (7 weeks old), weighing between 200 and 250 g, were taken.
The experimental groups utilized raw Orlistat, the commercial product, and a specific Orlistat formulation (BNC's), whereas the control group used nothing.
For five days, each experimental group was given 0.25 percent w/v HPMC aqueous solution containing Orlistat corresponding to 2.5 mg/kg body weight orally at 9 a.m. and 4 p.m.

The positive control group received 1 mL of DW orally as a comparison. The faces were collected after 5 days. The dry faces' fat was recovered. 2.5 g of dry faces samples were put into 50 mL conical tubes. Eight millilitres of propan-2-ol and five millilitres of cyclohexane were added to the tube, which was vortexed for two minutes. Five millilitres of cyclohexane were added, and the mixture was vigorously stirred for two minutes after that. 11 mL of DW were then added, and the mixture was vortexed for 2 minutes. Centrifugation was used to separate the phases for 10 min. at 2000 rpm. The supernatants were subsequently placed to a pear-shaped flask. For a second extraction, 20 mL of 10% (v/v) propan-2-ol in cyclohexane were vortexed for two minutes. After centrifugation, the cyclohexane phase was added to the original extract. The liquid was evaporated using a rotary evaporator, and the leftover material was then dried for an hour at 80°C in an oven. The residues were weighed and used to calculate the fat content in the faces (mg/g) based on the amount of fat that was left per unit weight of the dry faces.

STABILITY STUDY OF OPTIMIZED NANOCOMPOSITES

According to ICH requirements, an accelerated stability study was completed. The sample of improved nanocomposites was kept in a stability chamber at 75 ± 5% RH and 40 ± 2°C for three months. After 1, 2, and 3 months of a stability study, many characteristics including drug content, appearance, and in-vitro drug release were examined.

Result and Discussion
Reformulation Study
Preformulation study of Drug
Organoleptic Properties
Table represents the results obtained for the drug samples organoleptic characters such as colour, odour, and appearance.

Melting point of Orlistat
Table shows the Orlistat drug melting point.

Table: Melting point of Orlistat

Sample	Observed melting point	Reported melting point
Orlistat	46^0C	40-50^0C

Solubility

Orlistat was found to be soluble in methanol and chloroform and poorly soluble in water. Solubility of Orlistat were shown in Table.

Table: Solubility of Orlistat

Solvent	Observed solubility (mg/ml)	Reported solubility (mg/ml)
Water	0.028	0.05
Methanol	0.821	0.689

λmax of Olistat and construction of standard curve

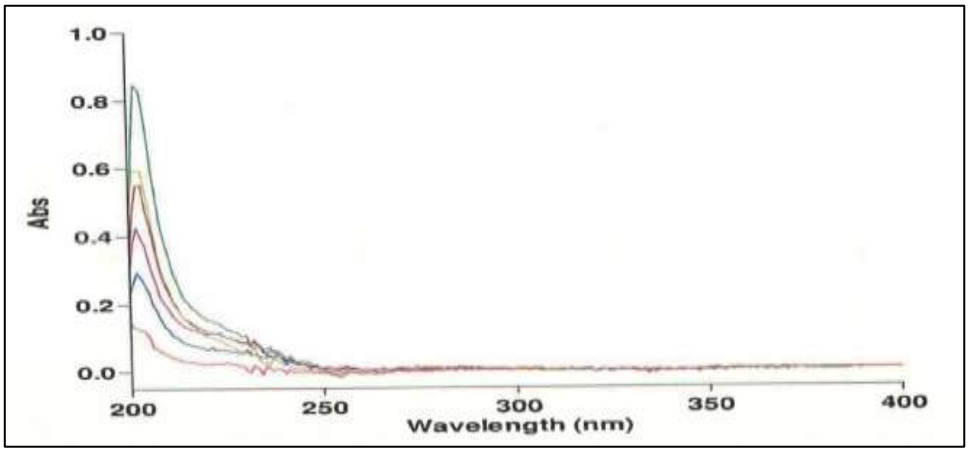

Fig. UV spectrum of orlistat

Chromatography

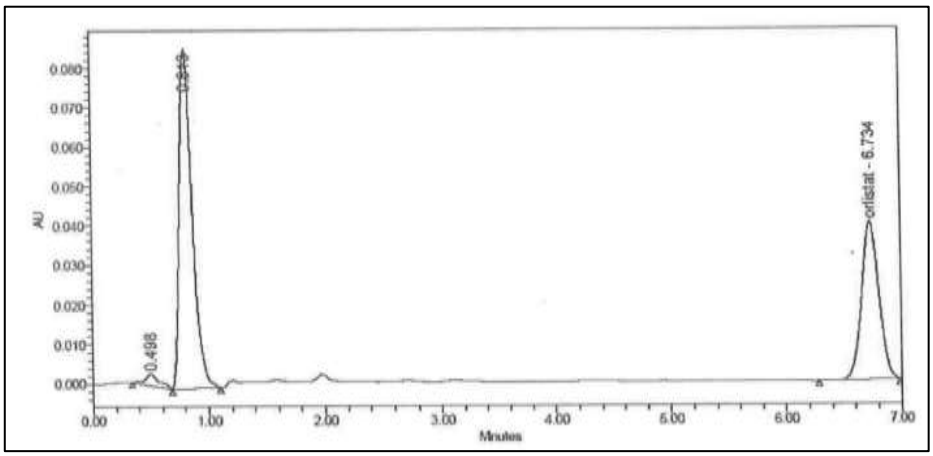

Figure: Chromatogram of orlistat solution in mobile phase for 120 µg/ml and 160 µg/ml

Table: Chromatogram peak descriptions for orlistat in methanol measured at 205 nm by HPLC method

Orlistat concentration (µg/ml)	Retention time	Average peak area ±SD	% Area	Pak height
40	6.744	107206±5.50	13.99	10343
80	6.742	210830±39.19	25.11	20286
120	6.738	319782±30.57	34.21	30829
160	6.734	420771±31.85	42.32	40932

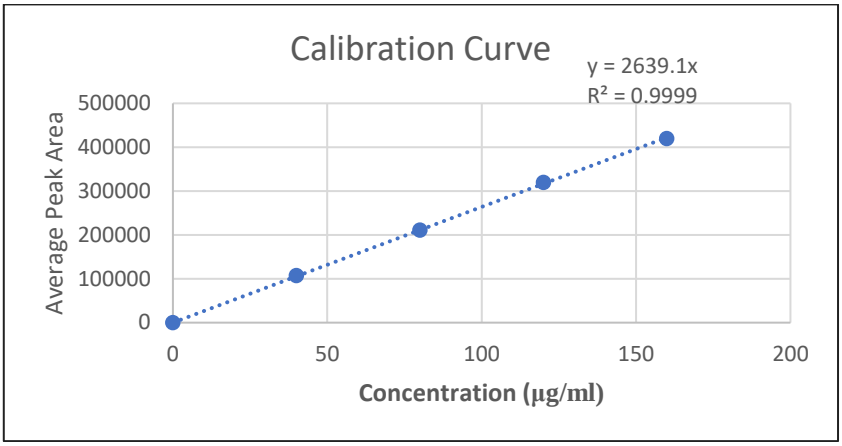

Fig. Standard curve of orlistat in methanol by HPLC method at 205 nm

Table: Regression coefficient values for orlistat calibration curve developed in methanol and mobile phase

Sr. No	Solvent system	Amax	r^2 values
1	Methanol	205	0.999
2	Mobile Phase (Acetonitrile: phosphoric acid, 90:10 v/v)	205	0.9991

Compatibility studies by FTIR analysis

FTIR experiments employing a Shimadzu, Japan IR-Spectrophotometer were used to determine the physical-chemical compatibility of the medicine orlistat with the formulation's constituents, Xanthum gum, gelatin powder, chitosan, acacia gum, and tragacanth. Figures and illustrate the recorded changes in the spectral heights and peak positions. And so forth. The Table had a list of the spectral descriptions.

Table: FTIR spectral descriptions of orlistat drug and its physical mixture with polymers

Functional group	Standard range (cm^{-1})	Orlistat (cm^{-1})	Excipients mixture(cm^{-1})	Orlistat and excipients mixture (cm^{-1})
C=O Stretching	1700-1725	1708.93	1722.43	1722.43
C-H Stretching in CH_2	2850-2960	2920.23	2926.01	2927.94
N-H Stretching	3500-3300	3332.99	3352.28	3334.94
C-H Deforming	875-895	871.82	872.23	872.12
C=C Aromatic stretching	1450-1600	1523.76	1456.1	1452.4

IR spectrum of Orlistat API Pellets

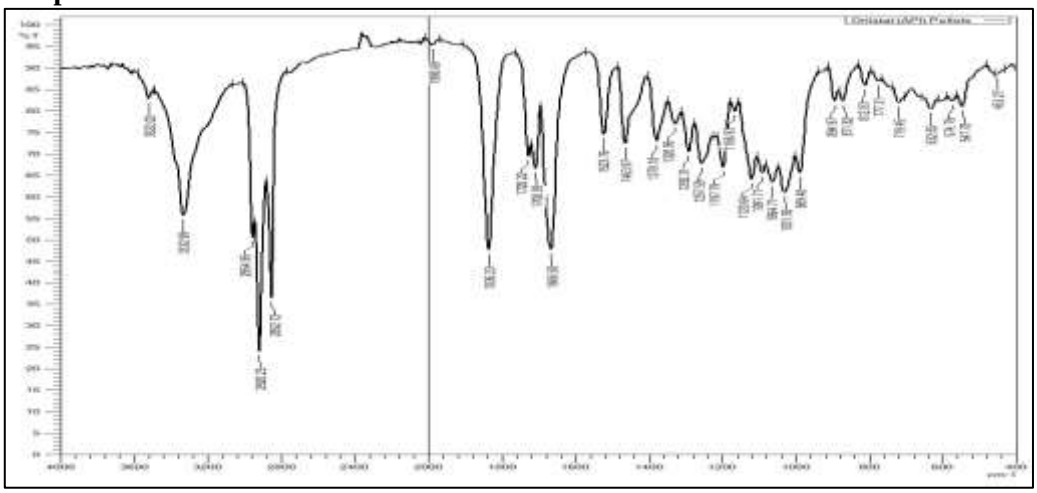

Fig. IR spectrum of Orlistat API Pellets

IR spectrum of Orlistat + excipients mixture

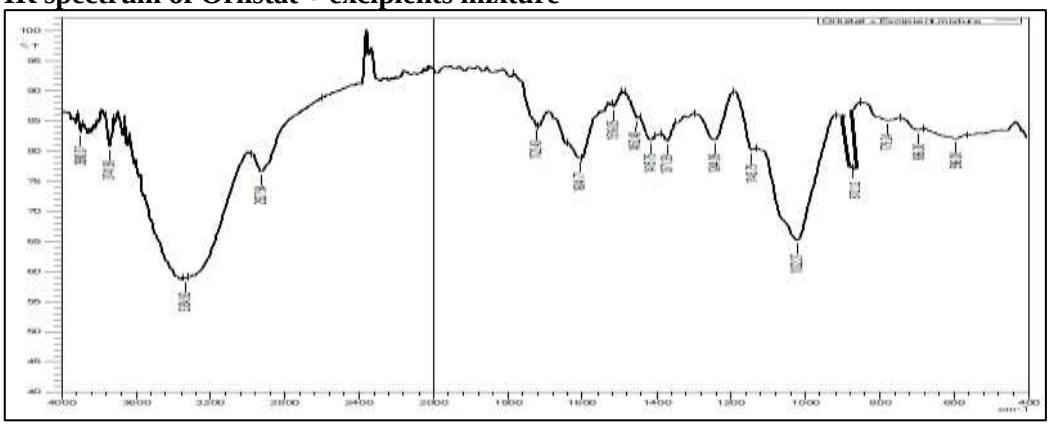

Fig. IR spectrum of Orlistat + Excipients mixture(Xanthum gum, gelatin powder, chitosan, acacia gum and tragacanth)

In vitro Drug release

Since solubility tests cannot forecast if a material's solubility grew better or worse, the in-vitro drug release was carried out. Drug solubility and dissolution are always adequately understood by the dissolution experiments of produced nanocomposites and drugs.

Table: Results of In-vitro dissolution test of pure Orlistat and developed optimised Nanocomposites

Time (min)	Pure Drug (%DR)	OGAN4 (%DR)	OCN4 (%DR)	OXN4 (%DR)	OTN4 (%DR)	OGN4 (%DR)
0	0	0	0	0	0	0
5	3.916 ± 0.49	31.81 ± 0.91	27.25 ± 0.56	21.37 ± 1.21	17.56 ± 0.64	18.37 ± 0.76
10	4.956 ±0 .85	44.45 ± 0.81	38.23 ± 0.76	37.37 ± 1.68	29.6 ± 1.28	27.37 ± 0.56
15	9.45 ± 0.16	62.06 ± 1.57	60.74 ± 0.87	51.54 ± 0.45	48.78 ± 1.54	48.84 ± 0.91
20	15.49 ± 0.66	71.98 ± 0.46	67.84 ± 1.39	59.37 ± 0.87	54.89 ± 0.78	55.74 ± 0.66
25	22.73 ± 1.87	79.59 ± 0.97	71.72 ± 1.64	62.32 ± 0.98	59.38 ± 1.49	59.51 ± 0.97
30	28.63 ± 0.84	**88.56 ± 0.43**	81.26 ± 0.97	69.78 ± 0.98	65.78 ± 0.75	62.74 ± 0.98

According to the findings of the dissolving analysis of the nanocomposites, all of the nanocomposites showed a noticeable improvement in the solubility rates when compared to the pure medication Orlistat. In comparison to pure orlistat, which released 28.63% of the medicine, OGAN4 had the greatest results among all nanocomposites, releasing 88.56% of the drug. Based on dissolution and solubility experiments, OGAN4 was subsequently chosen in order to develop the dosage form.

Fig. Dissolution profile of pure drug and optimised nanocomposites

Drug content analysis of nanocomposites

Analysing the drug content of the nanocomposites will reveal whether the drug is distributed uniformly throughout. It was found that between 66 and 92% of the medication can be included in the nanocomposites. Orlistat and acacia gum powder nanocomposites, OGAN4, demonstrate homogeneous drug dispersion. Analyses of drug content are displayed in Table.

Table: Drug content of Nanocomposites

Nanocomposites	OGAN4 (%DR)	OCN4 (%DR)	OXN4 (%DR)	OTN4 (%DR)	OGN4 (%DR)
Drug content	**92.73 ± 0.23**	82.81 ± 0.37	66.19 ± 0.24	75.78 ± 0.75	69.56 ± 0.34

The OGAN4 (Orlistat + Acacia gum powder) formulation of NCs was deemed the best among all developed formulations since it demonstrated the best solubility result at a 1:4 ratio. The investigation of the OGAN4 batch's drug content revealed a 92.73% concentration. The nanocomposites that displayed a greater increase in drug content release underwent batch optimisation.

CHARACTERIZATION OF OPTIMIZED NANOCOMPOSITES

Fourier-transform infrared spectroscopy (FTIR)

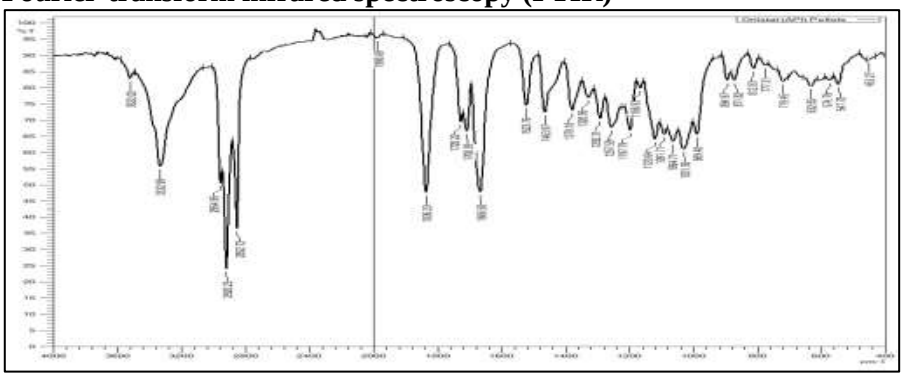

Fig. IR Spectrum of Orlistat API

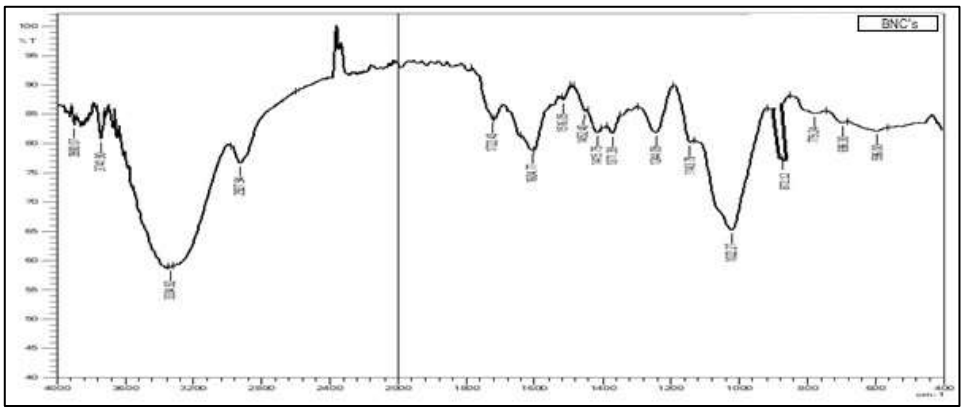

Fig. IR Spectrum of BNC's

In the FT-IR spectra of BNCs, the entire main peak visible in the pure drug is unaltered. After microwave irradiation of orlistat, FTIR measurements show that there is no chemical interaction between and polymer.

Differential Scanning Calorimetry (DSC)

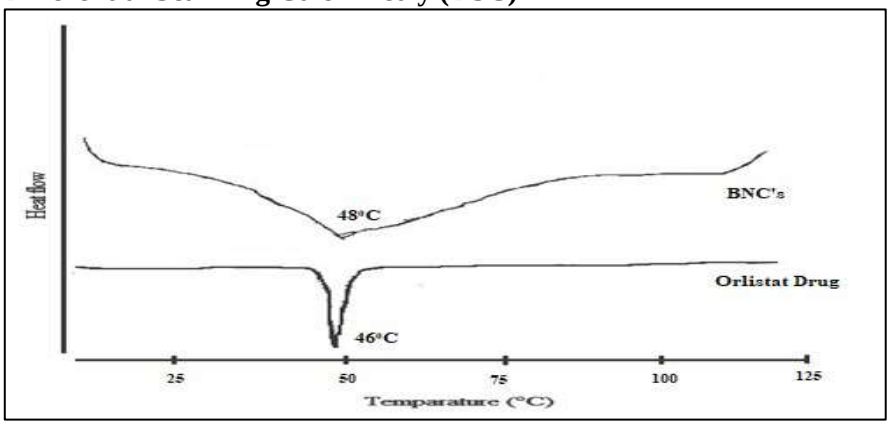

Fig. Thermogram of Orlistat API, Prepared BNC's

In the figure, pure drug (Orlistat) DSC thermograms and individual drug BNCs with Acacia are displayed. The melting point of orlistat at 46 0C is indicated by the DSC of pure orlistat, which has a prominent endothermic peak at that temperature. The DSC of manufactured BNCs revealed a modest temperature increase at 48 0C, which may be related to a decline in the drug's crystalline form. The drug's crystallinity is being reduced to a nanocrystalline state, as shown by a little change in melting point. The peak's enlargement suggests that much of the medication transforms into nanocrystalline form. It also concludes that drugs and polymers do not interact chemically. The medication is attached to the polymer as a result of the physical contact. These findings suggest that the melting point of crystalline nanoparticles decreases minutely as their crystal size decreases.

X-ray diffraction studies (XRD)

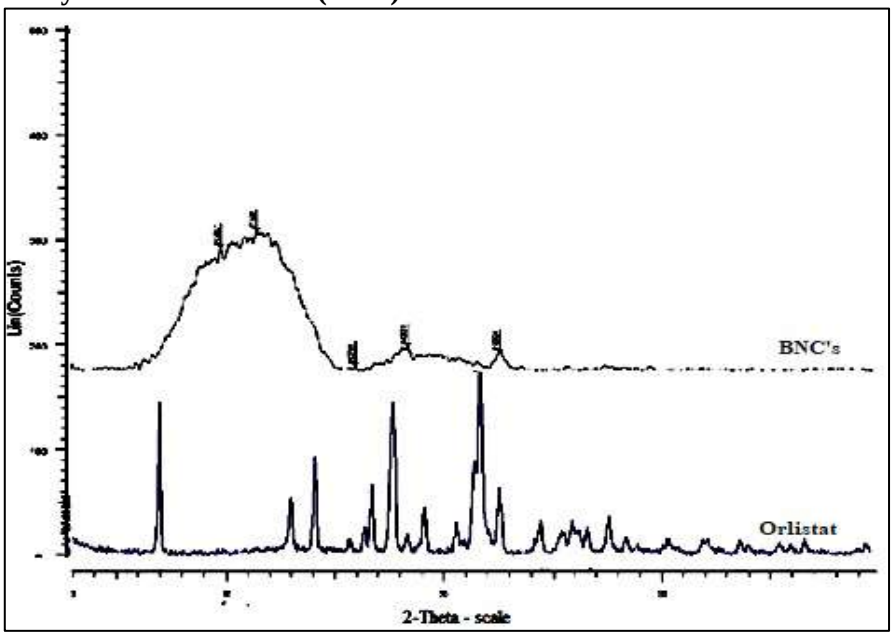

Fig. XRD study of Orlistat API, Prepared BNC's

To examine the physical condition of the drug and its BNCs, XRD was used. Pure orlistat has a crystalline peak in the range of 100 to 600 on the XRD pattern. The diffraction peaks at 5, 13, 14, 50, 17. 50, 19, 21, 24, 25. 50, 28, 30, 32, and 35 are recognisable. Orlistat's crystalline structure is indicated by its high peak at 22. While the BNC's XRD pattern exhibits diminished peak intensity as a result of lower crystallinity. Reduced medication size to the nano level may be the cause of the Bionanocomposites' decreased peak intensity.

Scanning electron microscopy (SEM)

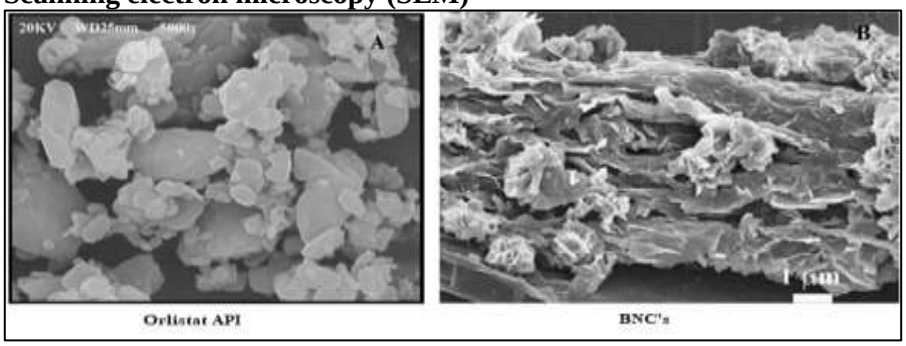

Fig. Image of SEM Orlistat API, Prepared BNC's

The surface morphology of the drug particles was examined by SEM investigations. Figure depicts the SEM of the Orlistat API and its BNCs. In contrast to the irregularly shaped and sized BNC particles, the orlistat particles had a spherical shape and surface. Figure amply demonstrates that Orlistat's spherical shape was entirely altered in BNCs exhibiting embedded Orlistat spheres in the matrix.

Transmission electron microscopy (TEM)

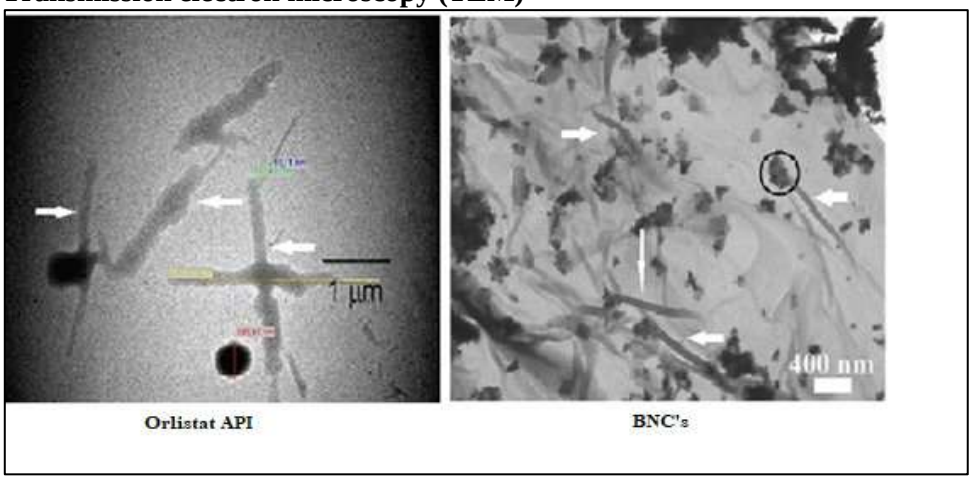

Fig. Images of TEM of Orlistat API, Prepared BNC's

The size of the medication particles contained in the orlistat was confirmed by TEM. Figure 1 displays TEM images of the medication orlistat in both its pure form and as bionanocomposites with acacia. The TEM results show that Orlistat is rapidly released from Bionanocomposites due to a loose network structure, which improves Orlistat's solubility and dissolving properties. The rod-shaped morphology of the Orlistat particles with a 1 m (1000 nm) diameter could clearly be seen. The surface black patches on BNCs may be shown by TEM to be made of the drug-dispersed acacia polymer. The looser structure of BNCs resulted in their reduced size, with an average diameter of 110 nm.

Evaluation of Immediate Release Tablet

Pre-Compression Evaluation Measurements were made of the Hausner's ratio of the NBC (OGAN4) formulation, Carr's index, and angle of repose. The table below shows the findings of pre-compression analyses of formulation combinations. The developed NBC formulation mixture has excellent flow characteristics, good compressibility, and a high Hausner's ratio, according to the results of the pre-compression investigation. Tablets may be made from the mixture with ease, and there are no flow issues. batch information for formulation.

Table: Formulation batches of IR tablets of OGAN4

Sr. No.	Ingredient	F1	F2	F3	F4
1	OGAN4	400	400	400	400
2	Microcrystalline cellulose	50	50	65	65
3	Sodium starch glycolate	30	40	30	40
4	Magnesium stearate	3	3	3	3
5	Talc	3	3	3	3

(All ingredients were in mg)

Table: Pre-Compression evaluation of IR tablet

Formulation	Angle of repose	Carr's index	Hausner's ratio
F1	33.69° ± 2.56	11.11 ± 1.15	1.125 ± 0.01
F2	32.39° ± 1.48	12.15 ± 0.50	1.136 ± 0.00
F3	32.66° ± 1.87	13.18 ± 0.61	1.110 ± 0.01
F4	33.82° ± 2.17	11.21 ± 0.75	1.121 ± 0.02

Data are means +/- SD, n=3

Post-Compression Evaluation

In order to evaluate the produced formulation post-compression, it was put through several tests, including ones for hardness, friability, content uniformity, disintegration time, and weight variance. All outcomes fall within the USP 30's permitted range.

Table: Post-Compression Evaluation of IR Tablet

Formulation	Weight variation (mg)	Hardness (kg)	% Friability	Drug content uniformity (%)	Disintegration time (s)
F1	486 ± 2.91	3.81 ±0.13	0.87± 0.06	99.2818± 0.61	69 ± 2.72
F2	498 ± 3.81	3.62 ± 0.21	0.75± 0.07	100.1813± 0.8	49 ± 3.15
F3	502 ± 4.29	3.51 ± 0.18	0.69± 0.01	98.1408± 0.57	78 ± 2.11
F4	504± 4.05	3.38 ± 0.11	0.55± 0.1	95.1739± 0.45	60 ± 3.21

(Mean ± SD) n=3

***In-vitro* dissolution study of IR tablet**

Tablet F2 was chosen for further characterization and an in vitro dissolving test was carried out to determine whether the medicine would release from the tablet as it had the shortest disintegration time out of the four tablet formulations. After 30 minutes, it was discovered that 91.45 ± 1.2 % of the medication had leaked.

Table: *In-Vitro* dissolution test of F2 tablet

Percent Drug Release (mean ± SD) n=3		
Time (min)	**F2 Tablet**	**Marketed tablet**
5	32.65 ± 2.2	27.45 ± 1.4
10	54.62 ± 2.1	45.65 ± 2.3
15	72.55 ± 1.2	63.43 ± 1.4
20	82.35 ± 1.1	70.34 ± 2.1
30	91.45 ± 1.2	75.65 ± 1.3
45	92.32 ± 1.3	76.34 ± 1.6
60	99.12 ± 1.4	78.65 ± 1.4

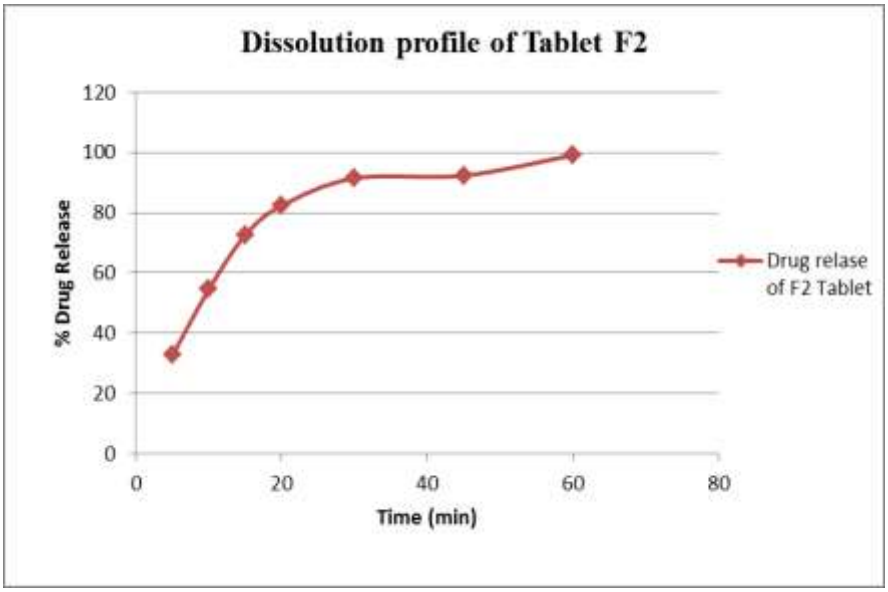

Fig. *In-vitro* dissolution test of F2 tablet

In-vivo study

Orlistat Fat Excretion via Faeces Studies

Day 5 after the fatty meal, raw Orlistat API, the commercial product, and the formulation from BNC. Control effects on the excretion of fat in rat faces. Rat faces in the control group's meal without orlistat had a fat content of 28.31 ± 4.21 mg/g. In comparison to the control group, the fat content in the faces increased significantly after administration of the commercial products raw Orlistat and BNCs to 44.61 5.97, and 44.61 ± 5.97, respectively. This meant that, as seen in the image, orlistat decreased lipase activity.

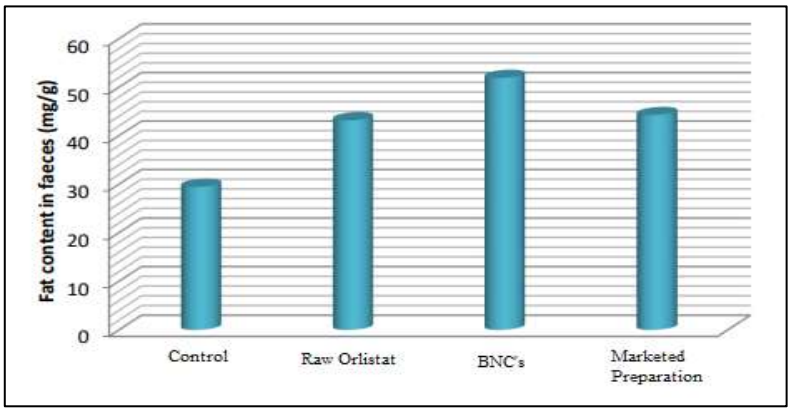

Figure: Effects of raw Orlistat, the marketed preparation and BNC's formulation on fat excretion in faeces of rat

STABILITY STUDY

To determine the impact of temperature and humidity on powder nanocomposites during storage period, stability research of the optimised ratio of orlistat (OGAN4) powder nanocomposites was conducted. Periodically, at 0 and 1, 2, and 3 months, nanocomposites were assessed for their drug content, appearance, and in-vitro drug release.
It is clear from the stability study results that the formulation shown in the table did not experience any significant changes in terms of drug content, appearance, or in-vitro drug release.

Table: Results of stability study

Duration (Months)	Appearance	Drug Content (%)	In vitro release (%)
0	Brownish fine powder	92.73 ± 0.23	88.56 ± 0.43
1	No change	91.46 ± 0.49	87.91 ± 0.31
2	No change	91.12 ± 0.54	87.64 ± 0.26
3	No change	91.52 ± 0.60	87.59 ± 0.33

Conclusion

The results of this study showed that natural carriers, like gum acacia, can be used to increase the solubility and, consequently, the dissolution of drug content in NCs IR tablets produced using microwave technology. The best nanocomposites from among the created batches were discovered to be those made with Gum Acacia OGAN4 (Orlistat + Acacia Gum Powder). A 16-fold increase in drug solubility was combined with a notable improvement in formulation dissolution performance. The primary accomplishment of this study is the uniform distribution of medication in carrier in a nanocrystalline form in optimised nanocomposites IR tablet, which is sufficiently stable and simple to make. It may be concluded that weakly soluble BCS class II pharmaceuticals like orlistat can be successfully enhanced in terms of solubility, dissolution, and hence bioavailability using microwave-generated NCs IR tablets.

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