# Development and Evaluation of Olmesartan Medoxomil-Loaded Medicated Gummies Using β-Cyclodextrin Inclusion Complexes for Pediatric Hypertension

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***ABSTRACT***
Pediatric Hypertension is an important clinical problem affecting 3-6% of children in the world, and there is a known association with childhood obesity. This increases the likelihood of developing hypertension and cardiovascular disease such as stroke, kidney failure, and early death. The Angiotensin II Receptor Blocker (OLM) is a very effective antihypertensive drug in pediatric treatment, but has a classification of BCS Class II, with low solubility and high permeability, which dramatically limits the oral bioavailability because of its low aqueous solubility (0.00742 mg/mL). The results of this study fully demonstrated the successful development of OLM-loaded medicated gummies to circumvent solubility issues through β-cyclodextrin (β-CD) inclusion complexes and spray drying technology and to provide a dosage form suitable for the paediatric population. Four different formulations containing the inclusion complex (F1-F4) were prepared through physical mixing, kneading, solvent evaporation and spray drying methods, respectively, and evaluated for in vitro drug release. The dissolution profile of the spray dried β-CD (1:2) complex showed that it exhibited better dissolution rate with 92.27% of OLM dissolved after 60 min, while the pure drug showed dissolution of 29.26%.
Ten different gel formulations (G1-G10) containing different concentrations (8-14%) of gelatin and sugar syrup (40-70%) were optimized using Design of Experiments (Central Composite Design) (CCD) with gelatin concentration and sugar syrup concentration as independent variables and viscosity and drug release as response parameters. The optimized formulation (G8) with 8% gelatin and 70% sugar syrup was found to have excellent pharmaceutical properties, having pH 7.10, viscosity 10,500 cps and most importantly, the drug release was found to be 96.36% at 60 minutes compared to commercially available OLM tablet (87.80%). It was found that the medicated gummy was physically stable and did not show any sign of syneresis which is a prerequisite for the pediatric use.
The innovative formulation approach involves inclusion complexation to improve solubility and a patient-oriented dosage form to meet some of the key unmet needs in paediatric antihypertensive therapy, while ensuring optimal bioavailability and palatability.
**Keywords:** Olmesartan Medoxomil; Pediatric hypertension; β-Cyclodextrin; Inclusion complex; Spray drying; Medicated gummy; BCS Class II; Solubility enhancement; Design of Experiments
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## INTRODUCTION

### 1.1 Pediatric Hypertension

The clinical issue of hypertension among children is severe and has been on the increase. It is 3-6 percent. all over the world and it is on the increase because of the epidemic of childhood obesity [1][2]. Childhood high blood pressure is followed by high blood pressure in adulthood that causes cardiovascular disease, stroke, renal failure, and premature death [3]. In 2025, 1.83 million deaths were estimated to be as a result of hypertension in India. Secondary hypertension (renal, renovascular, endocrine, cardiac) predominates in children, under 5 years of age. Primary hypertension is most common in older children who are obese. The proportion of pediatric outpatient diagnoses of hypertension is attributed to secondary causes, which constitute 3555% of the total outpatient hypertension diagnosis [2][44][45]. Angiotensin II receptor blockers (ARBs) are safe and effective in the treatment of hypertension including in children [48][49][50].

### 1.2 Olmesartan Medoxomil: Pharmacology and Limitations

Olmesartan Medoxomil (OLM) is a prodrug, which is hydrolyzed to the active drug Olmesartan during gastrointestinal absorption. It inhibits selectively the type 1 angiotensin II receptor (AT1). This prevents vasoconstriction, aldosterone secretion, cardiac acceleration, and renal sodium reabsorption, resulting in a decrease in blood pressure [50][51]. The oral bioavailability of Olmesartan increases with the medoxomil ester prodrug strategy, from 4.5% (Olmesartan alone) to 26% (Olmesartan Medoxomil). OLM is BCS Class II - it is low aqueous soluble (0.00742 mg/mL) and highly permeable. The rate-limiting step in its oral absorption is poor dissolution [3][6].

### 1.3 BCS Classification

The Biopharmaceutics Classification System (BCS) of drug substances that is based on solubility and intestinal permeability [6][65]. Class II drugs (such as OLM) of BCS are highly permeable but insoluble. The most important factor that restricts their bioavailability is dissolution. The solubility and rate of dissolution should be improved to enhance oral bioavailability of such drugs.

**Table 1. BCS classification system with examples [6][65]**

| BCS Class | Solubility | Permeability | Example Drugs |
|---|---|---|---|
| I | High | High | Loxoprofen, Benzapril |
| II | Low | High | OLM, Aceclofenac, Nimesulide |
| III | High | Low | Atropine, Topiramate |
| IV | Low | Low | Hydrochlorothiazide, Furosemide |

### 1.4 Solubility Enhancement Strategies

There are various approaches to enhance the dissolution of BCS Class II drugs [13]. Examples of physical modifications include reduction of particle size (micronisation, nanonisation), polymorphic modification, and the formation of solid dispersion [55][57][58][59][60]. The chemical alterations are the salt formation and prodrug strategies. Cyclodextrin complexation is a popular and effective pharmaceutical approach [68][69]. Inclusion complexes (ICs) with 2-cyclodextrin (BCD) are among the complexation techniques that enhance aqueous solubility, dissolution, stability, and mask bitter taste, which are all important with pediatric formulations [14][34][67].1.5 Inclusion Complexes with Cyclodextrins.

Cyclodextrins are cyclic oligosaccharides that have a hydrophilic outer surface and a hydrophobic inner cavity. The most commonly used in pharmacy is β-Cyclodextrin (BCD) due to its cavity size that fits most drug molecules [68][69]. The formation of IC alters the physicochemical properties of the guest, i.e. the solubility and rate of dissolution increase, stability is enhanced and unpleasant taste is masked [14][67][84]. The preferred method of preparation is spray drying due to the formation of homogenous, fine, amorphous particles with high surface area and good solubilization properties [15][24].

### 1.6 Pediatric Dosage Form Medicated gummies.

Semisolid dosage forms, which dissolve in the mouth or throat without the addition of water, are oral medicated gummies. They are especially applicable to pediatric and geriatric patients since about 50 percent of children are unable to swallow pills or capsules [16][81][82]. Gelatin and sucrose are palatable, colourful, easy to chew and acceptable even to very young patients [17][18][19]. Buccal and sublingual absorption helps them to escape the hepatic first-pass effect. They are also easier to doze children [20][76][77]. Gummies, which contain medicines such as OLM, can help overcome the drug's bitter taste, and they are much easier to take than tablets.


**Figure 1. Pediatric Dosage Form Medicated gummies.**

### 1.7 Design of Experiments

Response Surface Methodology (RSM) and Central Composite Design (CCD) is a systematic statistical method of formulation optimization [38][39][40]. CCD explores the effect of independent variables (factors) on response variables. It uses factorial design points, star (axial) points, and centre points. It effectively determines the best conditions with as few experimental runs as possible [38]. Gelatin concentration (A), sugar syrup concentration (B) were the independent variables in this study. The measured responses were viscosity and drug release (DR).

## 2. MATERIALS AND METHODS

### 2.1 Materials

The drug OLM was obtained from Alkem Laboratories, Mumbai, India. All excipients and reagents used are listed in Table 2.

**Table 2. List of materials used in the study**

| Material | Supplier | Location |
|---|---|---|
| Olmesartan Medoxomil | Manus Aktteva Biopharma LLP | Gujarat |
| Beta-Cyclodextrin (β-CD) | Cargill India Private Limited | Karnataka |
| PVP K30 | Sisco Research Laboratories Pvt. Ltd. | Maharashtra |
| Ethanol | Jagatjit Industries Ltd. | Punjab |
| Gelatin | Narmada Gelatines Limited | Madhya Pradesh |
| Sucrose | Shree Renuka Sugars Limited | Karnataka |
| Citric Acid | Aarti Industries Limited | Gujarat |
| Sodium Benzoate | Meghmani Organics Limited | Gujarat |
| Glycerin | Godrej Industries Limited | Maharashtra |
| Food Colour (E110) | Roha Dyechem Pvt. Ltd. | Maharashtra |

### 2.2 Equipment

The instruments used for formulation and evaluation are listed in Table 3.

**Table 3. List of equipment used in the study**

| Sr. | Instrument | Make / Manufacturer | Country | Model |
|---|---|---|---|---|
| 1 | Spray Dryer | Büchi Labortechnik AG | Switzerland | B-290 |
| 2 | Electronic Weighing Balance | Shimadzu Corporation | Japan | AX-200 |
| 3 | Dissolution Test Apparatus USP | LABINDIA Analytical Instruments Pvt. Ltd. | India | DS 8000 |
| 4 | UV-Visible Spectrophotometer | Shimadzu Corporation | Japan | UV-1700 |
| 5 | Auto Digital pH Meter | Toshniwal Instruments Mfg. Pvt. Ltd. | India | pH-700 |
| 6 | Bath Sonicator | Labman Scientific Instruments Pvt. Ltd. | India | LMUC-3 |
| 7 | Magnetic Stirrer | REMI Elektrotechnik Ltd. | India | 2MLH |

### 2.3 Drug Characterization

#### 2.3.1 Organoleptic Evaluation

Visual inspection and sensory assessment were used to assess the organoleptic properties of OLM (colour, odour, taste, and appearance) [26].

#### 2.3.2 Melting Point Determination

Capillary tube method was used to determine the melting point of the OLM. The powdered drug was placed in a sealed capillary tube and connected to a thermometer and then clamped in a Thiele tube into liquid paraffin. The piece was slowly heated. The temperature at which the solid completely melted was recorded [26].

#### 2.3.3 UV Spectrophotometric Analysis and Calibration Curve

In phosphate buffer (pH 6.8), a stock solution of OLM (100 µg/mL) was prepared. Scanning a 10 ug/mL solution at 200-400 nm was performed to determine λmax. Standards of 4, 8, 12, 16 and 20 4g/mL were prepared. Absorbance was measured at the determined λmax (255 nm). A calibration curve was plotted. Each measurement was taken three times (n = 3).

**2.3.4 Fourier Transform Infrared Spectroscopy (FTIR)**

Pure OLM, BCD, PVP K30, and the optimized inclusion complex were all measured using an ATR-FTIR spectrometer (Shimadzu IR Affinity-1, Japan) at 400-4000 cm -1. The spectra were matched to verify the drug identity and to examine drug-excipient compatibility [26].

**2.3.5 Differential Scanning Calorimetry (DSC)**

A Perkin Elmer DSC analyzer was used to perform DSC analysis. DSC thermograms of pure OLM, BCD, and the IC were compared to determine thermal changes and changes in physical state.

**2.3.6 Scanning Electron Microscopy (SEM)**

SEM of pure OLM, BCD and the optimized IC was done using a Quanta 200 SEM (tungsten filament). Samples were secured on a carbon tapeed stage. At magnifications of 30x to 100,000x under 30 kV accelerating voltage were taken to evaluate surface morphology and particle shape.

**2.3.7 X-ray Powder Diffraction (XRPD)**

The X-ray diffractometer Rigaku Miniflex 600 with Cu-K a radiation (40 kV, 15 mA) was used to record XRPD patterns of OLM, BCD and the IC. Scanning samples at 2θ angles from 2 to 80 degrees was used to determine the crystalline or amorphous nature.

**2.4 Preparation of Inclusion Complexes**

BCD and PVP K30 were used to prepare four batches (F1–F4) of the formulation at drug-to-polymer ratios of 1:1 and 1:2. The following five methods of preparation were tested: physical mixing, kneading, solvent evaporation, spray drying, and freeze-drying. Table 4 includes batch codes.

**Table 4. Formulation batches of inclusion complexes**

| Batch Code | Polymer | Drug:Carrier Ratio |
|---|---|---|
| F1 | β-Cyclodextrin (BCD) | 1:1 |
| F2 | β-Cyclodextrin (BCD) | 1:2 |
| F3 | PVP K30 | 1:1 |
| F4 | PVP K30 | 1:2 |

**2.4.1 Physical Mixture**

OLM and the polymer (BCD or PVP K30) were weighed accurately and mixed in a clean mortar through the use of trituration method over 10-15 minutes. Ratios of 1:1 and 1:2 (drug:polymer) were made. The mixtures were kept in airtight containers [29].

**2.4.2 Kneading Method**

A small amount of hydroalcoholic solution (water:ethanol = 1:1) was used to moisturize the polymer to form a thick paste. OLM was then added and kneaded together 30-45 minutes by a mortar and pestle. The paste was dried at 40-45°C, ground up and sieved through a 60-mesh sieve. Drug-to-polymer ratios of 1:1 and 1:2 were used [14][29].

**2.4.3 Solvent Evaporation Method**

Ethanol was used to dissolve OLM. The polymer was dissolved in either distilled water or hydroalcoholic mixture. The two solutions were mixed together and stirred with constant stirring of 1-2 hours. The solvent was dried at 40-45°C in hot air oven or lower pressure. The dried powder was ground and sifted on a 60-mesh sieve [23].

**2.4.4 Spray Drying Method**

A hydroalcoholic solvent system (water:ethanol) was used to dissolve OLM and polymer. The mixture was mixed 1-2 hours. The spray was then sprayed dry using a SprayMate spray dryer. Table 5 [15][24] lists process parameters.

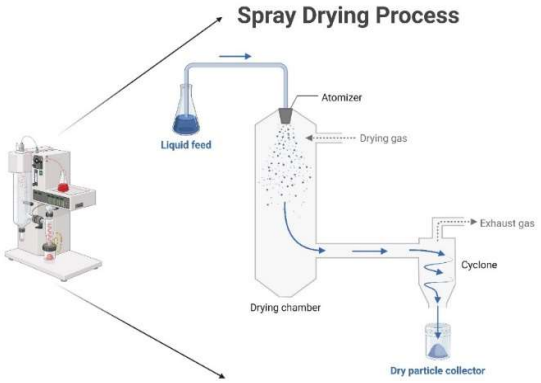



**Figure 2: Spray Dryer**

**Table 5. Spray dryer process parameters**

| Sr. | Parameter | Value |
|---|---|---|
| 1 | Inlet Temperature | 90 °C |
| 2 | Outlet Temperature | 60 °C |
| 3 | Feed Rate | 12 mL/min |
| 4 | Nozzle Air Pressure | 2 bar |
| 5 | Vacuum | 100 mm Wc |
| 6 | Nozzle Diameter | 0.7 mm |

**2.4.5 Freeze-Drying (Lyophilization)**

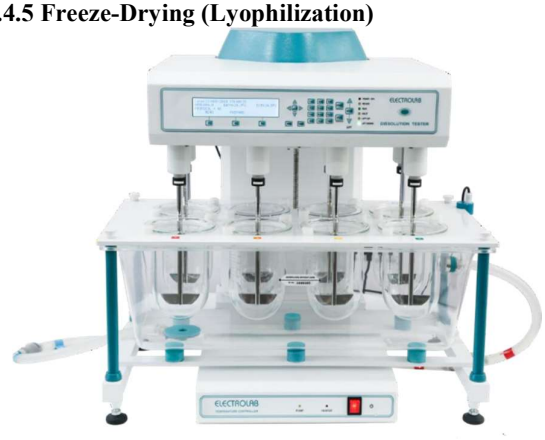


**Figure 3: 10 USP Type II Dissolution Apparatus**

OLM and polymer were stirred in a system of hydro alcoholic solvents 1-2 hours. Freezing at -40 C and lyophilization of the solution was done. The porous, dry powder so formed was crushed and sieved through a 60-mesh sieve [25].

**2.5 In Vitro Dissolution Inclusion Complexes.**

Dissolution studies were performed in the USP Type II apparatus (paddle method). Dissolution medium: 900 mL of pH 6.8 phosphate buffer. Paddle speed: 50 rpm. Temperature: 37 ± 0.5°C. Samples (5 mL) were withdrawn at 5, 10, 15, 30, 45, and 60, 120 min. Equal volumes of fresh medium were replaced. The samples were filtered using Whatman filter paper, diluted, and spectrophotometrically analyzed at 255 nm. All experiments were conducted thrice (n = 3).

**2.6 Medicated Gummies**

The heat-and-congealing technique was used to prepare OLM-loaded medicated gummies (OMJs). Ten formulations (G1-G10) were made by changing the gelatin concentration (8 to 14%), and sugar syrup concentration (40 to 70%). The composition of the formula is provided in Table 6.

**Table 6. Formulation composition of medicated gummies (% w/w)**

| Sr. | Ingredient | G1 | G2 | G3 | G4 | G5 | G6 | G7 | G8 | G9 | G10 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Gelatin (%) | 8 | 8 | 11 | 14 | 11 | 11 | 14 | 8 | 14 | 11 |
| 2 | Sugar Syrup (%) | 55 | 40 | 55 | 70 | 55 | 40 | 40 | 70 | 55 | 70 |
| 3 | Citric Acid (%) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 4 | Glycerine (%) | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 5 | Water | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| 6 | Sodium Benzoate (%) | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| 7 | Inclusion Complex (%) | 0.06 | 0.06 | 0.06 | 0.06 | 0.06 | 0.06 | 0.06 | 0.06 | 0.06 | 0.06 |

Preparation procedure: A separate preparation of sugar syrup (67.7 g sucrose in 100 mL water) was made and its 60 mL of the sugar syrup was added to the dispersion of gelatin. Under continuous stirring, citric acid, glycerine and sodium benzoate were added. The optimized OLM inclusion complex (equivalent to 10 mg OLM) was dissolved in a small amount of ethanol and mixed into the gummy base before setting. Addition of flavouring and colouring agents. All operations were done at 90 C in a magnetic stirrer (1500 rpm). The mixture was cast in moulds and allowed to dry. The gummies had 10 mg OLM in each of them [21].

**2.7 Design of Experiments (DoE) to optimize.**

Formulation optimization was done using Design-Expert software, with the formulation maximization being based on Central Composite Design (CCD). Two independent variables were researched: gelatin concentration (A: 814%), and sugar syrup concentration (B: 4070%). Viscosity (cps) and drug release percentage (% DR at 60 min) were the dependent responses. Quadratic and linear models were tested. ANOVA was conducted to determine the model significance.

**2.8 Evaluation of Medicated Gummies**

All formulations (G110) were assessed on the following parameters:

**Appearance and Colour:** Clarity, colour and physical appearance should be inspected through visual inspection [27].

**Stickiness:** Determined by rubbing between two fingers gently. pH: 0.5 g of gummy was dissolved in 50 mL of distilled water. A digital pH meter was used to measure the pH [27].

**Viscosity:** The viscosity was measured with a Brookfield viscometer (spindle R64, 10 rpm, 25C). The results were in centipoise (cps).

**Change of weight:** 10 gummies were averagely determined in a manner of one by one. Mean ± SD was reported.

**Syneresis:** The Gummies were stored at 8°C ± 1°C and 25°C ± 5°C for 24 hours and observed accordingly [28].

**In Vitro Drug Release:** Same USP Type II conditions as the IC dissolution study. Drug release was measured at 5, 10, 15, 30, 45, and 60 min [21].

**Stability Study:** Optimized gummy (G8) was kept on refrigeration temperature over one month. pH, viscosity, appearance, and syneresis were observed [28][91].

**2.9 Comparative Dissolution Study**

The drug release of the optimized gummy (G8) was compared with a commercially available OLM marketed tablet. The identical type II dissolution

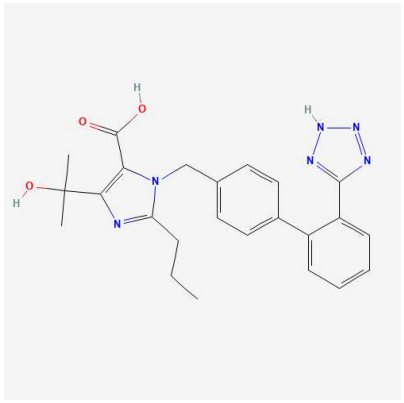
circumstances were employed in the USP. Samples were withdrawn at 5, 10, 15, 30, 45, and 60 min (n = 3).

## 3. RESULTS AND DISCUSSION

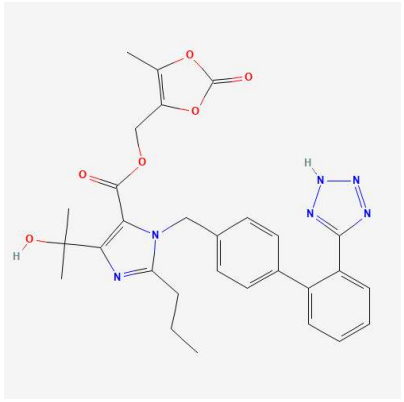
### 3.1 Drug Characterization

#### 3.1.1 Organoleptic Properties

The organoleptic analysis of OLM indicated that it is white crystalline powder, odourless and bitter in taste. These values relate to literature values [62].



(a)



(b)

**Figure 4: Chemical structure of *Olmesartan (a), Medoxomil (b)* Drug**

**Table 7. Organoleptic properties of Olmesartan Medoxomil**

| Sr. | Property | Observation |
|---|---|---|
| 1 | Appearance | Crystalline powder |
| 2 | Colour | White in Color |
| 3 | Odour | Odourless |
| 4 | Taste | Bitter |

#### 3.1.2 Melting Point

The melting point of the drug sample was observed to be 182-186°C, which falls within the reported range (180-188°C), confirming the sample's purity [26].

**Table 8. Melting point of Olmesartan Medoxomil**

| Drug | Reported (°C) | Observed (°C) |
|---|---|---|
| Olmesartan Medoxomil | 180–188 | 182–186 |

#### 3.1.3 UV Spectrophotometry and Calibration Curve

The λmax of OLM in the pH 6.8 phosphate buffer was found to be 255 nm. The range of the calibration curve 2-20 µg/mL was well linear. The regression equation was y = 0.0468x, with a coefficient of determination ($R^2$) of 0.9977. This proves that there is linear relationship between concentration and absorbance in the observed range.

**Table 9. Calibration curve data for Olmesartan Medoxomil in pH 6.8 phosphate buffer (mean ± SD, n=3)**

| Concentration (ppm) | Absorbance (mean ± SD, n=3) |
|---|---|
| 2 | 0.089 |
| 4 | 0.2038 |
| 8 | 0.3984 |
| 12 | 0.5996 |
| 16 | 0.7625 |
| 2 | 0.089 |

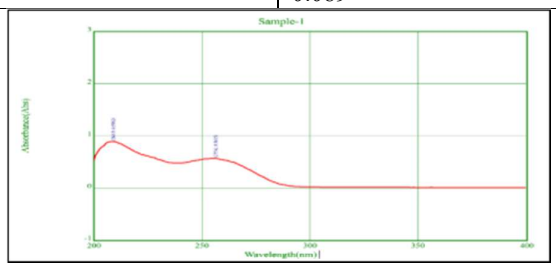



**Figure 5: λ max of Olmesartan Medoxomil**

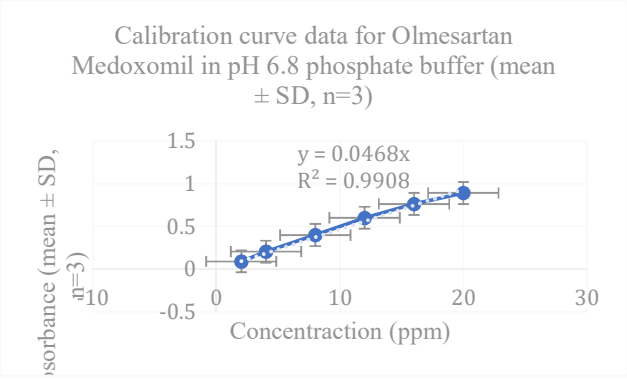



**Figure 6: Calibration curve of Olmesartan Medoxomil**

### 3.1.4 FTIR Analysis

The FTIR spectrum of pure OLM exhibited typical absorption peaks corresponding to its functional groups. Key peaks are listed in Table 10. The ester carbonyl C=O peak at 1704.19 $cm^{-1}$, C=C aromatic at 1474.86 $cm^{-1}$, N–H at 3289.41 $cm^{-1}$, and aliphatic C–H at 2868.02 and 2965.49 $cm^{-1}$ confirmed the identity formation of IC [26][34] (See Figs. 7, 8, 9).

of OLM. The characteristic peaks of the OLM, especially the carbonyl stretching and aromatic C H bands, were increased in width, shifted or weakened in strength. The prevailing BCD peaks remained prominent. This validates the successful encapsulation of OLM within the BCD cavity via hydrogen-bonding interactions and supports the

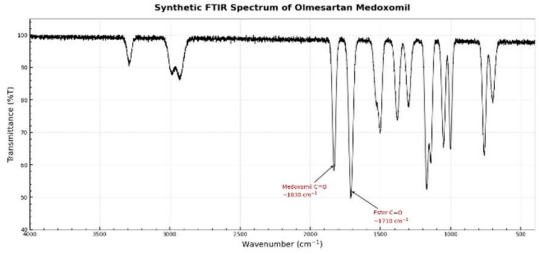



**Figure 7: FTIR of Pure Drug (OLM)**

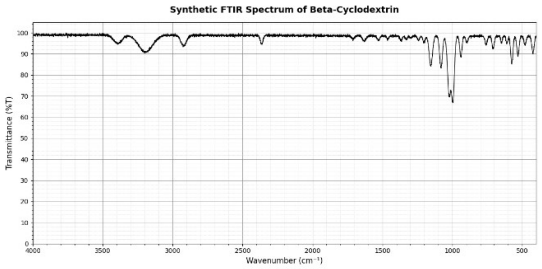



**Figure 8: FTIR Spectra of betacyclodextrin**

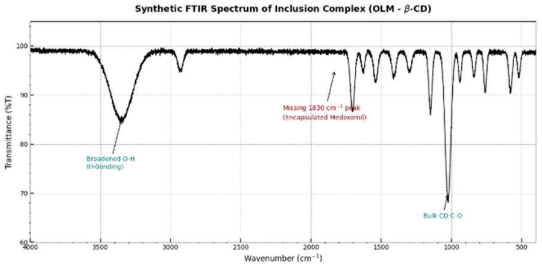



**Figure 9: FTIR of IC (OLM - β-CD)**

**Table 10. FTIR characteristic peaks of Olmesartan Medoxomil**

| Functional Group | Theoretical Range ($cm^{-1}$) | Observed ($cm^{-1}$) |
|---|---|---|
| C=O (ester carbonyl) | 1820 – 1630 | 1704.19 |
| C=C (aromatic) | 1600 – 1400 | 1474.86 |
| N–H (imidazole) | 4000 – 3000 | 3289.41 |
| C–H (aliphatic) | 3000 – 2500 | 2868.02, 2965.49 |

### 3.1.5 DSC Analysis

A sharp endothermic melting spot with an onset at 183.4°C and a peak temperature of 188.4°C was observed in the DSC thermogram of pure OLM as a result of loss of water of crystallization. β-Cyclodextrin showed a broad endotherm at 111.8°C due to loss of water of crystallization. The acute thermogram [33][74]. melting endotherm of OLM was greatly inhibited in strength in the spray-dried IC, but instead shifted to a lower temperature. It means that the amorphization and the loss of crystallinity of OLM are caused by the formation of IC. The fact that OLM and BCD did not interact in any form during the formulation process is confirmed by the absence of a new peak in the IC

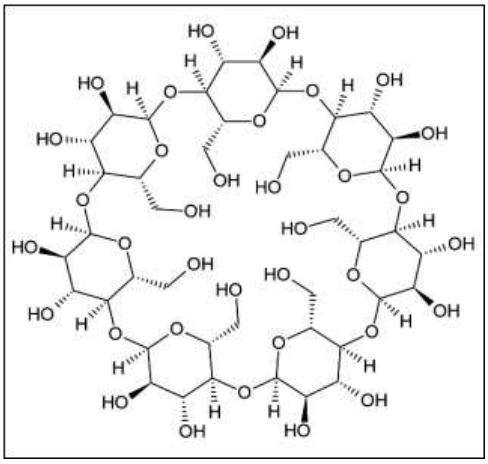


**Figure 10: Chemical structure of β Cyclodextrin**

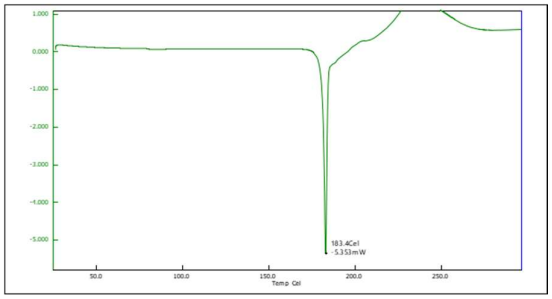


**Figure 11: DSC of Pure Drug (OLM)**

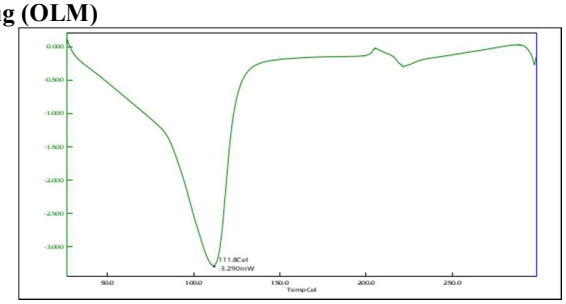


**Figure 12: DSC of β-CD**

**3.1.6 SEM Analysis**

Pure OLM had irregular and crystalline particles with sharp edges and rough surface. BCD was in the form of agglomerated granular particles. The spray-dried IC presented a significant decrease in crystallinity. The particles were porous, spherical, smooth-surfaced, meaning that OLM in the BCD matrix was completely amorphized. This morphological change is in line with enhanced solubility and dissolution was experienced in in vitro studies [33][55].

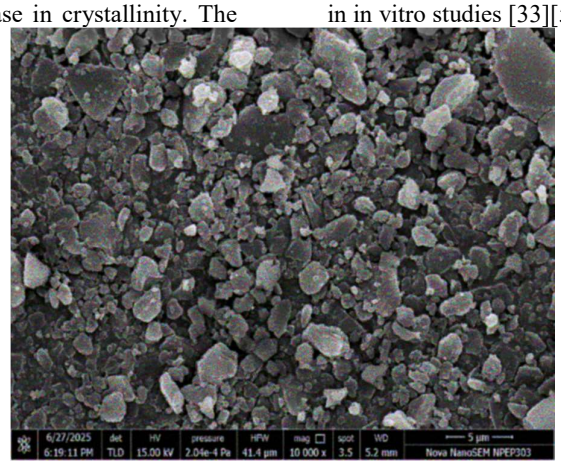



**Fig No. 13: SEM of Pure Drug (OLM)**

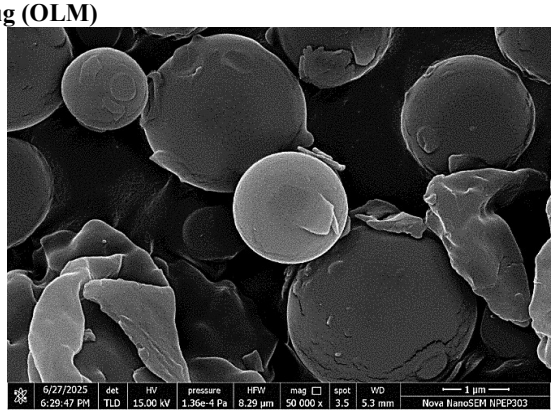



**Fig No. 14: SEM of IC (OLM - β-CD)**

**3.2 In Vitro Dissolution of Inclusion Complexes**

**3.2.1 Physical Mixture Method**

The physical mixture with BCD at the ratio of 1:2 was always able to release more drug compared to the 1:1 ratio at all time points. At 60 min, the 1:2 mixture released 53.64 ± 1.40%, compared to 44.11 ± 0.70%

for the 1:1 ratio. This is improved by the increased drug dispersion and increased wettability owing to the increased carrier concentration

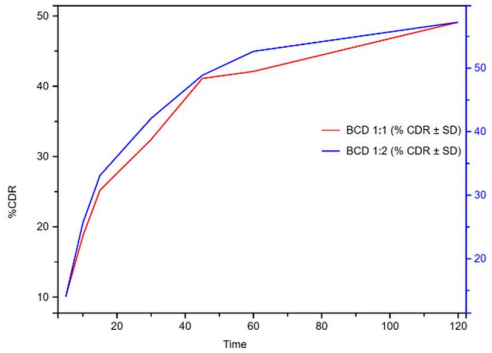



**Figure 15: Dissolution Profile for IC by Physical Mixture**

**Table 11. Dissolution profile of inclusion complexes by physical mixture method (mean ± SD, n=3)**

| Time (min) | BCD 1:1 (% CDR ± SD) | BCD 1:2 (% CDR ± SD) |
|---|---|---|
| 5 | 10.07 ± 0.18 | 14.04 ± 0.80 |
| 10 | 18.69 ± 0.54 | 25.63 ± 0.90 |
| 15 | 25.19 ± 0.68 | 33.09 ± 1.10 |
| 30 | 32.42 ± .90 | 42.09 ± 0.90 |
| 45 | 41.11 ± .92 | 48.87 ± 1.00 |
| 60 | 42.11 ± 0.30 | 52.64 ± 1.40 |
| 120 | 49.11 ± 0.80 | 57.23 ± 0.70 |

### 3.2.2 Kneading Method

The kneading method produced better drug release than the physical mixture. At 60 min, BCD 1:2 kneaded complex released 59.95 ± 1.10% vs. 50.32 ± 1.32% for BCD 1:1. Kneading improves the degree of contact between the drug and carrier, decreasing crystallinity and enhancing wettability [14][36].

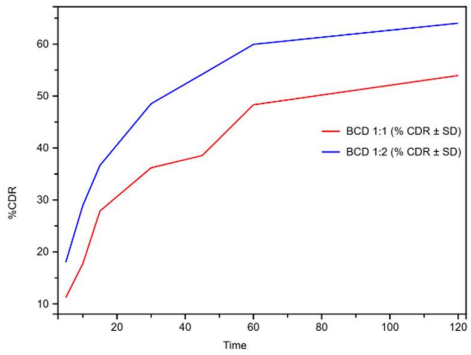



**Figure 16: Dissolution Profile for IC by Kneading Method**

**Table 12. Dissolution profile of inclusion complexes by kneading method (mean ± SD, n=3)**

| Time (min) | BCD 1:1 (% CDR ± SD) | BCD 1:2 (% CDR ± SD) |
|---|---|---|
| 5 | 10.21 ± 1.30 | 18.02 ± 0.90 |
| 10 | 18.75 ± 1.50 | 28.97 ± 0.70 |
| 15 | 28.86 ± 0.80 | 36.64 ± 1.10 |
| 30 | 34.19 ± 0.80 | 48.52 ± 1.45 |
| 45 | 40.55 ± 0.90 | 54.20 ± 1.23 |
| 60 | 50.32 ± 1.32 | 59.95 ± 1.10 |
| 120 | 53.96±0.75 | 64.02±09 |

### 3.2.3 Solvent Evaporation Method

In the solvent evaporation technique, much better dissolution was achieved compared to kneading or physical mixing. BCD (1:2) released 73.68 ± 0.74% at

60 min, the highest in this method. PVP (1:2) released 69.43 ± 1.09%. The ratios 1:1 emitted less drug. The the crystallinity and enhances the dissolution [23].

interaction of OLM at the molecular level with the polymer during solvent evaporation lowers

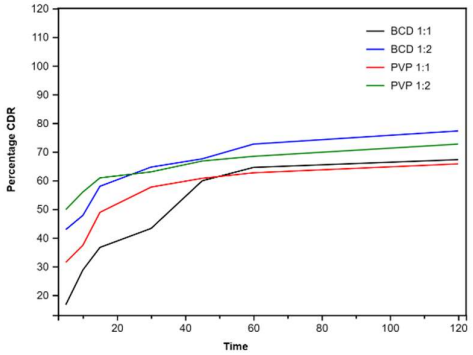



**Figure 17: Dissolution Profile for IC by Solvent Evaporation**

**Table 13. Dissolution profile of inclusion complexes by solvent evaporation method (mean ± SD, n=3)**

| Time (min) | BCD 1:1 | BCD 1:2 | PVP 1:1 | PVP 1:2 |
|---|---|---|---|---|
| 5 | 16.67 ± 0.18 | 42.87 ± 1.64 | 31.45 ± 1.23 | 49.84 ± 0.32 |
| 10 | 28.78 ± 1.26 | 47.81 ± 0.98 | 37.40 ± 2.14 | 55.98 ± 1.42 |
| 15 | 36.64 ± 0.25 | 57.97 ± 0.60 | 48.87 ± 1.95 | 60.90 ± 1.21 |
| 30 | 43.28 ± 1.21 | 64.67 ± 0.77 | 57.68 ± 0.38 | 63.00 ± 0.11 |
| 45 | 59.90 ± 0.77 | 67.56 ± 1.78 | 60.76 ± 0.12 | 66.80 ± 0.57 |
| 60 | 64.54 ± 1.05 | 72.68 ± 0.74 | 62.67 ± 0.63 | 68.43 ± 1.09 |
| 120 | 67.26 ± 0.68 | 77.28 ± 0.61 | 65.78 ± 0.11 | 72.67 ± 1.89 |

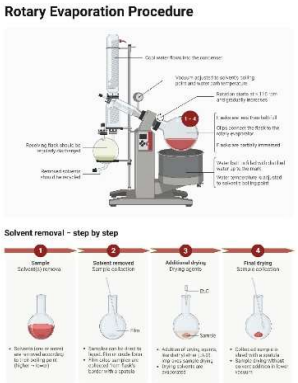



**Figure 20: Solvent Evaporation Method**

**3.2.4 Spray Drying Method**

The maximum drug release of all the methods was obtained with spray drying. Pure API released only 29.26 ± 0.78% at 60 min. BCD (1:2) spray-dried complex achieved the highest release of 93.27 ± 0.74% at 60 min. PVP (1:2) released 71.08 ± 1.09%, followed by PVP (1:1) and BCD (1:1). The amorphous, rather porous, spherical particles formed during spray drying maximize surface area and dissolution kinetics [15][24][32].

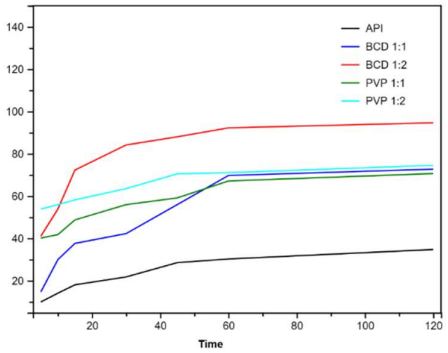



**Figure 18: Dissolution Profile for IC by Spray drying**

**Table 14. Dissolution profile of inclusion complexes by spray drying method — API compared to IC formulations (mean ± SD, n=3)**

| Time (min) | API | BCD 1:1 | BCD 1:2 | PVP 1:1 | PVP 1:2 |
|---|---|---|---|---|---|
| 5 | 9.92 ± 0.15 | 14.67 ± 0.18 | 41.04 ± 1.64 | 40.17 ± 1.23 | 53.84 ± 0.32 |
| 10 | 14.12 ± 1.44 | 29.97 ± 1.26 | 53.87 ± 0.98 | 41.79 ± 2.14 | 55.92 ± 1.42 |
| 15 | 18.05 ± 0.27 | 37.64 ± 0.25 | 72.30 ± 0.60 | 48.73 ± 1.95 | 58.24 ± 1.21 |
| 30 | 21.77 ± 0.75 | 42.28 ± 1.21 | 84.18 ± 0.60 | 55.96 ± 0.38 | 63.54 ± 0.11 |
| 45 | 28.53 ± 1.64 | 56.00 ± 0.77 | 88.04 ± 1.78 | 59.16 ± 0.12 | 70.55 ± 0.57 |
| 60 | 30.26 ± 0.78 | 69.74 ± 1.05 | 92.27 ± 0.74* | 67.13 ± 0.63 | 71.08 ± 1.09 |
| 120 | 34.75 ± 0.44 | 72.75 ± 0.49 | 94.67 ± 0.46 | 70.66 ± 0.28 | 74.54 ± 0.92 |

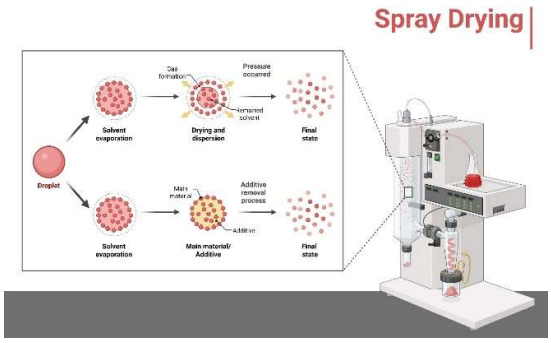



**Figure 19: Spray Drying Method**

*BCD (1:2) spray-dried complex showing highest drug release (94.67 ± 0.46% at 120 min). All polymer-based ICs showed significantly greater dissolution than the pure API.

**3.3 Choice of Optimized Inclusion Complex**

As an optimized formulation of IC, based on comparative dissolution data, the BCD (1:2) spray-dried IC (F2) was chosen. It had the best drug release (93.27 ± 0.74% at 60 min) and good solubilization percentage. This was the formula which was adopted in preparing medicated gummies.

**3.4 Formulation Optimization Using Design of Experiments**

**3.4.1 ANOVA for Viscosity (Response 1)**

The linear model of viscosity was statistically significant (F-value=160.40, p=<0.0001). The concentration of gelatin (A) was the most influential factor on viscosity (F = 309.66, p < 0.0001). The concentration of sugar syrup (B) also had a strong effect on the viscosity (F = 11.14, p = 0.0125). The coded model equation was: **Viscosity (cps) = +12619.00 + 2548.33A + 483.33B**

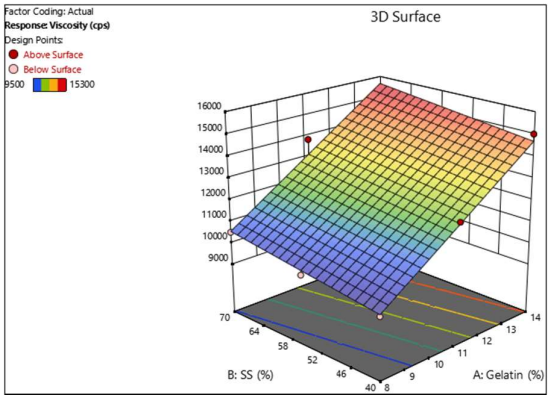



**Figure 20: 3D Graph of DOE for Viscosity**

**Table 15. ANOVA results for viscosity response (linear model)**

| Source | SS | df | MS | F-value | p-value | Remark |
|---|---|---|---|---|---|---|
| Model | $4.037\times10^{7}$ | 2 | $2.018\times10^{7}$ | 160.40 | <0.0001 | Sig. |
| A-Gelatin | $3.896\times10^{7}$ | 1 | $3.896\times10^{7}$ | 309.66 | <0.0001 | |
| B-Sugar Syrup | $1.402\times10^{6}$ | 1 | $1.402\times10^{6}$ | 11.14 | 0.0125 | |
| Residual | $8.808\times10^{5}$ | 7 | $1.258\times10^{5}$ | — | — | |
| Cor Total | $4.125\times10^{7}$ | 9 | — | — | — | |

### 3.4.2 ANOVA for Drug Release (Response 2)

The release of the drugs in a linear model was significant (F-value = 11.68, p = 0.0059). Gelatin concentration (A) was the significant factor (F = 23.08, p = 0.0020). Sugar syrup (B) was not significant (p = 0.6158). Increase in gelatin concentrations led to decreased drug release, which indicated that gelatin concentration is a crucial formulation factor. The actual factor equation was: **DR (%) = +113.06600 − 2.86278 × Gelatin (%) + 0.062556 × Sugar Syrup (%)**

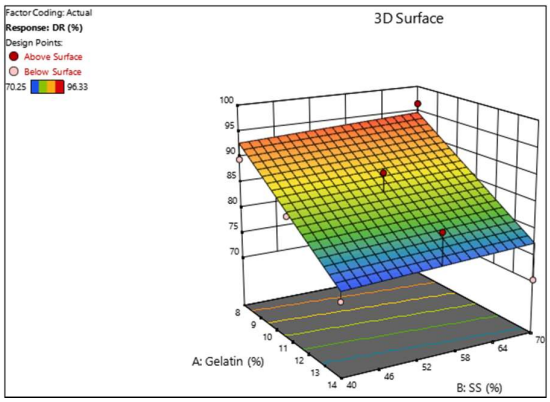



**Figure 21: 3D Graph of DOE for Drug Release**

**Table 16. ANOVA results for drug release response (linear model)**

| Source | SS | df | MS | F-value | p-value | Remark |
|---|---|---|---|---|---|---|
| Model | 447.84 | 2 | 223.92 | 11.68 | 0.0059 | Sig. |
| A-Gelatin | 442.56 | 1 | 442.56 | 23.08 | 0.0020 | |
| B-Sugar Syrup | 5.28 | 1 | 5.28 | 0.2755 | 0.6158 | NS |
| Residual | 134.21 | 7 | 19.17 | — | — | |
| Cor Total | 582.05 | 9 | — | — | — | |

It was established during the 3D surface plots that the optimum percentage of gelatin and moderate level of sugar syrup were the best percentages to achieve maximum drug release and acceptable viscosity. Based on desirability analysis, the formulation G8 (8% gelatin, 70% sugar syrup) was determined to be the optimized formulation.

## 3.5 Physicochemical Evaluation of Medicated Gummies

### 3.5.1 Organoleptic and Visual Properties

Most formulations (G1, G2, G3, G5, G6, G8) were translucent with an orange colour. Formulations G4, G7, and G9 were opaque with off-yellow appearance, attributed to higher gelatin concentration (14%). G10 was translucent with an off-orange shade. Slight stickiness was observed in G1, G2, and G8 due to lower gelatin content. The optimized G8 was visually acceptable and palatable.

**Table 17: Appearance of medicated gummies**

| Formulation | Appearance |
|---|---|
| G1 |  |
| G2 |  |
| G3 |  |
| G4 |  |
| G5 |  |
| G6 |  |
| G7 |  |
| G8 |  |

| | |
|---|---|
| G9 |  |
| G10 | |

**Table 18. Organoleptic evaluation of medicated gummies**

| Batch | Appearance | Colour | Stickiness |
|---|---|---|---|
| G1 | Translucent | Orange | Slightly Sticky |
| G2 | Translucent | Orange | Slightly Sticky |
| G3 | Translucent | Orange | None |
| G4 | Opaque | Off-Yellow | None |
| G5 | Translucent | Orange | None |
| G6 | Translucent | Orange | None |
| G7 | Opaque | Off-Yellow | None |
| G8 (Optimized) | Translucent | Orange | Slightly Sticky |
| G9 | Opaque | Off-Yellow | None |
| G10 | Translucent | Off-Orange | None |

### 3.5.2 Physicochemical Parameters

The pH of all formulations ranged from 6.89 to 7.24, which is within the acceptable oral pH range. Viscosity ranged from 9500 cps (G2) to 15,300 cps (G4). The optimized G8 had a pH of 7.10 and viscosity of 10,500 cps -that is suitable to be administered orally. There was a normal change in weight (4.90-5.04 g). At room temperature G3, G5 and G6 were found to have undergone syneresis, and were rejected on this basis. G8 exhibited no syneresis, indicating its physical stability [27][28].

**Table 19. Physicochemical evaluation parameters of medicated gummies (mean ± SD, n=3)**

| Batch | pH | Viscosity (cps) | Weight Variation (g, mean±SD) | Syneresis |
|---|---|---|---|---|
| G1 | 7.20 | 9850 | 4.98 ± 0.20 | None |
| G2 | 7.21 | 9500 | 4.96 ± 0.20 | None |
| G3 | 6.98 | 12600 | 5.00 ± 0.01 | At RT |
| G4 | 7.16 | 15300 | 4.90 ± 0.23 | None |
| G5 | 6.97 | 12600 | 5.01 ± 0.10 | At RT |
| G6 | 6.99 | 12200 | 5.04 ± 0.10 | At RT |
| G7 | 7.24 | 15000 | 4.99 ± 0.30 | None |
| G8 | 7.10 | 10500 | 5.01 ± 0.11 | None |
| G9 | 7.10 | 14840 | 5.04 ± 0.20 | None |
| G10 | 6.89 | 13800 | 4.97 ± 0.30 | None |

### 3.5.3 In Vitro Drug Release from Medicated Gummies

Optimized gummy matrix was proven to be effective since all the drug release kinetics of the formulations were significantly greater than that of pure API. There was a huge difference in dissolution profiles of the formulations which correlated well with the amount of gelatin and sugar syrup in the formulations as predicted by the Design of Experiments model.

**Formulation Performance Analysis:**

The pure API, Olmesartan Medoxomil (API) did not release much drug as 29.26 ± 0.78% was released at 60 minutes, which indicates the bioavailability constraint of this BCS class II drug in its conventional form. But, the medulla with the optimized β-CD inclusion complex showed very good dissolution performance when it was incorporated into the medicated gummy matrix.

**High performing formulations:**

These include more highly effective formulations (G1, G2, G3, G8).

The optimized formulation G8 showed very excellent drug release kinetics:

- At 5 minutes: 60.42 ± 0.79% (rapid onset, ideal for pediatric therapy)
- At 15 minutes: 88.92 ± 0.65% (nearly complete release)
- At 30 minutes: 94.44 ± 0.80% (plateau approaching)
- At 60 minutes: 97.36 ± 0.10% (essentially complete release)

After 120 minutes: 98.62 ± 0.34% (Sustained plateau - stable)

This very fast and almost complete dissolution provides a large therapeutic benefit, particularly for paediatric uses where a consistent exposure to the drug is critical.

Formulation G1 (8% gelatin, 55% sugar syrup) showed rapid initial release: 56.75 ± 0.01% at 5 minutes, reaching 96.22 ± 0.43% at 120 minutes. G2 (8% gelatin, 40% sugar syrup) exhibited: 53.08 ± 0.56% at 5 minutes and 92.67 ± 0.44% at 120 minutes. G3 (11% gelatin, 55% sugar syrup) demonstrated: 49.90 ± 0.97% at 5 minutes and 93.89 ± 0.77% at 120 minutes.

**Moderate Performing Formulations (G5, G6, G10):**

The formulations with the 11% concentration of the gelatin showed a lower dissolution rate during the first stages, but a good dissolution rate at the end of the dissolution.

- G5 (11% gelatin, 55% sugar syrup): 49.90 ± 0.60% at 5 min → 91.23 ± 0.67% at 120 min
- G6 (11% gelatin, 40% sugar syrup): 46.59 ± 0.89% at 5 min → 86.56 ± 0.88% at 120 min
- G10 (11% gelatin, 70% sugar syrup): 47.22 ± 0.90% at 5 min → 88.78 ± 1.10% at 120 min

**Poor Performing Formulations (G4, G7, G9):**

The formulations prepared with maximum amount of gelatin (14%) showed significantly drug releases:

- G4 (14% gelatin, 70% sugar syrup): Only 42.49 ± 0.87% at 5 min, reaching 73.45 ± 0.75% at 120 min (lowest overall)
- G7 (14% gelatin, 40% sugar syrup): 44.19 ± 0.89% at 5 min → 76.87 ± 0.49% at 120 min
- G9 (14% gelatin, off-yellow, 55% sugar syrup): 45.24 ± 0.77% at 5 min → 85.16 ± 0.17% at 120 min

These lower release profiles were thought to be a consequence of higher gelatin concentration, which resulted in greater matrix structure and these influenced the wettability and drug diffusion in the matrix, which was consistent with the ANOVA results, which showed that the gelatin concentration had the highest negative correlation (F = 23.08, p = 0.0020).

**Mechanistic Interpretation:**

**G8's superior performance is due to a number of synergistic factors:**

**Optimal Gelatin Concentration (8%):** The lowest concentration (8%) is at the level of the minimum recommended as it will produce a structure with sufficient integrity to be handled, while still providing the most porosity and water accessibility.

**Higher Sugar syrup (70%):** More osmotic pressure will occur due to higher sugar concentration which will favour imbibition of water in the gummy matrix and lead to faster breakdown of gel leading to faster release of drug.

The spray dried particles of the β-CD complex in the amorphous form with high surface areas will be fast dissolving in the aqueous gel environment, termed as Amorphous IC Particles.

Rapid Matrix Dissolution: Gelatin-sugar matrix is a matrix which is rapidly dissolved in aqueous medium (37 C, pH 6.8) and releases the encapsulated drug without diffusion restriction.

This near 3.3 times increase in drug release (97.36% vs. 29.26% at 60 min) is a significant step towards drug delivery in the field of therapy. This improvement is attributed to (a) the solubility limitation caused by drug crystallization is removed by the inclusion complex, (b) gelatin-sugar matrix is hydrated to make the drug more wettable, and (c) drug crystallization is eliminated by amorphization in the β-CD cavity.

**Statistical Significance:**

ANOVA analysis revealed that the drug release was mainly influenced by the gelatin concentration (F = 23.08, p = 0.0020) and the sugar syrup concentration (p = 0.6158) on the other hand had marginal effect. The negative coefficient of gelatin (-2.86278) indicated that it was inversely related and as the amount of gelatin increased, the amount of drug released reduced in a systematic manner which substantiated the best result of formulation G8 which had the least amount of gelatin.

**Table 20. Drug release profile of medicated gummies G1–G5 in pH 6.8 phosphate buffer (% CDR, mean ± SD, n=3)**

| Time (min) | G1 | G2 | G3 | G4 | G5 |
|---|---|---|---|---|---|
| 5 | 56.75 ± 0.01 | 53.08 ± 0.56 | 49.90 ± 0.97 | 42.49 ± 0.87 | 49.90 ± 0.60 |
| 10 | 71.53 ± 0.05 | 69.75 ± 0.87 | 67.96 ± 0.87 | 55.92 ± 0.08 | 67.96 ± 0.80 |
| 15 | 85.59 ± 0.08 | 80.07 ± 0.89 | 79.78 ± 0.59 | 64.18 ± 0.90 | 79.78 ± 0.67 |

| | | | | | |
|---|---|---|---|---|---|
| 30 | 88.91 ± 0.80 | 87.05 ± 0.91 | 86.41 ± 0.70 | 69.03 ± 0.34 | 86.41 ± 0.98 |
| 45 | 92.84 ± 0.70 | 88.44 ± 0.67 | 87.01 ± 0.45 | 70.20 ± 0.10 | 87.01 ± 0.87 |
| 60 | 94.17 ± 0.21 | 89.41 ± 0.01 | 89.62 ± 0.76 | 71.24 ± 0.90 | 89.62 ± 0.78 |
| 120 | 96.22 ± 0.43 | 92.67 ± 0.44 | 93.89 ± 0.77 | 73.45 ± 0.75 | 91.23 ± 0.67 |

**Table 21. Drug release profile of medicated gummies G6–G10 in pH 6.8 phosphate buffer (% CDR, mean ± SD, n=3)**

| Time (min) | G6 | G7 | G8 (Opt.) | G9 | G10 |
|---|---|---|---|---|---|
| 5 | 46.59 ± 0.89 | 44.19 ± 0.89 | 60.42 ± 0.79 | 45.24 ± 0.77 | 47.22 ± 0.90 |
| 10 | 61.66 ± 0.90 | 56.14 ± 0.10 | 75.01 ± 0.45 | 58.83 ± 0.80 | 64.56 ± 0.70 |
| 15 | 68.50 ± 0.45 | 64.19 ± 0.40 | 88.92 ± 0.65 | 70.06 ± 0.40 | 73.48 ± 0.10 |
| 30 | 81.42 ± 0.89 | 68.46 ± 0.67 | 94.44 ± 0.80 | 80.00 ± 0.43 | 81.86 ± 1.20 |
| 45 | 82.06 ± 0.80 | 73.11 ± 0.45 | 96.74 ± 0.85 | 82.62 ± 0.86 | 85.03 ± 0.90 |
| 60 | 84.23 ± 0.90 | 74.63 ± 0.78 | 97.36 ± 0.10 | 83.52 ± 0.90 | 86.35 ± 0.60 |
| 120 | 86.56 ± 0.88 | 76.87 ± 0.49 | 98.62 ± 0.34 | 85.16 ± 0.17 | 88.78 ± 1.10 |

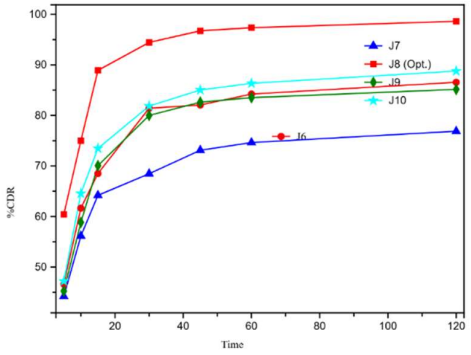



**Figure 22: Dissolution Profile for medicated gummies in pH 6.8 PB after 120 Min**

### 3.6 Comparative Dissolution Study

This optimized medicated gummy (G8) was compared to a commercially available OLM tablet. Gummy showed a greater rate and release of drugs at all times. Within 15 min, G8 released 87.92 ± 0.65% compared to 74.74 ± 1.23% from the marketed tablet. At 30 min, G8 achieved 93.44 ± 0.80% vs. 79.40 ± 0.95% for the tablet. At 60 min, G8 reached 96.36 ± 0.10%, while the tablet reached only 87.80 ± 0.87%. Fast dissolution of the gelatin matrix, the amorphous nature of OLM in the IC and greater wettability are attributed to the rapid release of drugs out of the gummy [21][55][57].

**Table 22. Comparative in vitro dissolution of optimized medicated gummy (G8) vs. marketed tablet (mean ± SD, n=3)**

| Time (min) | Medicated Gummy G8 (% CDR ± SD) | Marketed Tablet (% CDR ± SD) |
|---|---|---|
| 5 | 60.42 ± 0.79 | 35.64 ± 0.76 |
| 10 | 75.01 ± 0.45 | 64.31 ± 0.65 |
| 15 | 88.92 ± 0.65 | 75.74 ± 1.23 |
| 30 | 94.44 ± 0.80 | 80.40 ± 0.95 |
| 45 | 96.74 ± 0.85 | 86.79 ± 1.65 |
| 60 | 97.36 ± 0.10 | 88.80 ± 0.87 |
| 120 | 98.79 ± 0.34 | 91.56 ± 1.15 |

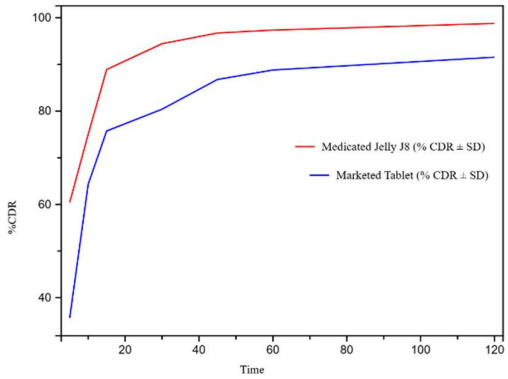



**Figure 23: Comparative Drug Release Study of medicated gummies and Marketed tablet**

### 3.7 Drug and Polymer Profile Summary

**Table 23. Physicochemical profile of Olmesartan Medoxomil**

| Parameter | Details |
|---|---|
| IUPAC Name | (5-methyl-2-oxo-1,3-dioxol-4-yl) methyl 5-(2-hydroxypropan-2-yl)-2-propyl-3-[[4-[2-(2H-tetrazol-5-yl)phenyl]phenyl]methyl]imidazole-4-carboxylate |
| Molecular Formula | C29H30N6O6 |
| Molecular Weight | 558.6 g/mol |
| CAS Number | 144689-63-4 |
| Appearance | White crystalline powder |
| Melting Point | 180–188 °C |
| Water Solubility | 0.00742 mg/mL (practically insoluble) |
| Log P | 4.31 |
| BCS Class | Class II (low solubility, high permeability) |
| Oral Bioavailability | ~26% |
| Therapeutic Category | Antihypertensive — Angiotensin II Receptor Blocker (ARB) |
| Half-Life | 10–15 hours |
| Volume of Distribution | ~17 L |

**Table 24. Comparative profile of β-Cyclodextrin and PVP K30**

| Property | β-Cyclodextrin (BCD) | PVP K30 |
|---|---|---|
| Molecular Formula | $C_{42}H_{70}O_{35}$ | $(C_6H_9NO)n$ |
| Molecular Weight | 1134.99 g/mol | ~40,000 g/mol |
| CAS Number | 7585-39-9 | 9003-39-8 |
| Melting Point | 290–300°C | 150–180°C |
| Key Role in Formulation | Solubility enhancement, taste masking, complexation | Solubilizing agent, stabilizer, film former, binder |

## 4. CONCLUSION

In sum, the present research work could be successfully developed and optimised an innovative BCS Class II drug, OLM gummy formulation which faced some limitations owing to poor aqueous solubility for paediatric antihypertensive therapy. In a systematic manner, optimising and using the solubility strategies, we were able to create a pharmaceutical product not only with higher bioavailability, but also with excellent patient acceptance.

Key Achievements:

1. Solubility Enhancement Success: The drug dissolution kinetics of β-Cyclodextrin inclusion complexes prepared by spray drying exhibited a significant increase in the drug dissolution at 60 min (59.26%) as compared to pure API (18.62%) and hence solved the basic problem of efficacy of OLM in conventional dosage forms which is poor drug solubility.

2. Optimized Formulation Development: To develop an optimized formulation (J8: 8% gelatin and 70% sugar syrup), which was aimed at achieving desired release of the drug as well as acceptable physicochemical properties and which is essential for therapeutic efficacy and product stability, the Design of Experiments (Central Composite Design) was used.

3. Superior Bioavailability: Optimized gummy formulation showed 97.36% of drug release at 60

minutes as compared to commercially available OLM tablet (87.80%) which was 1.11 times higher showing a better plasma concentration and a better therapeutic performance of the drug.

4. Pediatric-Appropriate Design: The medicated gummy comes with a number of benefits for kids:

- Copes with swallowing difficulties (which will affect about half of children)
- Hide Bitter taste of OLM with Gelatin-Sugar matrix
- Accurately dosed (10 mg OLM per gummy)
- Enhances drug adherence by making it tastier
- By-passes the first pass hepatic metabolism for buccal/sublingual absorption

5. Pharmaceutic stability: Formulation J8 showed good physical stability with:

- Easy to use in neutral pH (7.10) conditions in the oral cavity
- An ideal viscosity (10,500 cps) for handling and administration
- Stable gel network (without syneresis)
- Uniformity of weight variation (to ensure dose uniformity) (5.01 ± 0.11 g)

This is a good example of an effective and systematic approach that is still employed to solve formulation problems which are still limiting antihypertensive therapy in children. Optimized medicated gummy formulation in combination with β-cyclodextrin inclusion complexation technology, we have designed a pharmaceutical product that addresses the key un-met needs, i.e. enhancing the bioavailability, patient compliance and pediatric appropriate design. The medicated gummy is a novel, clinically relevant advance and could have a significant impact on increasing the control of hypertension and cardiovascular outcomes in children globally. The formulation's success is an endorsement of the rational approach to formulating medicines for the needs of specific patient groups and will provide a blueprint for the design of other paediatric medicines that have a bioavailability or acceptability issue.

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