Sesha Sai Durga Manyam *et al*, Int. Journal of Pharmaceutical Sciences & Medicine (IJPSM), Vol.8 Issue. 10, October- 2023, pg. 11-22

ISSN: 2519-9889
Impact Factor: 5.9

Formulation and Evaluation of Sustained Release Atorvastatin Tablets Using Natural Polymers, with a Focus on Okra Gum

Sesha Sai Durga Manyam[1]; Swetha Arumilli[2]; Prasanthi Pakalapati[3]; Prakash Nathaniel Kumar Sarella[4]

[1]Associate Professor, Aditya College of Pharmacy, Surampalem, saidurgapharmacy@gmail.com
[2]Associate Professor, Aditya College of Pharmacy, Surampalem, swetha.arumilli@gmail.com
[3]Associate Professor, Aditya College of Pharmacy, Surampalem, prashupharma@gmail.com
[4]Associate Professor, Aditya College of Pharmacy, Surampalem, sarellaprakash@acop.edu.in

DOI: 10.47760/ijpsm.2023.v08i10.003

Abstract

This research study presents the development and evaluation of sustained-release tablets of Atorvastatin using five distinct natural polymers, namely guar gum, xanthan gum, hibiscus gum, okra gum, and soya bean gum, at different drug-polymer ratios. The formulations underwent rigorous pre-compression and post-compression assessments to ensure their quality and efficacy. The utilization of natural polymers in drug formulations has gained significance due to their cost-effectiveness, biocompatibility, and eco-friendliness. In this study, we investigated the potential of these natural polymers to create sustained-release tablets, a vital need for long-term management of conditions like hypercholesterolemia. Atorvastatin, a BCS class-II drug, was chosen as the model drug for this study, as it plays a crucial role in managing cardiovascular diseases related to high blood pressure. The pre-compression tests ensured that the formulations met pharmacopoeial standards for characteristics such as bulk density, angle of repose, compressibility index, and Hausner's ratio. The post-compression studies confirmed that the tablets exhibited acceptable features, including hardness, friability, and weight variation. In vitro dissolution studies revealed that formulation F8, incorporating okra gum as the rate-retarding polymer, exhibited an impressive 98.5% drug release after 10 hours. This suggest that okra gum holds promise as a natural polymer for designing sustained-release drug formulations. Overall, this study provides valuable insights into the use of natural polymers for the controlled release of drugs, particularly Atorvastatin, and could pave the way for further research in this field.

Keywords: Atorvastatin, Sustained Release, Natural Polymers, Okra Gum, Drug Delivery.

1. Introduction

Cardiovascular diseases, including hypercholesterolemia, continue to be a leading cause of morbidity and mortality worldwide. Among the various therapeutic agents used to manage these conditions, Atorvastatin, a BCS class-II drug, has proven to be highly effective (Gradman and Alfayoumi, 2006; Teaima et al., 2021). Atorvastatin acts by inhibiting the enzyme 3-hydroxy-3-methylglutaryl-coenzyme (HMG-CoA) reductase, a key player in cholesterol production. However, its relatively short half-life, poor solubility, and pH-dependent solubility have led researchers to explore innovative drug delivery systems (Martsenyuk et al., 2019).

Sustained-release formulations offer a promising solution for managing long-term diseases, such as hypercholesterolemia, by optimizing drug release kinetics and reducing dosing frequency. This paper focuses on the development of sustained-release tablets of Atorvastatin, which is achieved by incorporating five distinct natural polymers: guar gum, xanthan gum, hibiscus gum, okra gum, and soya bean gum. The selection

ISSN: 2519-9889
Impact Factor: 5.9

of natural polymers aligns with the growing interest in eco-friendly and biocompatible excipients, offering benefits such as cost-effectiveness, low side effects, and a renewable supply (Sharma et al., 2010).

In this study, we investigate various drug-polymer ratios to create formulations that meet pharmacopoeial standards. The formulations undergo comprehensive pre-compression and post-compression assessments, including evaluations of bulk density, angle of repose, compressibility index, hardness, friability, and weight variation. The key objective is to develop sustained-release tablets that maintain their structural integrity while releasing Atorvastatin over an extended period.

Additionally, *in vitro* dissolution studies are conducted using the USP-II dissolution test apparatus to assess the drug release profiles of the different formulations in a simulated physiological environment. These studies aim to identify the most effective natural polymer for achieving the desired sustained release characteristics. This research holds promise not only for the management of hypercholesterolemia but also for developing cost-effective and eco-friendly drug delivery systems that can be locally sourced and produced.

2. Methodology

2.1 Materials

This study utilized Atorvastatin as the model drug. Natural polymers, including guar gum, xanthan gum, hibiscus gum, okra gum, and soya bean gum, were employed as rate-retarding excipients. Lactose was used to aid in formulation homogenization, while magnesium stearate and talc served as lubricants and anti-adherents during tablet compression. Methanol and distilled water were used for drug solution preparation and extraction of okra gum mucilage. Acetone was employed in the extraction of okra mucilage from *Abelmoschus esculentus.*

2.2 Preparation of standard calibration curve

A stock solution of Atorvastatin was prepared by dissolving 100 mg of the drug in 100 ml of methanol, contained in a 100 ml volumetric flask. This stock solution was expected to yield a concentration of 1000 µg/ml of Atorvastatin. The solution was vigorously mixed through shaking and subsequently subjected to sonication for approximately 10 minutes to ensure complete dissolution. To obtain a stock solution with a concentration of 100 µg/ml of Atorvastatin, 10 ml of Stock Solution 1 was diluted to 100 ml using methanol. This diluted stock solution was filtered through Whatman Filter Paper No.41 to remove any particulate matter and maintain solution clarity (Breaux et al., 2003).

A range of standard solutions was prepared by diluting Stock Solution 2. Concentrations of 2 µg/ml, 4 µg/ml, 6 µg/ml, 8 µg/ml, 10 µg/ml, and 12 µg/ml were achieved by adding the following volumes of Stock Solution 2 into separate test tubes: 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1 ml, and 1.2 ml, respectively. Methanol was added to each test tube to reach a total volume of 10 ml. Absorbance measurements were conducted on the prepared standard solutions at a wavelength of 246 nm using a UV spectrophotometer. The resulting absorbance values were correlated with the respective concentrations of Atorvastatin, forming the foundation for the calibration curve (Breaux et al., 2003).

Statistical analysis was performed to construct a linear regression model, determining the equation of the calibration curve. This equation was used to predict the concentration of Atorvastatin in test samples based on their absorbance readings. Additionally, the regression coefficient (R^2) was calculated to assess the linearity and reliability of the calibration curve, ensuring its suitability for accurate quantification and drug content determination in subsequent analysis procedures (Almeida et al., 2002).

2.3 Drug excipient compatibility using Fourier Transform Infrared (FTIR) Spectroscopy

In this study, both the pure drug and the drug: excipient mixtures at a 1:1 ratio were subjected to Fourier-transform infrared spectroscopy (FTIR) analysis using the potassium bromide (KBr) technique. FTIR spectra were recorded over the wavenumber range of 4000 to 400 cm^{-1} to comprehensively investigate the compatibility of the drug and its excipient, with particular attention to shifts in absorption bands, the emergence of new peaks, or the disappearance of existing peaks that might indicate potential incompatibilities,

ISSN: 2519-9889
Impact Factor: 5.9

ensuring a thorough assessment of their physical and chemical interactions in the pharmaceutical formulation (Chadha and Bhandari, 2014).

2.4 Preparation of Okra Mucilage

Okra mucilage was extracted from the fruits of Abelmoschus esculentus utilizing an organic solvent, acetone. The fruits of Abelmoschus esculentus were carefully sliced into small pieces. The sliced okra pieces were soaked in 1000 ml of distilled water. The soaked okra slices were subjected to boiling in a water bath for one hour at 80°C. This process facilitated the release and dispersion of okra mucilage into the water. After the one-hour boiling period, the okra mucilage was separated from the Abelmoschus esculentus fruits. The separated mucilage was precipitated from the filtrate by adding acetone. This step caused the mucilage to separate and form distinct precipitates. The precipitated mucilage was dried in an oven at 45°C until it was completely dry. Subsequently, the dried mucilage was milled using a mortar and pestle. The dry powder was then passed through an 80 mesh sieve to obtain a fine and uniform particle size. The processed okra gum mucilage was stored in a desiccator for later use (Khokra et al., 2012; Kumar et al., 2009).

2.5 Formulation of tablets

The sustained-release tablets of Atorvastatin were prepared using the direct compression method. For each of the ten formulations (F1 to F10), specific ratios of Atorvastatin and natural polymers (guar gum, xanthan gum, hibiscus gum, okra gum, and soya bean gum) were selected. The chosen ratios of Atorvastatin and polymers were combined (shown in Table 1) in a suitable container, and lactose was added to the mixture. The components were mixed thoroughly by trituration, ensuring even distribution of all ingredients. Magnesium stearate and talc were added to the mixture to act as lubricants. These were also thoroughly mixed with the other components until a uniform mixture was obtained. The required quantities of the mixture were accurately weighed and then compressed using a single rotary tablet press. The tablet press exerted the necessary pressure to form the sustained-release tablets (Banker, 1970a; Gohel and Jogani, 2005).

Table 1: Formulation of Atorvastatin calcium tablets

S.No	Drug/ Ingredients	Quantity of each ingredient in mg									
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	Atorvastatin calcium	100	100	100	100	100	100	100	100	100	100
2	Guar gum	100	200	-	-	-	-	-	-	-	-
3	Xanthan gum	-	-	100	200	-	-	-	-	-	-
4	Hibiscus	-	-	-	-	100	200	-	-	-	-
5	Okra	-	-	-	-	-	-	100	200	-	-
6	Soya bean	-	-	-	-	100	-	-	-	100	200
7	Lactose	285	185	285	185	285	185	285	185	285	185
8	Magnesium stearate	5	5	5	5	5	5	5	5	5	5
9	Talc	10	10	10	10	10	10	10	10	10	10

2.6 Bulk Density

The bulk density of the formulated mixtures was determined following the glass funnel method. A specific quantity of the mixture was allowed to flow through a fixed glass funnel into a measuring cylinder, and the

ISSN: 2519-9889
Impact Factor: 5.9

measurements of the radius (r) of the resulting powder pile and the height (h) of the heap from the ground were recorded. The angle of repose was then calculated using the formula:

$\theta = \tan^{-1}(h/r)$

The obtained values for the angle of repose were compared to pharmacopeial standards, with acceptable limits typically falling below 30°(Almutairy et al., 2020).

2.7 Tapped density

Following bulk density determination, the measuring cylinders were secured to a bulk density test apparatus and subjected to precisely 50 taps. The volume of the material in the cylinder after tapping, termed the tapped volume, was recorded. Tapped density was calculated as the mass of the sample divided by the tapped volume. The Carr's index was calculated using the formula:

Carr's Index = [(Tapped Density - Bulk Density) / Tapped Density] × 100.

According to pharmacopeial standards, Carr's index values should typically be below 15% for efficient powder flow and compression properties (Geldart et al., 2006).

2.8 Hausner's ratio

The Hausner's ratio, a parameter indicating flowability, was determined by dividing the tapped density by the bulk density. The resulting value represented the materials' ease of flow. The pharmacopeial limits for Hausner's ratio vary but generally indicate that values less than 1.25 are desirable for good flow properties, while ratios exceeding 1.25 suggest less favorable flow characteristics (Geldart et al., 2006).

2.9 Hardness test

The tablets' mechanical strength was evaluated using a Monsanto hardness tester, and an average of three trials was conducted for each formulation. The results were reported in terms of kilograms per square centimeter (Kg/cm^2). The obtained hardness values were compared to pharmacopeial standards to ensure that the tablets exhibited appropriate mechanical strength (Brniak et al., 2013).

2.10 Friability test

The tablets' resistance to abrasion and mechanical stress was assessed using a Roche friabilator. The percentage friability of the tablets was determined by measuring the weight loss due to the abrasion caused by repeated tumbling. Tablets that lost less than 1% of their initial weight were considered to meet the standard for friability, as per common pharmacopeial requirements (Banker, 1970b).

2.11 Weight variation test

A weight variation test was carried out to identify any deviations in tablet weight. Twenty tablets were randomly selected, and their individual weights were determined. The individual tablet weights were compared to the average weight of the tablets. The percentage deviation was calculated using the formula:

% deviation = [(W1 - W2) / W1] × 100,

where W1 represents the average weight of ten tablets and W2 is the individual tablet weight. Compliance with pharmacopeial standards was assessed based on the specified maximum allowable percentage difference (Pharmacopoeia, 2007).

2.12 Drug content uniformity

To assess the uniform distribution of the drug within the tablets, a content uniformity test was conducted. Ten tablets were crushed, and a quantity equivalent to 100 mg of the drug was dissolved in a selected solvent (e.g., methanol). The resulting solution was filtered, and its absorbance was measured using a UV spectrophotometer at the appropriate wavelength. Compliance with pharmacopeial standards for drug content uniformity was verified based on the determined drug concentration and its consistency within the tablets (Martsenyuk et al., 2019).

ISSN: 2519-9889
Impact Factor: 5.9

2.13 *In vitro* drug dissolution testing

In vitro drug dissolution studies were conducted using the United States Pharmacopeia (USP) dissolution test apparatus II. Phosphate buffer solution at pH 6.8, maintained at a temperature of 37.5°C to simulate physiological conditions. The dissolution apparatus was set to a rotation speed of 50 revolutions per minute (rpm) to ensure adequate mixing and agitation of the dissolution medium. A total volume of 900 ml of the dissolution medium was maintained in the dissolution chamber. During the dissolution test, 5 ml of the dissolution medium was periodically withdrawn at specified time intervals. To maintain sink conditions and ensure consistent conditions throughout the study, the withdrawal volume was immediately replaced with an equal volume of fresh dissolution medium at the same temperature. This process allowed for the continuous and controlled release of the drug from the tablets. The samples collected at different time intervals were used to determine the drug concentration. UV-spectrophotometry was employed to measure the absorbance of the samples at a wavelength of 246 nm, a suitable wavelength for the drug Atorvastatin. The absorbance readings were converted into drug concentrations using a pre-established calibration curve, and the cumulative drug release was calculated for each time point. The dissolution tests were conducted over a period of 12 hours, with periodic sample collection and analysis to monitor the drug release kinetics. The extended testing duration allowed for the assessment of the sustained release properties of the tablets over an extended timeframe (Amidon et al., 1995).

3. Results

3.1 Standard Calibration curve

The standard calibration curve for Atorvastatin, generated by plotting the concentration of Atorvastatin (in micrograms per milliliter, µg/ml) against the corresponding absorbance values at 246 nm, provides valuable information for quantitative analysis of Atorvastatin in the subsequent stages of the study. The results of the calibration curve are shown in Table 2 and Figure 1. At zero concentration (0 µg/ml), the absorbance was measured as 0, indicating that the blank solution did not exhibit any interference or background absorption at the specified wavelength. As the concentration of Atorvastatin increased from 2 µg/ml to 12 µg/ml, there was a proportional increase in the absorbance values. This demonstrates a linear relationship between the concentration of the drug and the absorbance at 246 nm. The regression coefficient for the calibration curve is 0.9995. This high value of the regression coefficient (close to 1) indicates an excellent linear correlation between the concentration and absorbance, suggesting that the calibration curve is robust and reliable for quantifying Atorvastatin concentrations in subsequent samples (Breaux et al., 2003). The increase in absorbance with increasing drug concentration signifies that the drug strongly absorbs light at 246 nm, making this wavelength suitable for quantifying Atorvastatin in the UV-spectrophotometric analysis (Breaux et al., 2003).

Table 2: Data for calibration curve in 6.8 pH phosphate buffer

S.No	Concentration of Atorvastatin µg/ml	Absorbance at 246 nm*
1	0	0
2	2	0.050 ± 0.05
3	4	0.094 ± 0.14
4	6	0.134 ± 0.09
5	8	0.178 ± 0.04
6	10	0.222 ± 0.21
7	12	0.269± 0.16

Mean ± SEM (n=3 observations)

ISSN: 2519-9889
Impact Factor: 5.9

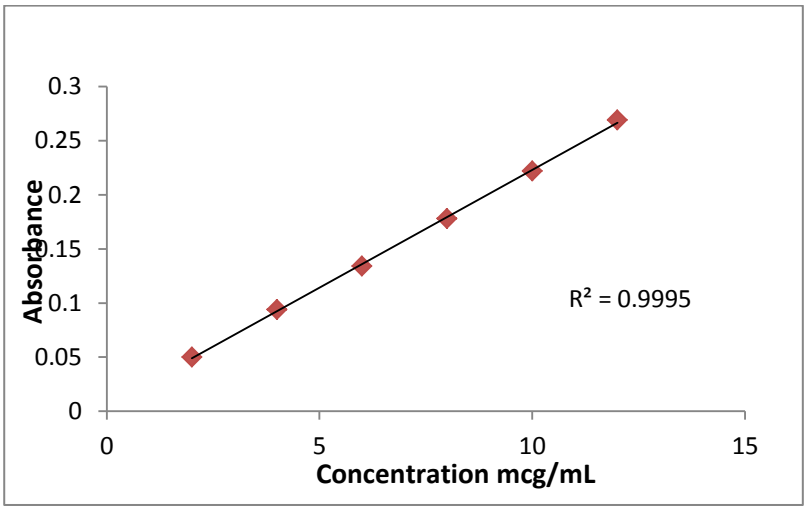

Figure 1: Calibration curve of atorvastatin in 6.8 pH phosphate buffer

3.2 FTIR Studies

The FTIR analysis was performed to investigate potential interactions between Atorvastatin and the selected excipients in the tablet formulation. In the FTIR spectra, several key functional groups associated with Atorvastatin were examined. Notably, the analysis revealed that the following functional groups, associated with Atorvastatin (shown in Figure 2), remained intact in the presence of the excipients (shown in Figure 3). The C-H stretching at 2972.43 band remained unchanged, suggesting the preservation of the C-H bonds. The C=C stretching band at 1560.48 remained unaltered, indicating the retention of the C=C bonds in Atorvastatin. The C=S stretching band at 1157.34 was unaffected, indicating that the C=S bond in Atorvastatin was preserved. Additionally, the FTIR analysis did not reveal any notable shifts or changes in the other C-H bending bands, including those at 880.54, 841.96, 814.96, and 749.38 cm^{-1}. These observations suggest that the structural integrity of Atorvastatin, as indicated by the retention of these functional groups, was maintained in the presence of the excipients. Overall, the FTIR results indicate that the excipients did not induce any significant alterations in the functional groups of Atorvastatin, and the drug's structural characteristics remained unaltered, confirming the absence of chemical interactions and incompatibilities between Atorvastatin and the excipients in the formulation (Chadha and Bhandari, 2014; Macian et al., 2021)

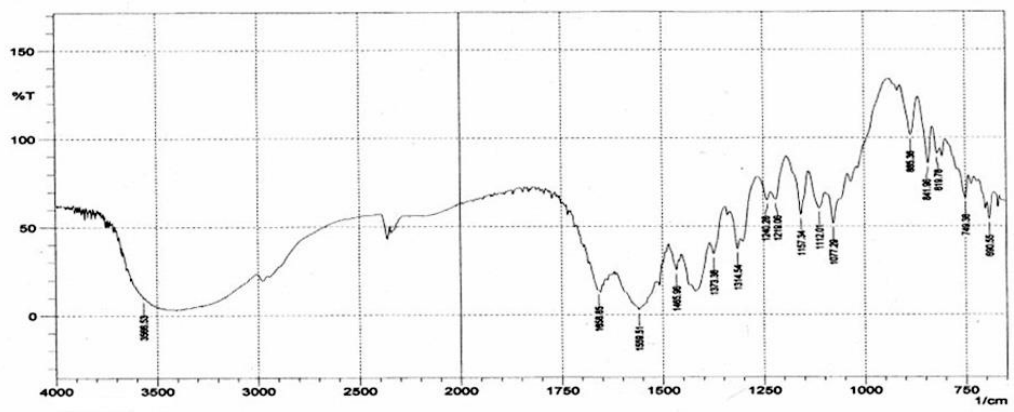

Figure 2: FTIR spectrum of pure drug

ISSN: 2519-9889
Impact Factor: 5.9

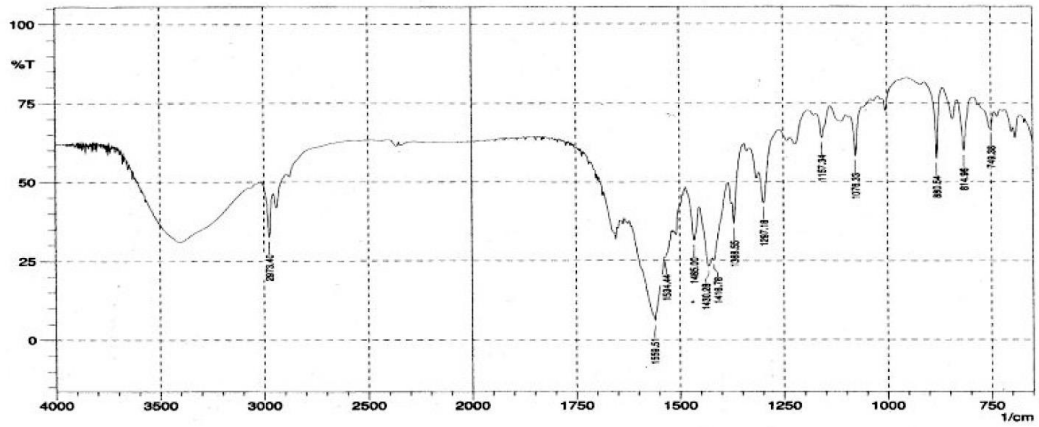

Figure 3: FTIR spectrum of pure drug + excipients

3.3 Precompression parameters

The results of the precompression parameters (indicated in Table 3) provide valuable insights into the physical characteristics of the formulated mixtures. These parameters are crucial in determining the suitability of the powder mixtures for subsequent tablet compression processes.

The angle of repose is an indicator of the flow properties of a powder. Lower values indicate better flowability. Formulations F1 and F3 had angles of repose of 25° and 22°, respectively, suggesting good flow properties. In contrast, formulations F4 to F10 exhibited slightly higher angles of repose, indicating relatively poorer flow characteristics (Geldart et al., 2006).

Bulk density refers to the mass of the powder divided by its bulk volume, encompassing both inter- and intra-particulate spaces. Formulation F3 had the lowest bulk density at 0.291 g/cc, indicating greater particle packing. Conversely, F4 to F10 had higher bulk densities, signifying looser packing of particles.

Tapped density reflects the mass of the powder in a more compact state after tapping, and it accounts for the compression of the powder. Formulations F4 to F10 exhibited higher tapped densities compared to F1 and F3, indicating their compaction under tapping conditions (Almutairy et al., 2020).

Carr's Index, also known as the compressibility index, assesses the compressibility of the powder. Lower values represent better compressibility. Formulations F1, F2, and F3 had Carr's Index values below 10%, suggesting good compressibility. In contrast, formulations F4 to F10 exhibited Carr's Index values above 8%, indicating reduced compressibility and potential challenges in tablet compression.

Hausner's ratio, a measure of flowability, is calculated as the ratio of tapped density to bulk density. Values less than 1.25 are generally considered indicative of good flow properties. Formulations F1, F2, and F3 had Hausner's ratios below 1.10, suggesting good flowability. Formulations F4 to F10 had higher Hausner's ratios, indicating relatively poorer flow properties.

Due to the poor flow properties, a direct compression method is chosen which allows for more content uniformity than wet granulation or slugging method (Geldart et al., 2006).

ISSN: 2519-9889
Impact Factor: 5.9

Table 3: Results of precompression parameters

Formulation	Angle of repose (°)	Bulk density (g/ cc)	Tapped density (g/ cc)	Carr's index (%)	Hausners ratio
F_1	25	0.292	0.328	10.97	1.123
F_2	22	0.291	0.317	8.20	1.089
F_3	29	0.323	0.398	18.84	1.232
F_4	30	0.345	0.388	11.08	1.124
F_5	25	0.368	0.402	8.45	1.092
F_6	25	0.286	0.365	9.32	1.135
F_7	27	0.301	0.322	9.05	1.025
F_8	28	0.295	0.311	10.10	1.108
F_9	24	0.321	0.314	9.65	1.201
F_{10}	28	0.265	0.320	8.69	1.130

3.4 Post compression parameters

The results for hardness, friability, and drug content uniformity are important quality control parameters in assessing the suitability and performance of the formulated tablets. The results of post compression parameters are shown in Table 4.

Hardness is a measure of the tablet's resistance to mechanical forces and provides insights into its strength. The results show that the hardness of the tablets for all formulations (F1 to F10) falls within a relatively narrow range, with values ranging from 3.1 to 3.8 Kg/cm². This indicates that the tablets possess satisfactory hardness, implying that they are robust enough to withstand handling and transport without breaking. The consistency in tablet hardness across formulations is a positive outcome, suggesting uniform tablet strength.

Friability is a measure of the tablet's tendency to break or crumble when subjected to abrasion during handling. It is desirable for tablets to exhibit low friability, typically less than 1%. The results demonstrate that all formulations meet this criterion, with friability values ranging from 0.25% to 0.40%. These low friability percentages suggest that the tablets maintain their structural integrity and do not experience excessive erosion during handling, which is a crucial quality attribute for oral dosage forms (Jain et al., 2008).

Drug content uniformity is a critical parameter that ensures consistent and accurate dosing of the active pharmaceutical ingredient (API) in each tablet. It is expressed as a percentage of the labeled drug content. The results indicate that formulations F2 and F4 exhibit the highest drug content uniformity with values of 98.2% and 97.3%, respectively. The other formulations also maintain acceptable drug content uniformity, with values above 94%, demonstrating that the tablets contain the specified amount of the drug, ensuring effective and consistent dosing for patients.

ISSN: 2519-9889
Impact Factor: 5.9

Table 4: Results of post compression parameters

Formulation	Hard ness Kg/cm^{2*}	Friability (%)	Drug content uniformity
F1	3.1 ± 0.25	0.25	95.8
F2	3.5 ±0.25	0.26	98.2
F3	3.2 ± 0.25	0.40	96.2
F4	3.8 ± 0.25	0.35	97.3
F5	3.6 ± 0.25	0.33	95.9
F6	3.2 ± 0.25	0.38	96.2
F7	3.3± 0.25	0.34	96.3
F8	3.2± 0.25	0.36	95.6
F9	3.6± 0.25	0.32	94.3
F10	3.5± 0.25	0.35	95.7

Mean ± SEM (n=3 observations)

3.5 *In vitro* drug release studies

The in vitro drug release results reveal formulations F7 and F8 as promising candidates for sustained drug delivery due to their controlled and extended release profiles. In contrast to other formulations that achieved complete drug release (100%) within 12 hours, F7 and F8 exhibited sustained action (results are shown in Table 5 and Figure 4). Formulations F7 and F8 both incorporating okra gum as the rate-retarding polymer, demonstrated controlled drug release profiles, achieving 95.2% and 94.1% drug release, respectively, by the end of the 12-hour study period. These results highlight their potential for sustained drug delivery, ensuring a more gradual and extended release of Atorvastatin. Formulation F8 showcased a consistent and gradual drug release pattern, indicating their ability to sustain therapeutic drug levels over an extended period. This sustained action is desirable for medications intended to maintain steady and effective treatment outcomes. The controlled release profiles of F7 and F8 make them suitable options for conditions where a prolonged and consistent drug presence in the body is beneficial, such as in the management of hypercholesterolemia. These formulations have the potential to enhance patient compliance and treatment effectiveness by reducing the frequency of dosing.

Formulations F7 and F8 stand out as formulations with controlled and sustained drug release characteristics. Their ability to release the drug gradually over 12 hours signifies their potential for optimizing therapeutic outcomes and patient adherence, especially in the context of managing chronic conditions like hypercholesterolemia (Agarwal and Murthy, 2015; Mombelli and Pavanello, 2013).

ISSN: 2519-9889
Impact Factor: 5.9

Table 5: Results of *in vitro* drug dissolution studies

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
1	16.0	15.5	16.8	14.2	13.7	9.9	7.2	11.5	16.1	12.0
2	18.2	23.7	26.5	20.3	22.8	19.3	15.4	19.5	25.7	20.2
3	22.6	34.8	30.8	37.7	30.2	25.8	26.2	24.3	34.1	29.3
4	28.5	40.2	43.3	42.1	42.7	36.2	38.1	39.5	41.5	37.5
5	35.2	52.5	56.5	55.0	56.3	42.1	47.4	45.6	52.2	48.2
6	48.5	63.6	69.0	73.0	60.2	50.2	51.0	52.1	61.5	58.5
7	64.1	78.7	77.0	88.9	72.4	73.5	63.2	62.8	70.1	62.1
8	73.3	86.2	86.4	94.6	86.7	86.2	70.2	71.7	83.3	76.3
9	89.2	89.5	88.1	98.2	88.4	92.1	81.4	80.9	90.2	87.2
10	90.1	92.3	99.8	98.8	95.4	98.1	85.2	82.3	95.3	91.2
11	92.4	98.1	99.9	99.1	97.8	98.7	90.7	92.1	98.2	98.2
12	98.7	100	100	100	98.9	99.5	95.2	94.1	100	100

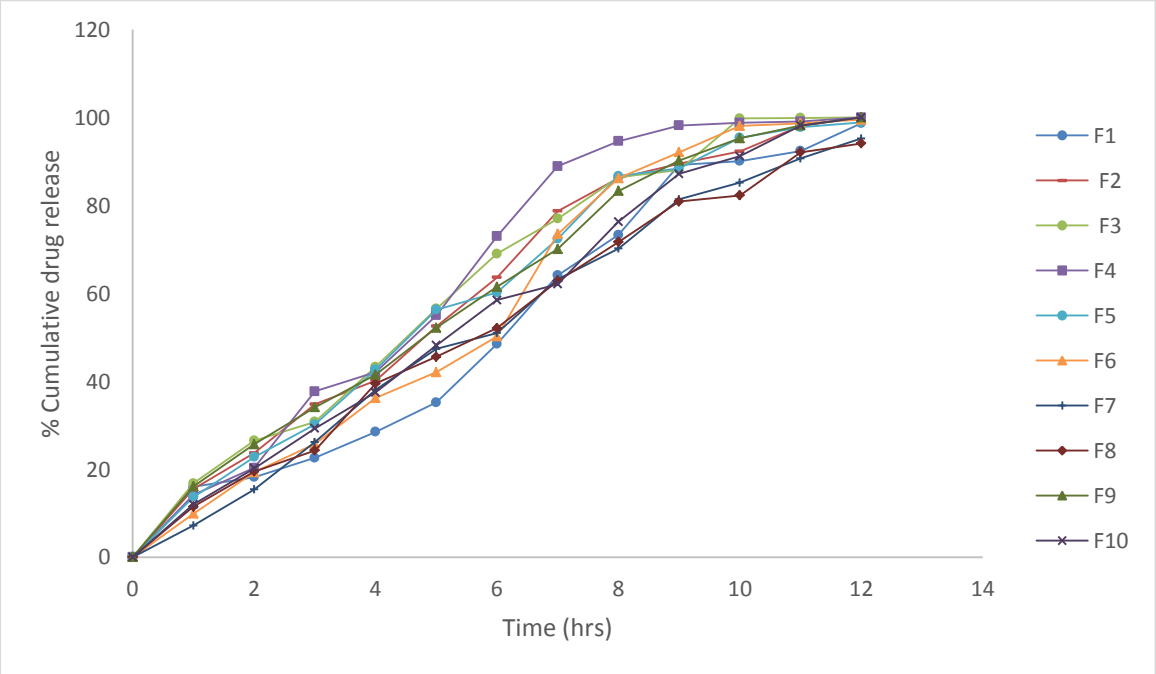

Figure 4: In vitro drug dissolution studies.

4. Discussion

The formulation of sustained-release tablets is a critical endeavor in pharmaceutical research, aiming to enhance patient adherence and therapeutic outcomes. In this study, natural polymers, including okra gum, were explored for their potential in achieving controlled drug release. The pre-compression and post-compression

ISSN: 2519-9889
Impact Factor: 5.9

studies provided valuable insights into the quality and uniformity of the formulated tablets, affirming their suitability for further evaluation (Banker, 1970a).

The standout results from this research were the sustained-release profiles observed in formulations F7 and F8, attributed to the inclusion of okra gum as the rate-retarding polymer. The ability to achieve controlled and extended drug release over 12 hours is a significant achievement, particularly for drugs like Atorvastatin used in the management of chronic conditions. This controlled release can lead to reduced dosing frequency, improving patient compliance and the overall effectiveness of treatment. Moreover, the utilization of natural polymers in drug formulations aligns with the principles of sustainability and patient safety, offering economic advantages and minimal side effects (Bhatia, 2016).

While the findings are promising, it's essential to acknowledge that further investigations, including in vivo studies and clinical trials, are necessary to validate the practical implications of these sustained-release formulations. Additionally, a comprehensive evaluation of stability, storage conditions, and long-term efficacy is warranted to ensure the suitability of these formulations for commercial use. Overall, this research lays the foundation for the development of patient-friendly and sustainable drug delivery systems with the potential to improve the management of chronic diseases (Rahman et al., 2022).

5. Conclusion

This study focused on the formulation of sustained-release tablets of Atorvastatin using various natural polymers. The pre-formulation and post-compression studies indicated the formulations' compliance with pharmacopeial standards, ensuring their quality and uniformity. Notably, formulations F7 and F8, incorporating okra gum, demonstrated controlled and sustained drug release profiles, making them promising candidates for prolonged drug delivery. These sustained-release formulations offer potential benefits in optimizing treatment outcomes and patient compliance, especially in the management of chronic conditions such as hypercholesterolemia. The results suggest the feasibility of utilizing natural polymers for designing effective and patient-friendly drug delivery systems. Further research and clinical studies are warranted to assess the practical implications of these sustained-release formulations in a therapeutic context.

References

[1]. Agarwal, S., Murthy, R.S.R., 2015. Effect of different polymer concentration on drug release rate and physicochemical properties of mucoadhesive gastroretentive tablets. Indian journal of pharmaceutical sciences 77, 705. https://doi.org/10.4103/0250-474X.174993

[2]. Almeida, A.M. de, Castel-Branco, M.M., Falcao, A.C., 2002. Linear regression for calibration lines revisited: weighting schemes for bioanalytical methods. Journal of Chromatography B 774, 215–222.

[3]. Almutairy, B.K., Khafagy, E.-S., Alalaiwe, A., Labrou, N.E., Aldawsari, M.F., Alshahrani, S.M., Alsulays, B.B., Alshetaili, A.S., Sultan Alshehri, Mohamed H Fayed, Fayed, M.H., 2020. Enhancing the Poor Flow and Tableting Problems of High Drug-Loading Formulation of Canagliflozin Using Continuous Green Granulation Process and Design-of-Experiment Approach. Pharmaceuticals 13, 473. https://doi.org/10.3390/ph13120473

[4]. Amidon, G.L., Lennernäs, H., Shah, V.P., Crison, J., 1995. A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharmaceutical research 12, 413–20.

[5]. Banker, G.S., 1970b. The Theory and Practice of Industrial Pharmacy. Journal of Pharmaceutical Sciences 59, 1531. https://doi.org/10.1002/jps.2600591046

[6]. Bhatia, S., 2016. Plant derived polymers, properties, modification & applications, in: Natural Polymer Drug Delivery Systems. Springer, pp. 119–184.

[7]. Breaux, J., Jones, K., Boulas, P., 2003. Analytical methods development and validation. Pharm. Technol 1, 6–13.

[8]. Brniak, W., Jachowicz, R., Krupa, A., Skorka, T., Niwinski, K., 2013. Evaluation of co-processed excipients used for direct compression of orally disintegrating tablets (ODT) using novel disintegration apparatus. Pharmaceutical development and technology 18, 464–474. https://doi.org/10.3109/10837450.2012.710238

[9]. Chadha, R., Bhandari, S., 2014. Drug–excipient compatibility screening—role of thermoanalytical and spectroscopic techniques. Journal of pharmaceutical and biomedical analysis 87, 82–97.

ISSN: 2519-9889
Impact Factor: 5.9

[10]. Geldart, D., Abdullah, E.C., Hassanpour, A., Nwoke, L.C., Wouters, I., 2006. Characterization of powder flowability using measurement of angle of repose. China Particuology 4, 104–107.
[11]. Gohel, M.C., Jogani, P.D., 2005. A review of co-processed directly compressible excipients. J Pharm Pharm Sci 8, 76–93.
[12]. Gradman, A.H., Alfayoumi, F., 2006. From left ventricular hypertrophy to congestive heart failure: management of hypertensive heart disease. Progress in cardiovascular diseases 48, 326–341. https://doi.org/10.1016/j.pcad.2006.02.001
[13]. Jain, S., Yadav, S.K., Patil, U.K., 2008. Preparation and evaluation of sustained release matrix tablet of furosemide using natural polymers. Research journal of pharmacy and technology 1, 374–376.
[14]. Khokra, S.L., Parashar, B., Dhamija, H.K., Kumar, K., Arora, S., 2012. Formulation and evaluation of novel sustained release multiple emulsion containing chemotherapeutic agents. Int J PharmTech Res 4, 866–72.
[15]. Kumar, R., Patil, S., Patil, M.B., Patil, S.R., Paschapur, M.S., 2009. Isolation and evaluation of disintegrant properties of fenugreek seed mucilage. International Journal of PharmTech Research 1, 982–996.
[16]. Macian, V., Tormos, B., García-Barberá, A., Tsolakis, A., 2021. Applying chemometric procedures for correlation the FTIR spectroscopy with the new thermometric evaluation of Total Acid Number and Total Basic Number in engine oils. Chemometrics and Intelligent Laboratory Systems 208, 104215. https://doi.org/10.1016/j.chemolab.2020.104215
[17]. Martsenyuk, V., Hroshovyi, T., Trygubchak, O., Klos-Witkowska, A., 2019. On machine learning approach for the design of pharmaceutical technology of tablets: Acetyl salicylic acid with atorvastatin, in: International Conference on Artificial Intelligence and Soft Computing. Springer, pp. 216–227.
[18]. Mombelli, G., Pavanello, C., 2013. Novel therapeutic strategies for the homozygous familial hypercholesterolemia. Recent Patents on Cardiovascular Drug Discovery (Discontinued) 8, 143–150.
[19]. Pharmacopoeia, I., 2007. Volume-1, published by The Indian Pharmacopoeia Commission, Central Indian pharmacopoeia Laboratory Govt. Of India, Ministry of Health & Family Welfare Sector-23, Raj Nagar, Ghaziabad-201 00.
[20]. Rahman, Md.M., Islam, F., -Or-Rashid, Md.H., Mamun, A.A., Rahaman, Md.S., Islam, Md.M., Meem, A.F.K., Sutradhar, P.R., Mitra, S., Mimi, A.A., Emran, T.B., Fatimawali, Idroes, R., Tallei, T.E., Ahmed, M., Cavalu, S., 2022. The Gut Microbiota (Microbiome) in Cardiovascular Disease and Its Therapeutic Regulation. Front Cell Infect Microbiol 12, 903570. https://doi.org/10.3389/fcimb.2022.903570
[21]. Sharma, V., Arora, V., Ray, C., 2010. Use of natural superdisintegrant in mouth dissolving tablet-an emerging trend. International bulletin of drug research 1, 46–54.
[22]. Teaima, M.H., Abdel-Haleem, K.M., Osama, R., El-Nabarawi, M.A., Elnahas, O.S., 2021. A promising single oral disintegrating tablet for co-delivery of pitavastatin calcium and lornoxicam using co-processed excipients: formulation, characterization and pharmacokinetic study. Drug Design, Development and Therapy 15, 4229. https://doi.org/10.2147/dddt.s332729.

A Brief Author Biography

Sesha Sai Durga Manyam– I am an Associate Professor in Aditya College of Pharmacy with over 6 years of experience in pharmaceutical drug development and research.

Swetha Arumilli– I am an Associate Professor in Aditya College of Pharmacy with over 7 years of experience in pharmaceutical drug development and research

Prasanthi Pakalapati – Associate Professor in Aditya College of Pharmacy with 10 years of experience in novel drug delivery systems and pharmaceutical research.

Prakash Nathaniel Kumar Sarella– Pharmaceutical scientist with a passion for innovative drug delivery solutions. Over 6 years of experience in drug delivery research and development. Expertise in nanomedicine, liposomes, polymer therapeutics, antibody-drug conjugates, and microneedle technologies.

