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Formulation, Development and Evaluation of Anti-diabetic Chewable Tablets

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Abstract: *The development and evaluation of anti-diabetic chewable tablets formulated with Sitagliptin require a comprehensive understanding of the drug's physical and chemical properties, as well as the pre-formulation studies conducted to assess its compatibility with excipients. In this study, Sitagliptin chewable tablets were prepared using the wet granulation method, ensuring uniformity and stability of the formulation. Various pre-compression parameters such as bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose were evaluated to assess the flowability and compressibility of the powder blends. The results indicated acceptable flow properties, with room for optimization to enhance tablet compression uniformity. Subsequent evaluation of the tablets focused on parameters including color, odor, taste, weight variation, diameter, thickness, hardness, and disintegration time. While the tablets exhibited uniformity in most parameters, variations in hardness and disintegration time among formulations were observed, suggesting the need for further optimization. Furthermore, drug content analysis revealed variability among batches, with batch F6 exceeding 100% drug content, necessitating careful consideration to ensure consistent drug delivery. Overall, this study highlights the importance of thorough formulation development and evaluation processes to ensure the quality, efficacy, and safety of anti-diabetic chewable tablets, thereby contributing to improved patient outcomes in diabetes management*

Keywords: Anti-diabetic, chewable tablets, Sitagliptin, formulation development, pre-formulation studies, tablet evaluation, drug content, optimization

I. INTRODUCTION

Chewable tablets are a type of oral dosage form that are designed to be chewed or masticated in the mouth before swallowing.[1,2] They are commonly used for medications intended for pediatric, geriatric, and patients who have difficulty swallowing conventional tablets or capsules. Chewable tablets offer several advantages over other oral dosage forms, making them a preferred choice for certain populations.[3,4]

Types of Chewable Tablets:

- **Traditional Chewable Tablets:** These are conventional tablets that are formulated with pleasant taste and texture to facilitate chewing and swallowing.
- **Fast-Disintegrating Chewable Tablets:** These tablets are designed to disintegrate rapidly in the mouth without the need for chewing. They dissolve or disintegrate quickly in saliva, making them easy to swallow without water.[5,6]

Advantages of Chewable Tablets:

- **Improved Patient Compliance:** Chewable tablets are particularly useful for patients who have difficulty swallowing solid dosage forms, such as children, elderly individuals, and individuals with certain medical conditions. They provide a convenient and palatable option for medication administration.
- **Enhanced Absorption:** Chewable tablets are designed to disintegrate or dissolve quickly in the mouth, allowing the drug to be absorbed more rapidly through the oral mucosa. This can result in faster onset of action compared to conventional tablets.

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- **Taste Masking:** Chewable tablets are formulated with flavors and sweeteners to enhance their taste, making them more acceptable and enjoyable for patients, especially children.
- **Flexible Dosing:** Chewable tablets can be easily divided or crushed to adjust the dose according to the patient's needs, which is particularly important for pediatric patients who may require lower doses. [7-10]

Applications of Chewable Tablets:

- **Pediatric Medications:** Chewable tablets are commonly used for pediatric medications, as they provide a more palatable and convenient alternative to conventional tablets or capsules.
- **Geriatric Medications:** Elderly individuals often face difficulty swallowing tablets or capsules due to age-related changes or medical conditions. Chewable tablets offer a suitable option for this population.
- **Nutritional Supplements:** Chewable tablets are used for delivering various nutritional supplements, such as vitamins, minerals, and dietary supplements, making them easier to consume for individuals with dietary deficiencies. [11]

II. MATERIALS AND METHOD

Drug Authentication

The sample was evaluated for its physical state, odor and color.

Pre formulation Studies

Pre formulation studies were performed on the drug, which included melting point determination, solubility and compatibility studies.

Infrared spectra analysis

Infrared spectrum of Sitagliptin was determined on Fourier Transform Infrared Spectrophotometer (FTIR-4100s) using KBr dispersion method [12]

PREFORMULATION STUDIES

- Pre-formulation testing is an investigation of physical and chemical properties of a drug substance alone and when combined with excipients.
- Pre-formulation studies yield necessary knowledge to develop suitable formulation for toxicological use. It gives information needed to define the nature of the drug substance and provide a dosage form. [12]

Formulation Development

Preparation of Sitagliptin chewable tablets

The preparation of Sitagliptin chewable tablets involves a series of steps, primarily utilizing the wet granulation method.

Initially, the ingredients are accurately weighed according to the formulation. Subsequently, these weighed ingredients are combined to form a damp mass, ensuring homogeneity of the mixture.

The damp mass is then screened through a sieve, typically with mesh size number 14, to obtain granules of uniform size. These granules are then dried to remove excess moisture, ensuring stability and facilitating subsequent processing steps.

Lubricants, such as stearic acid and magnesium stearate, are added to the dried granules to improve flow properties and prevent sticking during tablet compression.

After blending thoroughly, the granules are compressed into tablets using an 8-station rotary press tablet compression machine.

This process ensures uniformity in tablet weight, content, and physical characteristics, resulting in the production of high-quality Levamisole chewable tablets suitable for oral administration.[13]

Table 1: Preparation of Sitagliptin chewable tablets

Ingredient	F1	F2	F3	F4	F5	F6
Sitagliptin (mg)	50	50	50	50	50	50

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SLS (mg)	15	15	15	15	15	15
PVP (mg)	10	10	10	10	10	10
Lactose (mg)	218	221	224	-	-	-
Mannitol (mg)	-	-	-	218	221	224
SSG (mg)	6	3	-	6	3	-
Magnesium stearate	10	10	10	10	10	10
(mg)						
Stearic acid (mg)	5	5	5	5	5	5
Starch (mg)	47	47	47	47	47	47
Vanilla flavour (mg)	15	15	15	15	15	15
Sodium saccharin (mg)	4	4	4	4	4	4
Total weight (mg)	380	380	380	380	380	380

III. EVALUATION OF PRE COMPRESSION PARAMETERS

Bulk density

Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. Bulk density is determined by pouring pre sieved granules into a graduated cylinder via a large funnel and measure the volume and weight.

Tapped density:

Tapped density is determined by placing a graduated cylinder containing a known mass of granules and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. using the weight of the drug in the cylinder and this minimum volume, the taped density may be computed.

Carr's Index (CI)

Carr's index is measured using the values of bulk density and tapped density.

Hausner's Ratio: It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder or granules.

Angle of repose:

The manner in which stresses are transmitted through a bead and the beads response to applied stress are reflected in the various angles of friction and response..[14]

IV. EVALUATION OF TABLETS

General appearance:

The formulated tablets were assessed for its general appearance and observations were made for shape, color, texture and odor.

Hardness:

Hardness of the tablet was determined by using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force

Weight Variation

20 tablets were selected and weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it was within the permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for 300 mg tablets and none by more than double that percentage.

Friability test:

20 previously weighed tablets were placed in the friability apparatus, which was given 100 revolutions and the tablets were reweighed.

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Drug content:

20 tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 100 mg of Sitagliptin was transferred in to a 100 ml volumetric flask and the volume adjusted to 100ml with 0.1N HCl. Further 1ml of the above solution was diluted to 100 ml with 0.1N HCl and check the absorbance of the resulting solution was observed at 216nm.[15]

V. RESULTS AND DISCUSSION

Calibration curve

The calibration curve is a fundamental aspect of quantitative analysis, providing a relationship between the concentration of the analyte (Sitagliptin Phosphate) and its corresponding response (typically measured as absorbance or intensity). This curve is essential for accurately determining the concentration of Sitagliptin Phosphate in samples based on their absorbance values.

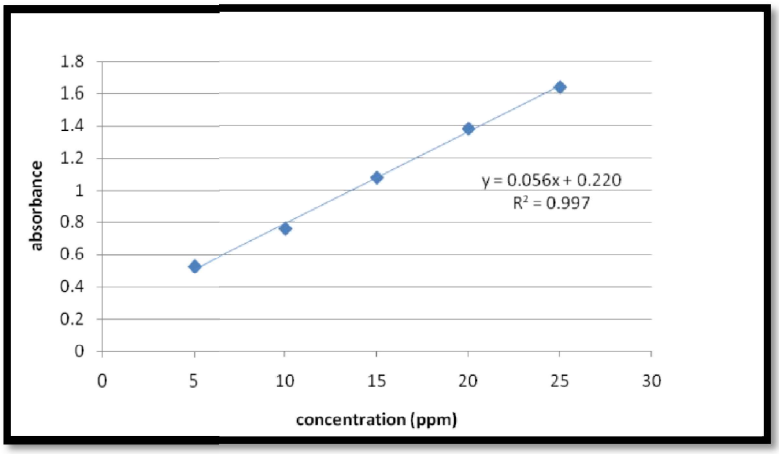

Fig 1: Calibration curve

IR spectra of pure Sitagliptin Phosphate

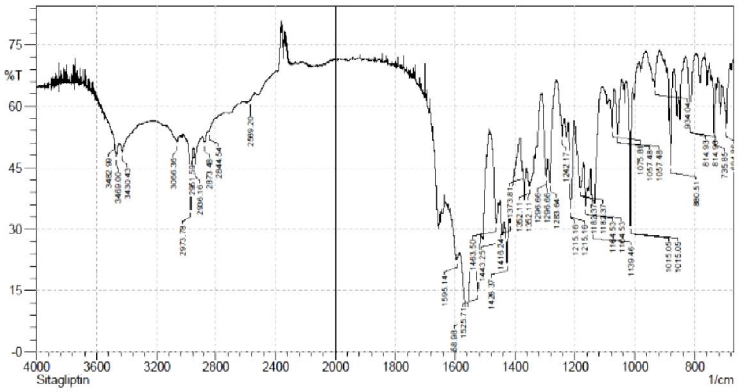

Fig 2: IR spectra of pure Sitagliptin Phosphate

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IR spectra of pure Sitagliptin Phosphate final formulation

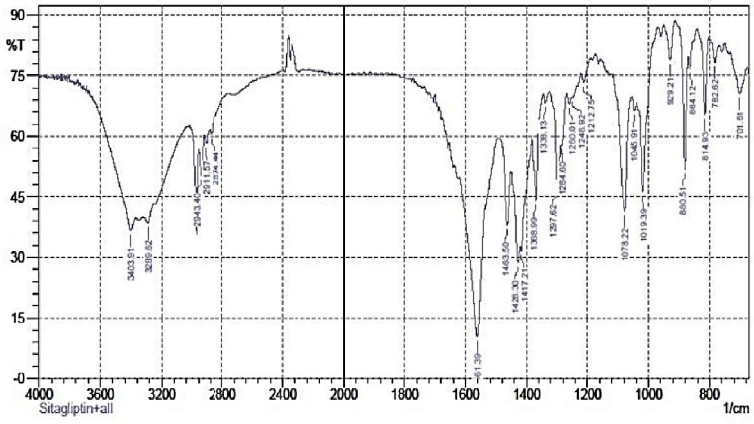

Fig 3: IR spectra of pure Sitagliptin Phosphate

VI. PRECOMPRESSIONAL STUDIES

The precompression studies provide valuable insights into the physical properties of the formulated herbal preparations prior to compression into tablets. The bulk density, tapped density, compressibility index, Hausner's ratio, and angle of repose are key parameters that influence the flowability and compressibility of the powder blends, thereby impacting the quality and uniformity of the final tablet product.

Table 2: Precompressional Studies

Formulation	Bulk Density	Tapped Density	Compressibility Index	Hausner's Ratio	Angle of Repose
F1	0.4	0.476	19	1.19	36.7
F2	0.408	0.50	22.5	1.22	42
F3	0.4	0.487	21.7	1.21	41.7
F4	0.416	0.512	23.2	1.23	42.5
F5	0.4	0.512	28	1.28	46
F6	0.416	0.512	23.27	1.23	43.2

The bulk density values of the formulations range from 0.4 to 0.416 g/cm^3, indicating the density of the powder blend before compression. Generally, a lower bulk density suggests better flow properties of the powder. The tapped density values, which represent the maximum packing density achieved after tapping, range from 0.476 to 0.512 g/cm^3. The compressibility index, calculated as a percentage, reflects the degree of powder densification and is an indicator of flowability. In this study, the compressibility index ranges from 19% to 28%, with lower values indicating better compressibility.

Hausner's ratio, calculated by dividing the tapped density by the bulk density, provides an indication of the flowability of the powder blend. Values close to 1 suggest good flow properties, while higher values indicate poor flow. In this study, Hausner's ratio ranges from 1.19 to 1.28, indicating acceptable to moderate flow properties of the formulations.

The angle of repose, which is the maximum angle at which the powder pile remains stable, is another measure of powder flowability. Higher angles of repose suggest poorer flow properties. In this study, the angle of repose ranges from 36.7° to 46°, indicating fair to poor flow properties of the formulations.

Overall, the results of the precompression studies suggest that while the formulations exhibit acceptable flow and compressibility properties, there is room for optimization to enhance flow properties and ensure uniform tablet compression. Further optimization of the formulation parameters may be necessary to improve tablet manufacturability and product quality.

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Evaluation of tablet

The evaluation of tablets involves assessing various parameters to ensure their quality, performance, and compliance with regulatory standards.

Table 3: Evaluation of tablet

Sr. No	Parameter	F1	F2	F3	F4	F5	F6
1	Colour	White	White	White	White	White	White
2	Odour	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant
3	Taste	Vanilla like	Vanilla like	Vanilla like	Vanilla like	Vanilla like	Vanilla like
4	% Weight variation	1.3195 ± 0.7905	1.3205 ± 0.2575	1.3255 ± 0.2525	1.3195 ± 0.7905	1.3575 ± 0.5875	1.3205 ± 0.2575
5	Diameter (cm)	0.9 ± 0.05	0.9 ± 0.05	0.9 ± 0.05	0.9 ± 0.05	0.9 ± 0.05	0.9 ± 0.05
6	Thickness (cm)	0.5 ± 0.02	0.5 ± 0.02	0.5 ± 0.02	0.5 ± 0.02	0.5 ± 0.02	0.5 ± 0.02
7	Hardness	3 kg	4.2 kg	2.6 kg	3.8 kg	3 kg	3.2 kg
8	Disintegration time	14 min	18 min	21 min	17 min	20 min	25 min

The results of the tablet evaluation for formulations F1 to F6 are summarized below:

Colour: All formulations exhibit a consistent white color, indicating uniformity in tablet appearance.

Odour: Each formulation has a pleasant odor, suggesting no significant variations in the scent among the tablets.

Taste: Tablets from all formulations have a vanilla-like taste, indicating uniformity in flavor across the different formulations.

% Weight Variation: The percentage weight variation for each formulation falls within acceptable limits, indicating consistency in tablet weight among different batches.

Diameter: The diameter of tablets from all formulations is consistent at 0.9 ± 0.05 cm, demonstrating uniformity in tablet size.

Thickness: Tablets from all formulations have a uniform thickness of 0.5 ± 0.02 cm, indicating consistency in tablet dimensions.

Hardness: The hardness of tablets varies among formulations, with values ranging from 2.6 kg to 4.2 kg. While some formulations exhibit slightly lower or higher hardness values, all tablets demonstrate sufficient mechanical strength to withstand handling and transportation.

Disintegration Time: The disintegration time of tablets varies among formulations, with values ranging from 14 to 25 minutes. Longer disintegration times may indicate slower dissolution rates, which could affect drug release and bioavailability.

Overall, the evaluation results suggest that while the tablets exhibit uniformity in color, odor, taste, weight variation, diameter, and thickness, there are variations in hardness and disintegration time among the formulations. Further optimization may be required to improve consistency in these parameters and ensure the quality and performance of the tablets for effective therapeutic outcomes.

% Drug content

The drug content analysis provides crucial information about the amount of active pharmaceutical ingredient (API) present in each tablet formulation.

Table 4: % Drug content

Batch no.	% Drug content
F1	93.16
F2	96.47
F3	100.81

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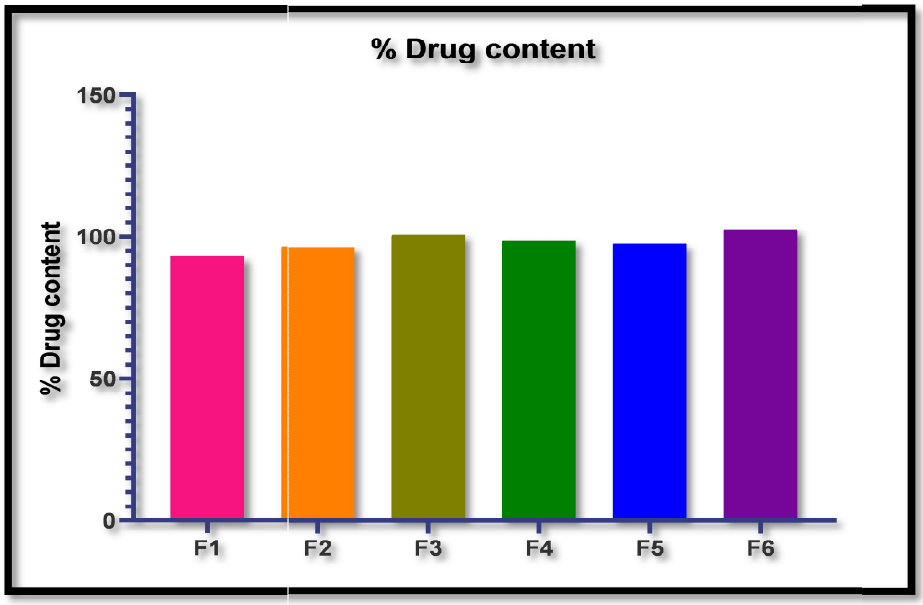
F4	98.78
F5	97.56
F6	102.58



These results indicate the variability in drug content among the different batches. While most batches fall within an acceptable range, batch F6 exceeds 100%, suggesting a higher concentration of the API than intended. Such deviations may impact the efficacy and safety of the tablets and require further investigation to ensure consistent drug delivery and therapeutic outcomes. Overall, monitoring drug content is essential to maintain the quality and performance of pharmaceutical formulations.

VII. CONCLUSION

In conclusion, the development and evaluation of anti-diabetic chewable tablets formulated with Sitagliptin involve a systematic approach encompassing pre-formulation studies, formulation development, and tablet evaluation. The study demonstrated the importance of assessing physical and chemical properties, optimizing formulation parameters, and evaluating tablet characteristics to ensure quality, efficacy, and safety. While the tablets exhibited uniformity in many parameters, variations in hardness, disintegration time, and drug content among formulations highlight the need for further optimization and refinement. Overall, this study contributes valuable insights into the formulation and evaluation processes of anti-diabetic chewable tablets, paving the way for improved therapeutic outcomes and patient adherence in diabetes management. Further research and optimization efforts are warranted to enhance the performance and consistency of these tablets, ultimately benefiting individuals with diabetes worldwide.

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