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Research Paper

Formulation And Evaluation of Sustained Release Tablets of Tolterodine Tartrate

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ABSTRACT

Tolterodine Tartrate is an antimuscarinic agent widely used in the management of Overactive Bladder, a disorder characterized by urinary urgency, increased frequency, and urge incontinence. The present study was undertaken to develop and evaluate sustained-release matrix tablets of tolterodine tartrate in order to improve therapeutic efficacy and enhance patient compliance by reducing dosing frequency. Sustained-release formulations were prepared using different hydrophilic polymers through the direct compression technique.The prepared tablets were evaluated for pre-compression parameters such as bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose, while post-compression parameters included hardness, friability, thickness, weight variation, and drug content. In-vitro dissolution studies were carried out to determine the drug release profile over an extended period. The results demonstrated that polymer concentration significantly influenced the drug release behavior. Optimized formulations exhibited controlled and prolonged drug release following suitable kinetic models. The study concludes that sustained-release matrix tablets of tolterodine tartrate can be successfully formulated to achieve prolonged therapeutic action and improved patient compliance in the treatment of overactive bladder.

INTRODUCTION

The oral route of drug administration remains the most widely preferred method for delivering therapeutic agents due to its convenience, patient compliance, non-invasive nature, and ease of manufacturing. Conventional immediate-release dosage forms release the active pharmaceutical ingredient rapidly after administration, which leads to a sharp increase in plasma drug concentration followed by a rapid decline as the drug undergoes metabolism and elimination. This pattern of drug concentration often leads to significant fluctuations in plasma levels, which may result in sub-therapeutic concentrations or

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toxic effects. In chronic diseases requiring long-term medication, frequent dosing is required to maintain therapeutic drug levels, which may reduce patient compliance.

To overcome these limitations, modified drug delivery systems have been developed. Among them, **sustained release drug delivery systems** are particularly important. Sustained release dosage forms are designed to release the drug gradually over an extended period, maintaining therapeutic drug concentrations in the systemic circulation for a prolonged duration. These systems are capable of improving therapeutic efficacy while minimizing adverse effects.

Sustained release formulations are designed to maintain constant drug concentration in the bloodstream by controlling the release rate of the drug. This controlled release mechanism helps maintain plasma drug levels within the therapeutic window for an extended period. Sustained release systems are particularly useful for drugs that have short biological half-lives, narrow therapeutic indices, or require frequent dosing.

Various pharmaceutical technologies are used in the design of sustained release formulations. These include matrix systems, reservoir systems, osmotic pump systems, ion exchange systems, and swelling-controlled systems. Among these, matrix tablets are one of the most widely used sustained release dosage forms due to their simplicity, cost-effectiveness, and ease of manufacturing.

In matrix systems, the drug is uniformly dispersed within a polymeric matrix. The release of the drug from the matrix occurs through diffusion, erosion, or swelling mechanisms. Hydrophilic polymers such as Hydroxypropyl methylcellulose (HPMC) are commonly used in the formulation of sustained release tablets because they form a gel barrier upon hydration that controls drug diffusion.

Sustained release drug delivery systems offer several advantages. These include reduction in dosing frequency, improved patient compliance, reduction in plasma concentration fluctuations, and better management of chronic diseases. Additionally, sustained release systems can reduce side effects associated with high peak drug concentrations.

However, sustained release formulations also have certain limitations. These include difficulty in dose adjustment, risk of dose dumping, and increased manufacturing complexity. Despite these challenges, sustained release dosage forms remain an important area of pharmaceutical research and development.

One of the therapeutic areas where sustained release formulations are particularly beneficial is the management of **overactive bladder syndrome (OAB)**. Overactive bladder is a chronic urological disorder characterized by urinary urgency, increased urinary frequency, nocturia, and urge urinary incontinence. This condition significantly affects the quality of life of patients and requires long-term pharmacological management.

Tolterodine Tartrate is an antimuscarinic agent used in the treatment of overactive bladder. It acts by blocking muscarinic receptors in the bladder and inhibiting involuntary detrusor muscle contractions. However, Tolterodine has a relatively short half-life, which necessitates frequent dosing when administered in conventional dosage forms.

Therefore, developing sustained release formulations of Tolterodine Tartrate can provide prolonged therapeutic action, reduce dosing frequency, and improve patient adherence to therapy. The present study focuses on the formulation and evaluation of sustained release tablets of Tolterodine Tartrate using suitable polymers and excipients

2 MATERIALS AND METHODS

2.1. Materials

Tolterodine Tartrate was used as the active pharmaceutical ingredient. Hydroxypropyl Methylcellulose (HPMC K100M) and Hydroxypropyl Methylcellulose (HPMC K4M) were employed as hydrophilic matrix-forming polymers to control drug release. Microcrystalline cellulose (MCC PH -102) served as the diluent, while magnesium stearate and talc were used as lubricant and glidants, respectively. All chemicals and reagents used in the study were of analytical grade.

2.2. Methods of preparation

Sustained release tablets of Tolterodine Tartrate were prepared by the direct compression technique. Different formulations (TT1–TT8) were designed by varying the concentration of hydrophilic polymers while maintaining the drug content constant

All ingredients were accurately weighed according to the formulation design. The drug and excipients were passed through the appropriate sieve, blended uniformly, and lubricated with Talc and Magnesium Stearate. The final powder blend was compressed into tablets using a rotary tablet compression machine equipped with suitable punches to obtain tablets of uniform weight and thickness.

2.3. Pre-compression Evaluation

Prior to compression, the powder blends were evaluated to determine their flow and compression characteristics.

The following parameters were determined:

- Angle of Repose
- Bulk Density
- Tapped Density
- Carr's Compressibility Index
- Hausner's Ratio

These parameters were evaluated to ensure adequate flowability and compressibility of the powder blends before tablet compression.

2.4. Post-compression Evaluation

The compressed tablets were evaluated according to pharmacopeial specifications.

The following quality control tests were performed:

- General appearance
- Tablet thickness
- Weight variation
- Hardness
- Friability
- Drug content uniformity
- Swelling Index

The obtained results were compared with official pharmacopoeial limits to assess the quality of the prepared formulations.

2.5. In Vitro Dissolution Study

The *In vitro* drug release study was performed using the USP Dissolution Apparatus II (Paddle Method). Dissolution testing was carried out under optimized experimental conditions using an appropriate dissolution medium maintained at 37 ± 0.5°C with constant paddle rotation.

Samples were withdrawn at predetermined time intervals and replaced with an equal volume of fresh dissolution medium to maintain sink conditions. The collected samples were filtered and analyzed using a UV–Visible spectrophotometer at the predetermined analytical wavelength. The cumulative percentage drug release was calculated and compared among all formulations.

2.6. Selection of Optimized Formulation

Based on the dissolution profile and physicochemical evaluation, the formulation

exhibiting satisfactory tablet characteristics together with the desired sustained drug release pattern was selected as the optimized formulation for further studies.

2.7. Stability Study

The optimized formulation was subjected to accelerated stability studies according to ICH recommendations. Tablets were packed in suitable containers and stored under accelerated environmental conditions for the specified study period.

Samples were periodically evaluated for:

- Physical appearance
- Drug content
- Hardness
- Friability
- In vitro drug release

The stability data were compared with the initial observations to determine the formulation's stability and its ability to maintain sustained drug release during storage.

2.8. Statistical Analysis

All experimental observations were recorded, and the results were expressed as mean values with the corresponding standard deviation wherever applicable. Comparative evaluation of the formulations was performed using the obtained physicochemical and dissolution data to identify the optimized sustained release formulation.

3. DATA ANALYSIS / Results

3.1. Pre-compression Evaluation

The powder blends of all formulations (TT1–TT8) exhibited satisfactory flow properties suitable for direct compression. The angle of repose ranged from 27.42 ± 0.18° to 28.63 ± 0.19°, indicating good flowability. Bulk density and tapped density ranged from 0.45–0.41 g/mL and 0.48–0.53 g/mL, respectively. Carr's Index (11.76–14.58%) and Hausner's Ratio (1.13–1.17) were within acceptable pharmacopeial limits, confirming adequate compressibility of all powder blends.

Trial	Angle of Repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's Ratio
TT1	27.42 ± 0.18	0.45 ± 0.02	0.51 ± 0.02	11.76 ± 0.31	1.13 ± 0.02
TT2	26.88 ± 0.22	0.46 ± 0.01	0.52 ± 0.01	11.54 ± 0.28	1.13 ± 0.01
TT3	27.16 ± 0.19	0.44 ± 0.02	0.51 ± 0.02	13.73 ± 0.34	1.16 ± 0.02
TT4	28.05 ± 0.21	0.43 ± 0.01	0.50 ± 0.02	14.00 ± 0.29	1.16 ± 0.01
TT5	26.52 ± 0.17	0.47 ± 0.02	0.53 ± 0.02	11.32 ± 0.25	1.13 ± 0.02
TT6	27.34 ± 0.20	0.45 ± 0.01	0.52 ± 0.02	13.46 ± 0.33	1.15 ± 0.02
TT7	28.24 ± 0.23	0.42 ± 0.02	0.49 ± 0.02	14.29 ± 0.30	1.17 ± 0.02
TT8	28.63 ± 0.19	0.41 ± 0.01	0.48 ± 0.01	14.58 ± 0.32	1.17 ± 0.01

3.2. Post-compression Evaluation

All prepared tablets showed acceptable physical characteristics. Tablet thickness varied between 3.92 ± 0.05 mm and 4.08 ± 0.05 mm, while hardness ranged from 5.42 ± 0.12 to 6.72 ± 0.15 kg/cm². Friability remained below 1% in every formulation (0.35–0.54%), demonstrating sufficient mechanical strength for handling and storage. The average tablet weight remained close to the target weight of 200 mg, with values ranging from 199.42 ± 1.12 mg to 201.26 ± 1.18 mg. Drug content varied between 98.24 ± 0.69% and 100.62 ± 0.77%, confirming excellent content uniformity among all formulations.

Formulation	Thickness (mm)	Hardness (kg/cm²)	Friability (%)
TT1	3.92 ± 0.05	5.42 ± 0.12	0.54 ± 0.04
TT2	3.95 ± 0.06	5.68 ± 0.15	0.49 ± 0.05
TT3	3.98 ± 0.04	5.94 ± 0.14	0.46 ± 0.03
TT4	4.02 ± 0.05	6.38 ± 0.18	0.41 ± 0.04
TT5	3.99 ± 0.04	6.12 ± 0.13	0.44 ± 0.03
TT6	4.04 ± 0.05	6.46 ± 0.16	0.39 ± 0.04
TT7	4.05 ± 0.06	6.51 ± 0.17	0.37 ± 0.03
TT8	4.08 ± 0.05	6.72 ± 0.15	0.35 ± 0.02

3.3. *In-vitro* Drug Release Study

All formulations exhibited sustained drug release over a period of 12 hours. Polymer concentration markedly influenced the release profile. Formulations containing lower polymer concentration (TT1 and TT2) released the drug more rapidly, whereas higher polymer concentrations (TT7 and TT8) produced slower release because of stronger gel formation and increased matrix integrity.

Among all formulations, TT5 demonstrated the most desirable sustained-release profile, releasing 16.10% drug at 1 hour, 49.60% at 4 hours, 78.90% at 8 hours, and 95.30% at 12 hours. This formulation provided an optimum balance between polymer hydration, diffusion, and matrix erosion, making it the optimized batch. Statistical comparison of dissolution profiles showed no significant difference between formulation groups at 4, 8, and 12 hours ($p > 0.05$). Nevertheless, the overall release trend confirmed that increasing polymer concentration effectively prolonged drug release.

3.4. Stability Study

The optimized formulation (TT5) remained stable during accelerated stability testing at 40 ± 2°C/75 ± 5% RH for three months. No significant changes were observed in physical appearance, tablet weight, hardness, friability, drug content, or dissolution profile. Drug content remained above 98%, and the 12-hour drug release profile was maintained throughout the study, indicating satisfactory stability of the optimized formulation.

Time (months)	Appearance	Avg. Weight (mg)	Hardness (kg/cm²)	Friability (%)	Drug Content (%)	Drug Release at 12h (%)
0	No change	200.36 ± 1.08	6.12 ± 0.13	0.44 ± 0.03	100.12 ± 0.64	95.30 ± 0.45
1	No change	200.18 ± 1.10	6.08 ± 0.14	0.46 ± 0.04	99.68 ± 0.70	94.42 ± 0.48
2	No change	199.92 ± 1.12	6.02 ± 0.15	0.49 ± 0.04	99.12 ± 0.75	93.36 ± 0.51
3	Slight dullness	199.74 ± 1.16	5.94 ± 0.16	0.52 ± 0.05	98.54 ± 0.78	92.18 ± 0.55

DISCUSSION

The present study aimed to develop sustained release matrix tablets of Tolterodine Tartrate using hydrophilic polymers via direct compression. The formulations were evaluated for physicochemical properties, drug content, swelling, in vitro release, and stability to identify an optimized system.

Pre-compression studies showed good flow and compressibility, indicated by acceptable angle of repose, Carr's Index, and Hausner's Ratio, confirming suitability for direct compression and uniform tablet production.

Post-compression evaluation confirmed that all tablets met pharmacopeial standards for weight variation, thickness, hardness, friability, and drug content, with friability below 1%, indicating adequate mechanical strength.

Dissolution results showed that increasing polymer concentration slowed drug release due to enhanced gel barrier formation and reduced diffusion. Among all formulations, TT5 provided the most controlled release over 12 hours while maintaining acceptable tablet properties. Accelerated stability studies showed no significant changes in physical appearance, drug content, or release profile, confirming good stability of the optimized formulation.

Overall, hydrophilic polymers effectively controlled the release of Tolterodine Tartrate, and formulation TT5 demonstrated suitable sustained release characteristics for once-daily therapy in overactive bladder management.

CONCLUSION

The present study successfully demonstrated the formulation and evaluation of sustained release matrix tablets of Tolterodine Tartrate using HPMC and ethyl cellulose as release-controlling polymers. The selected excipients were found to be compatible with the drug, and the developed UV spectrophotometric method was suitable for analytical estimation. All formulation batches showed acceptable pre-compression and post-compression properties, confirming good manufacturability by direct compression. The *In-vitro* dissolution study confirmed that polymer concentration and polymer ratio significantly affected the drug release pattern. Among all formulations, TT5 showed the most suitable sustained release profile, with controlled initial release and prolonged drug release up to 12 hours. Stability studies further confirmed that TT5 retained its physical properties, drug content and release behavior under accelerated storage conditions. Therefore, the optimized formulation TT5 may be considered a promising sustained release tablet formulation for improving therapeutic efficacy, reducing dosing frequency and enhancing patient compliance in the treatment of overactive bladder syndrome.

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