Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
JPP 2019; 8(5): 1937-1940
Received: 11-07-2019
Accepted: 15-08-2019

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A review on extended release matrix tablet for overactive bladder

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Abstract
Darifenacin is extended for treatment of urge incontinence or increased urinary frequency that creates urgency in patients with overactive bladder and thus once a day extended release tablet eliminates the multiple dosing and the half life of drug is 13 hours. Extended release dosage forms release drug slowly, so that plasma concentrations are maintained at a therapeutic level for a prolonged period of time as usually between 8 and 24 hours. By incorporating the dose for 24hrs into one tablet from which the drug is slowly released, peaks of high plasma concentration and troughs of low plasma concentrations can be prevented. Avoids the high blood concentration. Maintain therapeutic concentration over prolonged periods. Film coating of tablet will mask the bitter taste of drug and also protect from moisture during storage.

Keywords: extended release, tablet, overactive bladder

Introduction

Overactive bladder [1, 6]

- "Overactive bladder causes a sudden urge to urinate and the urge may be difficult to stop, and overactive bladder may lead to the involuntary loss of urine (urge incontinence)."
- "If you have an overactive bladder, you may feel embarrassed, isolate yourself, or limit your work and social life as the good news is that a brief evaluation can determine whether there a specific cause for your overactive bladder symptoms."
- "The management of overactive bladder often begins with behavioural strategies, such as fluid schedules, timed voiding and bladder-holding techniques using your pelvic floor as if these initial efforts don't help enough with your overactive bladder symptoms, medication are available."
- "Overactive bladder is a common and distressing disorder that imposes significant financial and quality of life costs and the current therapeutic paradigm aims to decrease detrusor over activity via blockade of bladder M3 muscarinic receptors, the primary cholinergic receptors responsible for detrusor contraction."
- "However, systemic antimuscarinic adverse effects, such as dry mouth and constipation, limit the tolerability of antimuscarinic treatment and therefore, a uroselective M3 receptor antagonist would be considered optimal therapy for overactive bladder."
- "The frequent need to urinate may occur during the day, at night, or both, if there is loss of bladder control then it is known as urge incontinence as more than 40% of people with overactive bladder have incontinence as about 40% to 70% of urinary incontinence is due to overactive bladder as it is not life-threatening most people with the condition have problems for years."
- "Overactive bladder is a condition where there is a frequent feeling of needing to urinate to a degree that it negatively affects a person's life and the cause of overactive bladder is unknown as the risk factors include obesity, caffeine, and constipation.
- Poorly controlled diabetes as poor functional mobility and thus chronic pelvic pain may worsen the symptoms and people often have the symptoms for a long period of time before seeking treatment and the condition is some time identified by care givers.
- "Diagnosis is based on a person's signs and symptoms and requires other problems such as urinary tract infections or neurological conditions to be excluded."
- "The amount of urine passed during each urination is relatively small and pain while urinating suggests that there is a problem other than overactive bladder

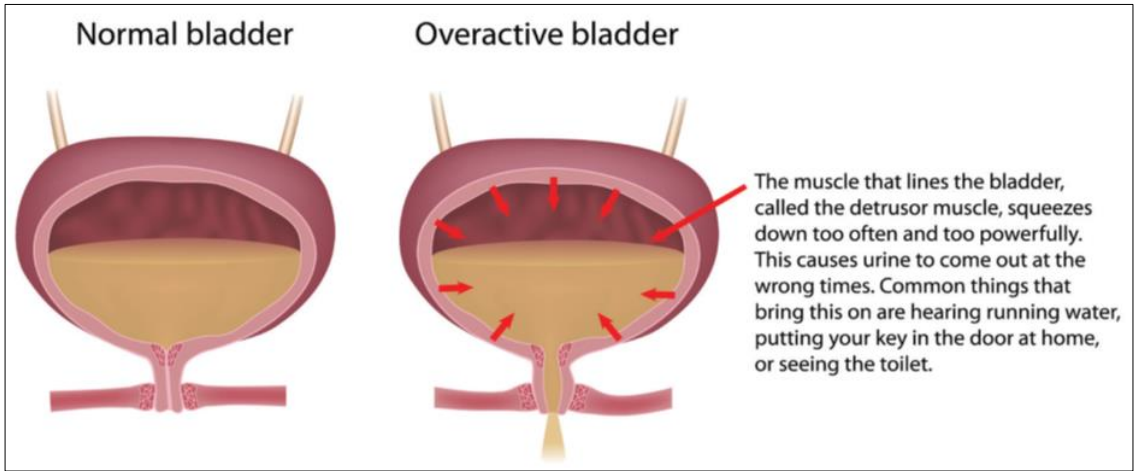

Fig 1: Overactive Bladder

Signs and symptoms

- Overactive bladder is characterized by a group of four symptoms:
- Urgency
- Urinary frequency
- Nocturia
- Urge incontinence

Introduction to Matrix Tablet

- Matrix tablet is defined as "Oral solid dosage form in which active pharmaceutical ingredient is uniformly dispersed throughout polymeric matrices (hydrophilic or hydrophobic) which retards the drug release rate.
- Matrix tablets are the type of controlled drug delivery systems, which release the drug in continuous manner.
- Diffusion controlled systems also known as matrix systems are very popular for sustained release formulations (Colombo *et al*. 2000). The can be divided up into different types of mechanisms by which they prolong drug release, these includes reservoir matrix systems, monolithic matrix systems and osmotic pump systems.

A. Classification based on the characteristics of rate controlling material

1. Hydrophillic type matrix
2. Hydrophobic type matrix
3. Lipid type matrix
4. Biodegradable type matrix
5. Mineral type matrix
6. Macroporous system
7. Microporous system
8. Non-porous System

Mechanism of drug release from matrix tablet [17, 18]

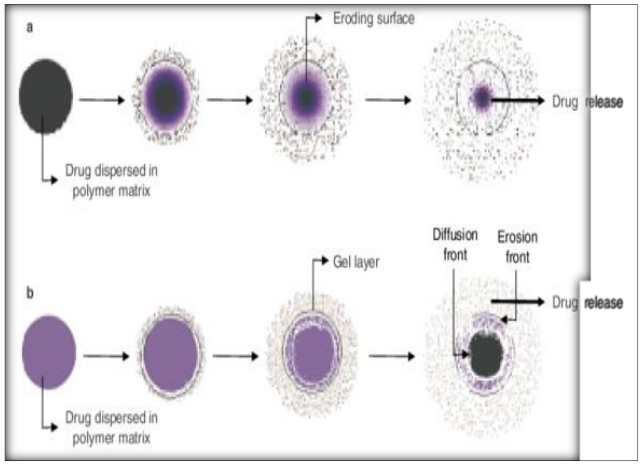

Fig 2: Disadvantage

Advantage

1. Maintains therapeutic concentrations over prolonged periods.
2. Avoids the high blood concentration.
3. Reduction in toxicity by slowing drug absorption.
4. Minimize the local and systemic side effects.
5. Improvement in treatment efficacy.
6. Better drug utilization.
7. Minimize drug accumulation with chronic dosing.
8. Can be made to release high molecular weight compounds.
9. Increase the stability by protecting the drug from hydrolysis or other derivative changes in GIT.
10. Reduction in health care cost.
11. Usage of less total drug.
12. Improvement of the ability to provide special effects. Ex: Morning relief of arthritis through bed time dosing.
13. Improved patient compliance.

Disadvantage

1. The remaining matrix must be removed after the drug has been released.
2. Greater dependence on GI residence time of dosage form.

3. Increased potential for first-pass metabolism.
4. Delay in onset of drug action.
5. Release rates are affected by food and the rate transit through the gut.
6. Release rate continuously diminishes due to increased diffusional resistance and decrease in effective area at the diffusion front.

Polymers used in matrix tablet

A) Hydrogels

1. Poly-hydroxyethyle methylacrylate (PHEMA)
2. Cross-linked polyvinyl alcohol (PVA)

B) Soluble polymers

1. Polyethylene glycol (PEG)
2. Polyvinyl alcohol (PVA)

C) Biodegradable polymers

1. Polylactic acid (PLA)
2. Polyglycolic acid (PGA)

D) Non-biodegradable polymers

1. Polyethylene vinyl acetate (PVA)
2. Polydimethyl siloxane (PDS)

E) Mucoadhesive polymers

1. Polycarbophil,
2. Sodium Carboxymethyl cellulose

F) Natural gums

1. Xanthan gum
2. Guar gum

Factors [7, 8]

❖ **Biological Factors Influencing Release From Matrix Tablet**

- Biological half-life.
- Absorption.
- Metabolism
- Distribution
- Protein binding
- Margin of safety

Physicochemical Factors Influencing Release from Matrix Tablet [10]

- Dose size:
- Ionization, pka and aqueous solubility
- Partition Coefficient

Materials and Method

Table 1: The percentage friability

Name of materials	Uses	Company Name
Darifenacin Hydrobromide	To treat an overactive bladder	SUN Pharma
HPMC K4M	Gelling agent, Release retarding agent	Vishal chem
HPMC K100M	Gelling agent, Release retarding agent	Vishal chem
Magnesium stearate	Lubricant	Vishal chem
Xantham Gum	Binding agent	Vishal chem
Lactose anhydrous	Diluents	Vishal chem
Talc	Glident	Vishal chem
Opadry orange	Colouring agent	Vapi care pharma

Method

Collecting of all excipients & drug (Darifenacin)
↓
Sifting
↓
Drug mixing with excipients
↓
Sifting of Drug -Excipients
↓
Blending
↓
Tablet compression
↓
Film coating

Results and Discussion

Evaluation of tablets

All batches of prepared tablets were evaluated for various parameters like hardness, friability, thickness, weight variation, content uniformity, in-vitro dissolution studies.

Tablet hardness

The crushing strength (Kg/cm2) of prepared tablets was determined by using Monsanto hardness tester. The hardness tests was performed for each batches of prepared tablets in triplicate manner.

Friability

Friability test was done by Roche Friabilator. Twenty tablets were weight (Wo) and were subjected to combined effect of attrition and shock by utilizing a plastic chamber that revolve at 25 rpm dropping the tablets at a distance of 6 inch with each revolution, operated for 100 revolutions. The tablets were dusted and reweighed (W) after completion of 100 revolutions. The percentage friability (Table 1) was calculated using following formula.

$$\% \text{ Friability} = W0 - W / W0 \times 100$$

Friability test

Friability test is performed to evaluate the ability of the tablet to withstand wear and tear in packing, handling and transporting.

Thickness

Ten tablets from each batch of formulations were selected randomly and thickness of tablets was measured using vernier caliper. The average value of thickness was calculated.

Weight Variation

For uniformity of weight, twenty tablets from each batch of formulation were selected at random and determined their individual weights by using electronic balance. Then, average weight and standard deviation of the tablets was calculated.

Uniformity of drug content

Assay of extended release tablets of Darifinacin was done in distilled water to find out the amount of drug present in one tablet. For this test, 5 tablets were weighed and powdered in a glass mortar and 200 mg of the powder equivalent to 8 mg of drug was placed in a stoppered 100 mL volumetric flask and dissolved in 100 mL water. The resulting solution was filtered and absorbance was measured at λmax 277 nm using UV visible spectrophotometer. The concentration of Darifinacin in milligram per milliliter (Table 1) was obtained from standard calibration plot of drug.

***In-vitro* drug release studies**

In-vitro release of Darifinacin from extended release tablets were determined using USP type II dissolution apparatus in 900 mL of phosphate buffer (pH 6.8) at constant temperature of 37° ± 0.5 °C at 50 rpm. Aliquots (5 mL) of the solutions were withdrawn from the dissolution apparatus at different time intervals and replaced with fresh dissolution medium to maintain the sink condition. These aliquots were filtered and the absorbance of these solutions were measured by using a double beam ultra-violet spectrophotometer at 277 nm against fresh phosphate buffer solution as blank. All the studies were conducted in triplicate and percent drug release was calculated by using the following formulae and the % drug release shown in Table 3.13.

% Drug Release = K × Absorbance

Where K can be calculated by using the equation as follows

K = Std. conc. × vol. of dissolution media × dilution factor × 100 / std. abs. × dose × 1000

Conclusion

Around 70% People are suffering from Overactive Bladder Disease, Which leads to Constioation and Obesity. To treate this Disease Darifinacine is Effective Drug, It is Class –II drug. Extended Release Matrix Tablet of Darifinacin Prove best choice.

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