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A REVIEW ON PULSATILE DRUG DELIVERY SYSTEM OF PERINDOPRIL ERBUMINE USING MODIFIED PULSINCAP TECHNOLOGY

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ABSTRACT

Pulsatile drug delivery systems (PDDS) are gaining significant attention in pharmaceutical research because they deliver drugs at a predetermined time after a specific lag period, thereby synchronizing drug release with the body's circadian rhythm. Perindopril Erbumine is an angiotensin-converting enzyme inhibitor widely used in the management of hypertension and cardiovascular disorders. Conventional dosage forms may not provide optimal therapeutic outcomes due to fluctuations in blood pressure during early morning hours. Modified Pulsincap technology offers a promising approach for chronotherapeutic delivery of Perindopril Erbumine by releasing the drug after a programmed lag time. The present review discusses the principles, rationale, formulation approaches, mechanism, advantages, evaluation parameters, and applications of pulsatile drug delivery systems with special emphasis on modified Pulsincap technology for Perindopril Erbumine.

KEYWORDS: Drug content uniformity, Weight variation, Lag time determination, In vitro dissolution studies, Swelling index, Stability studies.

INTRODUCTION

Pulsatile drug delivery systems are time-controlled drug delivery systems designed to release the drug rapidly after a predetermined lag time. These systems are particularly useful in diseases exhibiting circadian rhythm, such as hypertension, asthma, arthritis, peptic ulcer, and cardiovascular disorders. The main objective of PDDS is to deliver the drug at the right time, in the right amount, and at the right site.

Hypertension and cardiovascular events commonly show peak incidence during early morning hours. Therefore, chronotherapeutic drug delivery of antihypertensive drugs like Perindopril Erbumine can improve therapeutic efficacy and reduce side effects. Modified Pulsincap technology is one of the most promising capsule-based pulsatile systems developed to achieve delayed and rapid drug release after a desired lag time.

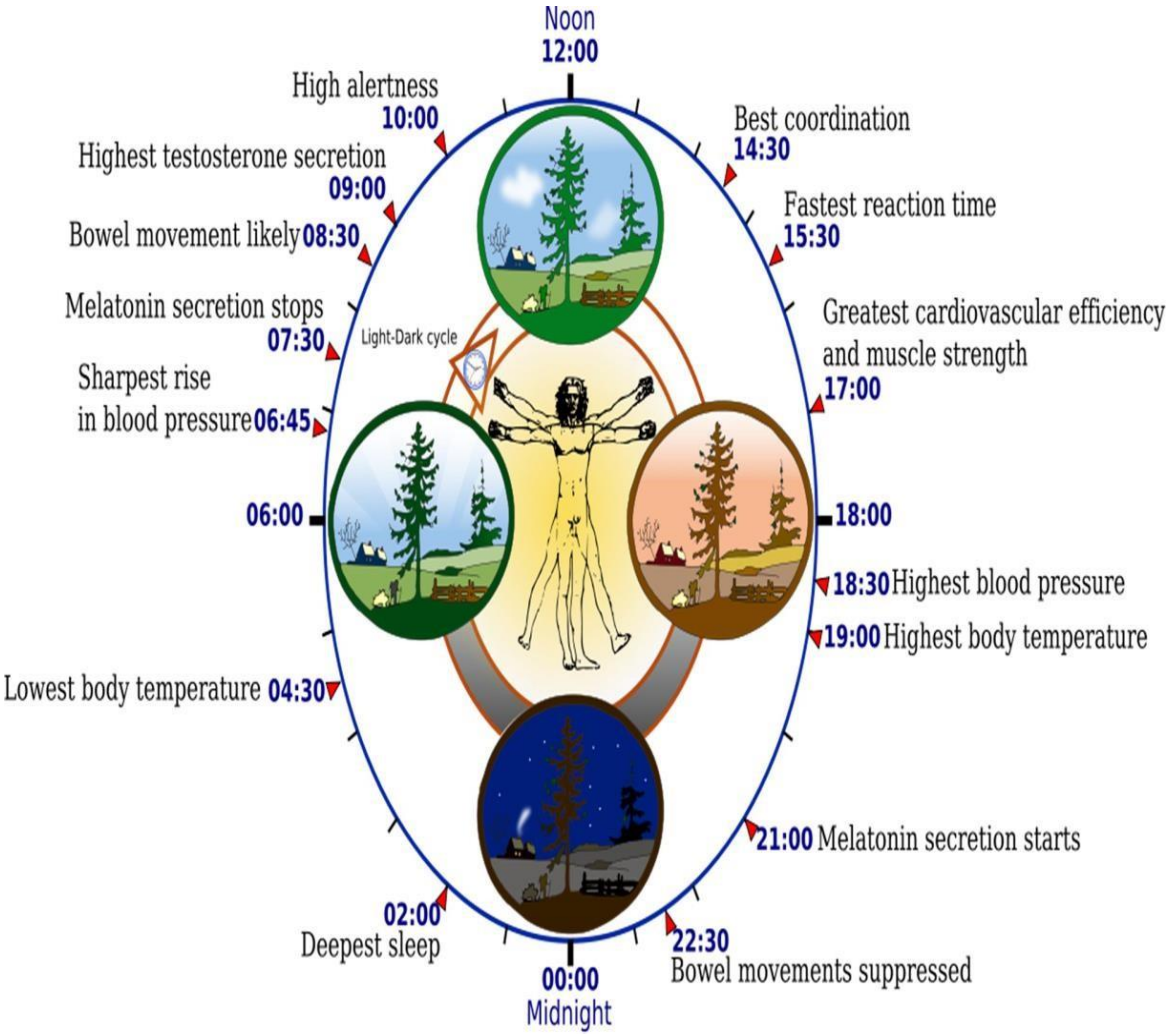


Figure: ***Cycle Of Circadian Rhythms.***

Pulsatile Drug Delivery System

- A pulsatile drug delivery system is characterized by.
- Rapid and complete drug release
- Presence of lag time before release
- Site-specific or time-specific delivery
- Synchronization with circadian rhythm
- These systems are mainly classified into:
- Time-controlled systems
- Stimuli-induced systems
- Externally regulated systems
- Capsule-based systems such as Pulsincap are widely used because of their simple design and controlled lag-time characteristics.

Chronotherapy and Hypertension

Blood pressure follows a circadian rhythm and generally increases sharply during the early morning period. This phenomenon is called the "morning surge." Cardiovascular complications such as myocardial infarction and stroke are more common during this period. Chronotherapeutic delivery of antihypertensive agents can provide maximum drug concentration when required most.

Perindopril Erbumine is suitable for pulsatile delivery because

- It has a short biological half-life
- Morning administration is therapeutically advantageous
- It is used in chronic cardiovascular conditions
- Controlled release can improve patient compliance

Perindopril Erbumine

Perindopril Erbumine is an ACE inhibitor used in.

- Hypertension
- Congestive heart failure
- Prevention of cardiovascular complications

Physicochemical Properties

- Drug class: ACE inhibitor

- Solubility: Freely soluble in water
- Half-life: Short biological half-life
- Indication: Hypertension and cardiovascular disorders
- Dose: Usually 4–8 mg

Because hypertension symptoms are more severe during early morning hours, pulsatile delivery of Perindopril Erbumine can improve therapeutic effectiveness.

DRUG PROFILE

PERINDOPRIL ERBUMINE

Chemical name: (2S, 3αŚ 7αŚ)-1-[(S)-N-[(S)-1-Carboxyl- butyl] alanyl] hexahydro-2-indoline carboxylic acid.

Empirical Formula: C23H43N3O5

Description:

Nature : White crystalline powder

Solubilty : Freely soluble in water

Log p : 2.6

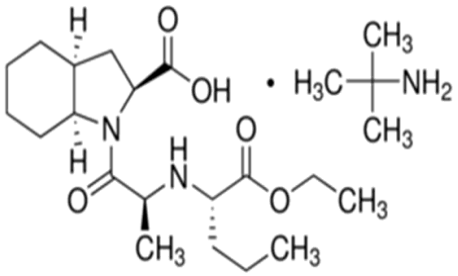
(Octanol/Water)

Melting Point : 126-128˚c Molecular weight : 441.61

Identification :

λmax at 215 nm in UV spectrophotometer.

Structure.



Pharmacodynamic Properties

Perindopril, an angiotensin-converting enzyme inhibitor, is a prodrug that the liver transforms into the active metabolite perindoprilat. By competing with the angiotensin converting enzyme, perindoprilat, the active metabolite, prevents angiotensin I from becoming angiotensin II. It is a negative feedback modulator of renin activity and a vasoconstrictor. Plasma renin rises and blood pressure falls as a result of the lower amounts. Kininase II, an enzyme that breaks down the vasodilator bradykinin and is similar to ACE, may likewise be

impacted by perindoprilat.

Properties of pharmacokinetics

- Rapid absorption following oral delivery.
- Parent chemical half-life is one hour, whereas active metabolite half-life is three to seven hours.
- Oral bioavailability: 25% for perindoprilat and 75% for perindopril
- Clearance: 219–36
- milliliters per minute [Oral administration]
- Metabolism: An enzyme in the liver transforms 30–60% of perindopril into the active metabolite perindoprilat.
- The mean renal clearance is 23.3-28.6 ml/min, while the total body clearance is 219-362 ml/min.
- Treatment indication: hypertension and stable coronary artery disease.
- Dosage: Tablet: 2 mg, 4 mg, 8 mg; maximum dose: 16 mg daily.
- side effects: Anaphylactoid responses, coughing, angioedema, hyperkalemia, postural hypotension, neutropenia, agranulocytosis, nausea, vomiting, and dizziness are some of the side effects.

Interactions between drugs

Diuretics: After starting perindopril erbumine treatment, patients using diuretics, particularly those who started lately, may occasionally have an abnormal drop in blood pressure. Diuretics used concurrently had no effect on the pace or degree of perindopril absorption and excretion. However, diuretics decreased the bioavailability of perindoprilat, which was linked to a reduction in plasma ACE inhibition.

Supplements containing potassium and diuretics that spare potassium: Perindopril erbumine may raise serum potassium due to its ability to reduce the synthesis of aldosterone. The use of potassium supplements, potassium sparing diuretics (such as amiloride, triamterene, and spirolactone), or medications that can raise serum potassium levels (such as cyclosporine, heparin, and indomethacin) might raise the risk of hyperkalemia. The patient's serum potassium level should be regularly checked, and such medications should be administered cautiously if concurrent usage is recommended.

Lithium: In individuals undergoing concurrent ACE inhibitor and lithium treatment, elevated blood lithium levels and signs of lithium toxicity have been seen. These medications should be used together carefully, and serum lithium levels should be checked often.
Focus is advised. Using a diuretic might make lithium poisoning much more likely.

Digoxin: Digoxin has not been demonstrated to have an impact on plasma digoxin concentrations when co-administered with perindopril erbumine in a controlled pharmacokinetic investigation; however, digoxin may have an impact on the plasma concentration of perindopril/perindoprilat.

Overdosing and Treatment: Diarrhea, anxiety, coughing, tachycardia, palpitations, bradycardia, hypotension, circulatory shock, electrolyte imbalances, renal failure, and hyperventilation are all possible side effects of taking too many ACE inhibitors. It is advised to provide a regular saline solution intravenously to cure overdosing. The patient should be put in the shock position if hypotension develops. If an intravenous catecholamine or an angiotensin II infusion is available, these treatments may also be tried. Hemodialysis is one way to take perindopril out of the general population. For bradycardia that is resistant to treatment, pacemaker therapy is recommended. It is important to regularly check serum electrolytes, creatinine levels, and vital signs.

Storage: A dry, dark, and cold environment is ideal for its storage.

Extra cautions: Avoid using potassium supplements without first seeing a doctor. Avoid taking during pregnancy.

Angioedema history is a contraindication.
[ACE inhibitors may harm or even kill the baby during pregnancy.] Hypersensitivity and Hypotension to Perindopril

Brand names include Aceon, Coversyl Plus, Povinace, and Apoperindopril.

Modified Pulsincap Technology

Modified Pulsincap technology is a capsule-based pulsatile delivery system designed to release the drug after a predetermined lag period.

Structure of Modified Pulsincap

The system generally consists of.

- Water-insoluble capsule body
- Drug reservoir
- Hydrogel plug
- Enteric coating or polymer coating
- The hydrogel plug controls the lag time by swelling or erosion. After the lag period, the plug is expelled, resulting in rapid drug release.

Mechanism of Drug Release

- Capsule enters gastrointestinal tract
- Water penetrates through capsule shell
- Hydrogel plug swells gradually
- Plug gets expelled after predetermined lag time
- Rapid release of Perindopril Erbumine occurs

Advantages of Modified Pulsincap Technology

- Site-specific drug delivery
- Time-controlled drug release
- Improved bioavailability
- Reduced dosing frequency
- Better patient compliance
- Synchronization with circadian rhythm
- Reduced side effects
- Suitable for chronotherapeutic diseases

Polymers Used in Modified Pulsincap

Common polymers used include:

- Hydroxypropyl methylcellulose (HPMC)
- Polyethylene oxide
- Carbopol
- Ethyl cellulose
- Sodium alginate
- These polymers control swelling, erosion, and lag time.

The formulation of Perindopril Erbumine modified Pulsincap involves

- Preparation of drug reservoir
- Selection of suitable capsule body
- Preparation of hydrogel plug
- Assembly of capsule components
- Coating process
- Evaluation studies
- Evaluation Parameters

Important evaluation tests include

- Drug content uniformity
- Weight variation
- Lag time determination
- In vitro dissolution studies
- Swelling index
- Stability studies

Applications of Pulsatile Drug Delivery System

PDDS are useful in diseases with circadian rhythm such as.

- Hypertension
- Asthma
- Arthritis
- Diabetes mellitus
- Peptic ulcer
- Hypercholesterolemia

Limitations

Despite advantages, PDDS have some limitations:

- Complex manufacturing process
- Higher production cost
- Risk of dose dumping
- Difficulty in maintaining precise lag time
- Stability issues
- Future Perspectives

Advancements in polymer science and chrono pharmaceutical technology are expected to improve pulsatile drug delivery systems. Modified Pulsincap technology may become more effective with.

- Smart polymers
- Nanotechnology-based systems
- Improved capsule materials
- Personalized chronotherapy
- Future research may focus on enhancing stability, reproducibility, and commercialization of Perindopril Erbumine pulsatile formulations

CONCLUSION

Pulsatile drug delivery systems represent an advanced approach for chronotherapeutic management of hypertension and cardiovascular disorders. Modified Pulsincap technology provides a reliable method for achieving delayed and rapid release of Perindopril Erbumine after a predetermined lag time. This system improves therapeutic efficacy, minimizes side effects, and enhances patient compliance by synchronizing drug release with circadian rhythms. Therefore, modified Pulsincap technology has great potential in the development of effective chronotherapeutic formulations for cardiovascular diseases.

Microspheres for continuous release after a predetermined lag period and an immediate release dosage were used in the successful development of a time-controlled chronomodulated pulsatile perindopril erbumine drug delivery system.

According to the investigation's findings, pulsincap dosage forms of perindopril erbumine may be an effective way to manage hypertension in the morning. (2–4 am)

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