RESEARCH PAPER

Formulation and Evaluation of Prednisolone Sustained-Release Matrix Tablets Using HPMC Polymers

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ABSTRACT

Prednisolone, a corticosteroid widely prescribed for the long term management of chronic inflammation disorders, presents a pharmacokinetic challenge due to its relatively short biological half-life, which necessitates frequent dosing and compromises patient adherence. The present study aimed to develop and evaluate a 200 mg sustained release matrix tablet of Prednisolone using HPMC as the primary release-retarding polymer. Preformulation characterisation conducted via FTIR and melting point determination confirmed the physiological compatibility of the drug with selected excipients. Tablets were prepared by wet granulation incorporating HPMC at varying concentrations, and the resultant granules exhibited favourable flow behavior with an angle of repose below 40°. Post-compression evaluation confirmed compliance with the pharmacopoeial standards, with weight variation within 7.5% and friability not exceeding 1%. In-vitro dissolution studies performed using USP Apparatus II (Paddle system) at 50 rpm in 900 ml of dissolution medium demonstrated controlled, progressive drug release, achieving approximately 92% cumulative release over 8 hours. The developed formulation presents a technically sound and therapeutically meaningful approach to reducing frequency, sustained plasma drug concentration within the therapeutic range, and improving treatment outcomes in patients with chronic inflammatory conditions.

Key words: Prednisolone, HPMC, Sustainable Release, Matrix tablet, USP Apparatus II.

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Introduction

Prednisolone is a synthetic corticosteroid that belongs to the glucocorticoid class of steroid hormones[1]. It is widely employed in clinical practice to manage a broad spectrum of conditions, including allergic disorders, chronic inflammatory diseases, autoimmune pathologes, certain malignancies, electrolyte disturbances, and dermatological conditions[2,3]. Among the specific conditions addressed are adrenocortical insuficiency, hypercalcemia, rheumatoid arthritis, dermatitis, ocular inflammation, asthma, multiple sclerosis, and phimosis[4]. The drug is versatile in its route of administration; it may be taken orally, administered intravenously, applied as a topical cream, or insailled as eye drops[5].

Side effect profile

Short-term administration of prednisolone is commonly associated with nausea, difficulty in concentrating, sleep disturbances, heightened appetite, and generalized fatigue. Psychiatric manifestations, although less frequent, are reported in approximately 5% of patients. When used over extended periods, corticosteroids tends to cause bone density loss, muscular weakness, opportunistic fungal infections, and increased skin frability. Although brief use during the later stages of pregnancy is generally regarded as acceptable, prolonged use or use during early pregnancy carries a risk of adverse fatal outcomes, albetit infrequently. Prednisolone is derived from hydrocortisone (cortisol) via the glucocorticoid synthesis pathway[6,7].

Historical and clinical context

Prednisolone was first identified and approved for therapeutic use in 1955 and has since been incorporated into the World Health Organization's List of Essential Medicines, underscoring its global clinical significance. It is widely accesible as a generic formulation. In the United States alone, its ranked as the 146th most frequently prescribed drug in 2023, with prescription volumes exceeding three million[5,7].

Medical applications

Mechanism of Anti – Inflammatory action

At lower therapeutic doses, prednisolone functions primarily as an anti-inflammatory agent, whereas

higher doses confer immunosuppressive properties[8]. Its mechanism involves the inhibition of the inflammatory cascade, which is triggered by various stimuli. Specifically, it suppresses tissue edema, fibrin deposition, capillary dilation and proliferation, leukocyte migration, fibroblast activity, collagen deposition, and ultimately, scar tissue formation.[9]

Systemic use

Given its predominantly glucocorticoid activity with minimal mineralocorticoid effects, prednisolone is therapeutically useful for a diverse range of inflammatory and autoimmune conditions.[10] These include asthma, uveitis, pyoderma gangrenosum, rheumatoid arthritis, urticaria, angioedema, ulcerative colitis, pericarditis, temporal arteritis, Crohn's disease, Bell's palsy, multiple sclerosis, cluster headaches, vasculitis, acute lymphoblastic leukemia, autoimmune hepatitis, systemic lupus erythematosus, Kawasaki disease, dermatomyositis, post-myocardial infarction syndrome, and sarcoidosis[11,12].

It is also used to manage allergic responses, ranging from seasonal allergies to drug-induced hypersensitivity reactions. Additionally, prednisolone may be used as an immunosuppressive agent following organ transplantation, and at lower doses, it is used in replacement therapy for patients with adrenal insufficiency secondary to Addison's disease[13].

Topical use : Ophthalmology

Topical prednisolone is widely used in ophthalmology. It is administered as eye drops for conditions such as chemical or thermal corneal injuries, foreign body-related ocular injury, eye inflammation, mild-to-moderate non-infectious allergies, eyelid and conjunctival disorders, postoperative ocular inflammation, and optic neuritis[14]. Potential ocular side effects include elevated intraocular pressure (glaucoma), blurred vision, ocular discomfort, delayed wound healing, optic nerve scarring, posterior subcapsular cataracts, and urticaria; however, the exact incidence rates remain undetermined[15].

Prednisolone eye drops are contraindicated in patients who demonstrate hypersensitivity to the drug and in those with ocular tuberculosis, herpes zoster ophthalmicus, raised intraocular pressure, or fungal eye infections.[16]

Prednisolone acetate ophthalmic suspension is a sterile formulation designed to reduce ocular swelling, redness, pruritus, and allergic responses. It has also been investigated as a potential treatment for bacterial keratitis.[17] Specific indications for ophthalmic use include allergic and bacterial conjunctivitis, marginal keratitis, uveitis, endophthalmitis, Grave's ophthalmopathy, herpes zoster keratitis, postsurgical inflammation, radiation-and chemically induced corneal damage, myringosclerosis prevention, herpes simplex stromal keratitis, and post-laser peripheral iridotomy inflammation in patients with primary angle-closure suspects.[18]

Adverse effects

Prednisolone administration is associated with a range of adverse effects.

This includes :

- Increased appetite and body weight
- Nausea
- General malaise
- Heightened susceptibility to infection
- Cardiovascular complications

Dermatological reactions may include:[19]

- Facial flushing
- Skin bruising
- Skin thinning
- Rash
- Oedema
- Impaired wound healing
- Abnormal hair growth

Metabolic disturbances include : [20]

- Hyperglycaemia - necessitating dosage adjustments in diabetic patients
- Menstrual irregularities
- Impaired hormonal responsiveness, particularly during physiological stress, such as surgery or illness, and electrolyte imbalances characterized by elevated blood pressure, hypernatremia, hypokalemia, and metabolic alkalosis.[21]

Gastrointestinal effects may include the following:

- gastric mucosal inflammation
- transient elevation of hepatic enzymes
- increased risk of peptic ulceration

Musculoskeletal complications include:

- muscle weakness and wasting
- steroid-induced osteoporosis
- long bone and vertebral fractures
- tendon rupture

Neurological manifestations may include seizures, headaches, and vertigo. Behavioral and psychiatric disturbances are also recognized, with aggression being particularly prevalent, especially with oral administration.[23]

In rare cases, nasal septum or bowel perforations may occur. Abrupt discontinuation of prednisolone following prolonged or high-dose therapy may cause adrenal insufficiency. Mania and hypomania are recognized as psychiatric sequelae, albeit less common.[24]

Pregnancy and Breastfeeding

Despite the absence of large-scale human studies, animal models have demonstrated the potential for teratogenicity, most notably an elevated incidence of cleft palates. Prednisolone has been detected in human breast milk following maternal administration. Its systemic use is associated with measurable levels in breast milk, which may adversily affect neonatal growth.[25] Accordingly,

the use of prednisolone during breastfeeding is generally discouraged. Its use during pregnancy is recommended only when the anticipated clinical benefit clearly outweighs the potential risk to both the mother and fetus.[26]

Ocular side effects (Local)

With prolonged topical ocular use, prednisolone may contribute to posterior subcapsular cataract formation, which can impair reading vision by obstructing the light path to the retina. Long-term use can also lead to progresive corneal or scleral thinning, which, if untreated, may progress to corneal perforation[27]. Furthermore, sustained corticosteroid eye drop use can cause elevated intraocular pressure, potentially damage the optic nerve, and reduce visual acuity. Patients receiving corticosteroid eye drops for > 103 consecutive days typically require ongoing monitoring of intraocular pressure, particularly those with pre-existing glaucoma.[28]

Pharmacology

Pharmacodynamics

As a lipophilic glucocorticoid, prednisolone readily crosses cell membranes and binds to glucocorticoid receptors (GCRs) in the cytoplasm. This binding triggers the release of chaperone proteins and facilitates the translocation of the glucocorticoid-receptor complex into the nucleus within approximately 20 min [29].Once inside, the homodimer complex interacts with glucocorticoid response elements (GREs) on DNA, modulating gene expression. Interactions with positive GREs promote the synthesis of anti-inflammatory proteins, whereas negative GRE binding suppresses the transcription of pro-inflammatory genes.[30]

Prednisolone inhibits key inflammatory mediators, including nuclear factor-kappa B (NF-κB), activator protein-1 (AP-1), and nuclear factor of activated T-cells (NFAT), while upregulating anti-inflammatory signals, such as interleukin-10.[31] Collectively, these effects inhibit prostaglandin synthesis, suppress neutrophil demargination and apoptosis, and inhibit phospholipase A2, thereby reducing the production of arachidonic acid-derived inflammatory mediators.[32]

Pharmacokinetics

Prednisolone exhibits a relatively short plasma half-life of 2–4 h and has a broad therapeutic window. It is 70–90% bound to plasma proteins, primarily to albumin.[33]

Both prednisolone phosphate and prednisolone acetate undergo ester hydrolysis in vivo to yield the active form of prednisolone, which then follows the standard metabolic pathways. Co-administration with potent CYP3A4 inhibitors, such as ketoconazole, has been shown to increase plasma prednisolone concentrations by approximately 50% due to reduced clearence. Elimination occurs predominantly via the kidneys, with excretion in urine as sulfate conjugates and glucuronide metabolites.[34]

Relationship with Prednisone

Prednisone is a pharmacologically inactive prodrug that undergoes hepatic biotransformation to its active metabolite, prednisolone, following systemic absorption.[35]

Chemistry

Prednisolone is a synthetically derived pregnane corticosteroid that is structurally analogous to prednisone, differing only by two fewer hydrogen atoms at the C11 position. It is also known by several chemical designations, including δ1-cortisol, δ1-hydrocortisone, 1,2-dehydrocortisol, and 11β,17α,21-trihydroxypregna-1,4-diene-3,20-dione.[36.37]

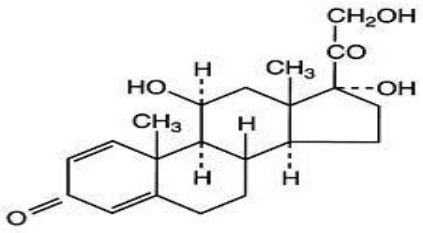

Figure 1 : Structure of Prednisolone

Drug Interactions :

The concurrent use of prednisolone eye drops with ophthalmic nonsteroidal anti-inflammatory drugs (NSAIDs) may potentiate adverse effects, including drug toxicity, and may further delay wound healing. Systemic drug interactions include co-administration with immunosuppressants such as azathioprine or ciclosporin, antiplatelet agents such as clopidogrel, anticoagulants such as warfarin or dabigatran, and NSAIDs such as aspirin, celecoxib, and ibuprofen.[38,39]

Special Populations

Paediatrics :

In children, particularly those below 6 years of age, prolonged use of prednisolone eye drops carries a dose-dependent risk of raising intraocular pressure, with younger children demonstrating heightened susceptibility. [40,41]

Mechanism of sustained-release system

Sustained-release (SR) oral delivery systems are frequently designed using dissolution as the primary time-limiting step, owing to their relative ease of formulation. For drugs with high intrinsic solubility, a common strategy involves incorporating the active pharmaceutical ingredient (API) into a matrix or carrier with a significantly lower dissolution rate. [42,43]

In systems governed by diffusion layer control, the rate-limiting step is the migration of the drug from the solid surface through a stagnant, unstirred liquid film into the bulk solution. Under steady-state

conditions, this kinetic process is characterized by the Noyes-Whitney equation: [45]

$$dc/dt = K_D A (C_s - C)$$

Where,

- dc/dt is the dissolution rate (change in concentration over time).
- K_D is the dissolution rate constant that reflects the permeability of the diffusion layer.
- A denotes the effective surface area of the dissolved solid.
- C_s is the saturation solubility of the drug in a specific dissolution medium.
- C is the concentration of the drug in the bulk solution at time, t.
- Dissolution formulation solution is categorised as
- Encapsulation dissolution control
- Matrix dissolution control

1.Encapsulation-Based dissolution control (reservoir system): [46]

This approach involves applying a rate-limiting, slowly erodible coating to individual drug particles or granules. These coated multiparticulates offer formulation flexibility, as they can be processed into compressed tablets (often referred to as "spacetabs") or encapsulated within hard gelatin shells (e.g., "spansule" delivery systems) [47]. The release profile is governed by the thickness and physicochemical properties of the coating material, which dictate the rate at which the core is exposed to the dissolution medium. [48]

2. Matrix-Based dissolution control

In matrix-controlled systems, the active pharmaceutical ingredient (API) is homogeneously compressed with a slowly dissolving carrier to create a monolithic solid dosage form. The kinetics of drug availability are primarily determined by the rate of aqueous flux into the tablet matrix. This penetration is a function of the internal architecture of the system, specifically its porosity and tortuosity. Furthermore, the incorporation of hydrophilic excipients and the inherent wettability of particle surfaces serve as critical modulators of the overall dissolution rate.

1. Diffusion-controlled release is of two types:
2. Encapsulation diffusion control
3. Matrix diffusion control

1.Encapsulation diffusion control (reservoir system)

Diffusion-controlled encapsulation or reservoir systems utilize a water-insoluble polymeric membrane to sequester a central drug core. Unlike dissolution-based coatings, this membrane remains intact; the drug partitions from the core into the polymer barrier and subsequently diffuses into the surrounding physiological fluid. The release rate is typically driven by the concentration gradient across the membrane and is influenced by the permeability of the polymer and the partition coefficient of the drug.

The rate of drug release is given by the equation

$$d_m/d_t = ADK\,\Delta c$$

where,

A = Area

D = Diffusion constant

K = Partition coefficient of the drug between the membrane and the drug core

Δc = The concentration difference across the membrane

2. Matrix diffusion control

In matrix-dispersion systems, the solid active pharmaceutical ingredient (API) is uniformly distributed within a lipophilic or hydrophilic polymeric network. The primary determinant of the release kinetics is the rate of molecular diffusion through the polymer matrix, rather than the intrinsic dissolution rate of solid drug particles. In this model, the matrix acts as a fundamental barrier to drug liberation.

Excipient profile:

1. HPMC K100 : Hydroxypropyl methyl cellulose

A high-viscosity grade of Hypromellose used primarily as a rate-controlling polymer in hydrophilic matrix systems. It forms a robust gel layer upon hydration, regulating the sustained release of the active pharmaceutical ingredients (API).

2. Lactose :

A widely used diluent or filler known for its excellent compression properties and physical stability. It is often employed to increase the bulk volume of the formulation, ensuring content uniformity in low dose tablets.

4. Starch :

A versatile excipient that typically functions as a disintegrant or binder. In its native form, it facilitates the breakup (disintegration) by wicking moisture into the dosage form, though it can also provide structural integrity to the granules.

5. Talc :

A hydrous magnesium silicate used as a glidant or anti-adherent. It improves the flowability of a powder blend by reducing interparticulate friction and prevents the formulation from sticking to the punch faces during compression.

6. Magnesium stearate :

The most common lubricant used in tablet manufacturing. It reduces friction between the tablet mass and the die wall during ejection, ensuring a smooth manufacturing process and preventing mechanical defects in the final dosage form.

Table 1 : Ingredients required

S No.	Ingredients	% w/w	Amount per tablet (mg)	Used as :
1.	Prednisolone	2.5 %	5 mg	Active pharmaceutical ingredient
2.	HPMC K100	30 %	60 mg	Matrix forming sustained release polymer
3.	Lactose	60 %	120 mg	Diluent
4.	Starch	5%	10 mg	Binder
5.	Talc	1.5 %	3 mg	Glidant
6.	Magnesium stearate	1%	2 mg	Lubricant
	Total	100 %	200 mg	-

Method of Preparation :

Step 1 : Weighing

Weigh all the ingredients properly using weighing balance and butter paper .

Step 2 : Shifting

Pass prednisolone, HPMC,and lactose through a #40 mesh sieve to ensure uniform particles size and remove aggregates.

Step 3 : Dry blending

Then mix the sifted API and excipients in a Rapid Mixer Granulator (RMG) or a double cone blender for 10-15 minutes to ensure a homogenous mix.

Step 3: Binder preparation

Dissolve PVP K-30 in the solvent (IPA is often preferred for prednisolone to minimize moisture-related degradation) until a clear, viscous solution is formed.

Step 4 : Addition of Binder

Slowly add the binder solution to the dry mix while maintaining the constant stirring.

Step 5 : Wet massing

Continue mixing until a Slug or Snowball consistency is achieved. If using an RMG, monitor the impeller and chopper speed to avoid over – granulation.

Step 6 : Wet Screening

Pass the wet mass through a #10 or #12 mesh sieve to create uniform granules .

Step 7 : Drying

Dry the granules in a fluidized bed dryer (FBD) or Tray dryer at 40 °C- 45 °C.

Note : Dry until the Loss of Drying (LOD) is between 1%-3%. Over drying can cause tablet capping, while under- drying causes sticking.

Step 8 : Dry Screening

Pass the dried granules through a 20 # mesh sieve to achieve the final granules size of compression .

Step 9 : Lubrication

Add the extra-granular materials (Magnesium Stearate and Talc) to the dry granules. Blend for 3-5 minutes. Over-blending here can waterproof the granules and retard disintegration excessively.

Step 10: Compression

Compress the tablets using a rotary tablet press.

Note : Target hardness – Generally higher for Sustained release tablet (7-10 kg/cm^2) to ensure the matrix stays intact during the initial phase of dissolution.

Pre formulation studies :[50,51]

1. Organoleptic Properties ----

Table 2 : Organoleptic properties

S No.	Properties	Observation	Inference
1.	Appearance	Crystalline	Indicates a stable solid-state structure
2.	Color	White to pale yellowish-white	Standard color for high-purity API
3.	Odor	Odorless	Absence of volatile impurities or degradation
4.	Taste	Slightly bitter	Characteristics of many H2-receptor antagonists
5.	Texture	Fine, free-flowing powder	Good for uniform mixing with HPMC

2. Flow Properties ----

A. Bulk density :

Procedure – Carefully weigh your 1-gram sample . Pour a sample into a 10 ml measuring cylinder and note the reading.

Formula : Bulk density = Mass / Bulk volume

Figure 2 : Bulk density

B. Tap density :

Procedure – Carefully tap the cylinder on a soft rubber mat from a height of 3 mm until the volume is constant .

Formula : Tapped density = Mass / Tapped volume

Figure 3 : Tapped density

C. Angle of repose :

Mount the dispenser : Fix the pipette tip on a stand so the opening exactly 2-3 cm above the centre of your platform .

Slow addition : Carefully pour your 1 g sample into the tip . Do not vibrate the stand .

Form the cone : Allow the powder to drop onto the platform until it forms a symmetrical cone that covers the entire surface of your platform .

S No.	Parameter	Observation 1	Observation 2	Average	Inference
1.	Bulk density	0.32	0.34	0.33	Indicates initial packing state
2.	Tap density	0.45	0.47	0.46	Maximum packed density after mechanical tapping
3.	Carr's index	28.8	27.6	28.2	Poor
4.	Hausner's ratio	1.40	1.38	1.39	Poor
5.	Angle of repose	42 °	44 °	43 °	Slightly poor

Measure height : Use the depth gauge of a digital callipers to measure from the peak of the powder cone down to the surface to the platform .
Measure Radius : If the powder covers your platform perfectly , r = diameter/2
Formula of Angle of repose : $\tan \theta = h/r$

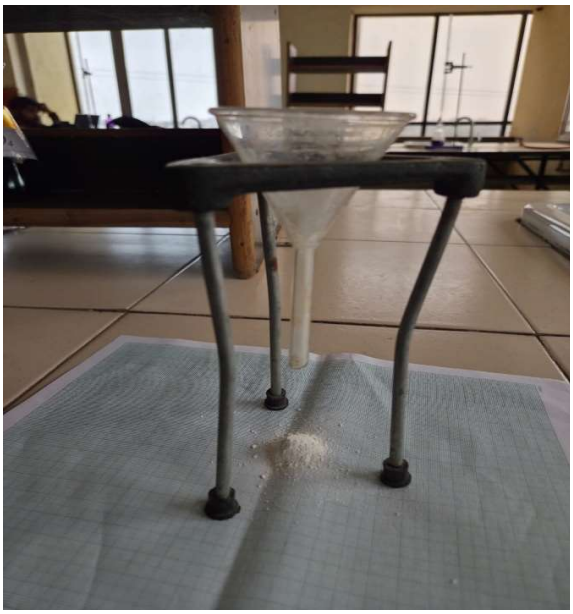

Figure 4 : Angle of repose

Table 3 : Flow properties

4. Melting point :

Procedure :

1. Prepare the thiele tube – Fill the thiele tube with liquid paraffin or silicone oil just above the top side arm inlet
2. Sample packing – Pack the Prednisolone into a capillary tube 2-3 mm height.
3. Attach to thermometer – Use a small rubber band to attach the capillary to the thermometer. The bottom of the capillary must be level with the mercury bulb of the thermometer.
4. Heating – Apply the Bunsen burner flame only to the side arm of the Thiele tube . Heat the side arm steadily until the temperature reaches (145 °- 150 °) C. Reduce the flame or move the burner in and out to slow rise to (1 °-2 °) C per minute.

Observation – Note the temperature where the first particle of API melts up to all the particles in the capillary tube melts completely.

Figure 5 : Melting point

Result : **Table 4 : Melting point**

Temperature	Standard	Observed 1	Observed 2	Observed 3	Average
T 1 (Temperature at which the first particle melts)	230 °	228 °	229°	228°	228 °
T 2(Tempera ture at which	235 °	233 °	234°	232°	233 °

HPLC method for Prednisolone Analysis:[50]

Chromatographic system : The analysis was performed using a reversed- phase C18 column (250*4.6 mm, 5 micrometre). The mobile phase consisted of a mixture of Water and Methanol(60:40 v/v), delivered isocratically at a flow rate of 0.9 mL/min. Detection was carried out at a wavelength of 254 nm with an injection volume 20 microlitre.

Sample preparation : A stock solution was prepared by dissolving 10 mg of prednisolone powder in 100 ml of mobile phase (100 microgram/mL). For the analytical working solution (10 microgram/mL), a 1 ml aliquot of the stock was diluted to 10 ml with the mobile phase. All solution were filtered by PVDF membrane prior to injection.

Result :

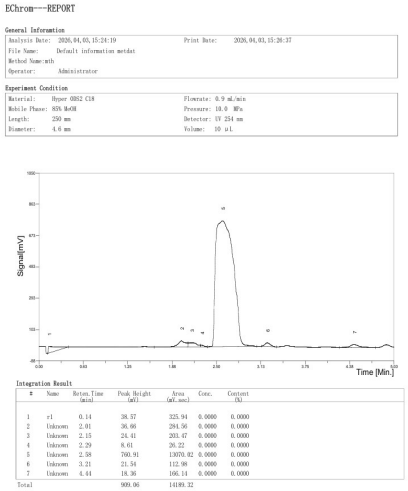

Figure 6 : HPLC test

UV-Visible Spectroscopy analysis :[51]

Procedure :

1. Preparation of Standard and Sample solution –

   - Stock solution preparation –

     Weigh 5 mg of prednisolone and put it in a 50 ml volumetric flask. Add 10 ml of methanol to the flask. Sonicate it for 2-3 minutes . Makeup the volume up to 50 ml with the use of methanol .

   - Working solution preparation –

     Pipette out 0.5 ml from the stock solution and put it in a 10 ml volumetric flask. Similarly take out 1 ml, 2 ml, 3 ml, and 4 ml and put each in different volumetric flask of 10 ml.

     Dilute each flask using 10 % methanol water up to 10 ml and mix it well.

2. Analytical procedure –

- Baseline correction –

  The instrument was first run with a blank sample (solvent : Methanol) across the specific wavelength range.

- Wavelength determination –

  The working solution was then scanned to determine the wavelength of maximum absorbance. For prednisolone drug it is recorded as 246 nm.

- Absorbance measurement –
  Repeat this experiment for every sample concentration to ensure reproducibility.

No.	Sample name	Absorbance	Concentration (mg/mL)
01	Sample 1	-3.585	-5.3745
02	Sample 2	0.153	0.2286
03	Sample 3	0.187	0.2807
04	Sample 4	0.134	0.1937
05	Sample 5	0.108	0.1621
06	Sample 6	0.011	0.0168

Table 5 : UV Spectroscopy result

Evaluation testing :[53,54]

Hardness test –

Procedure :

Apparatus used : Monsanto

Put the tablet between the jaws of the apparatus and apply force until it fracture.

Result :

Table 6 : Hardness test

Tablet	Hardness (kg/cm^2 or Newton)
Tablet 1	6.4
Tablet 2	6.2
Tablet 3	6.4
Average	6.3

Weight variation test –

Procedure : Weigh 20 tablets individually and calculate its average weight.

Result –

Table 7 : Weight variation

Parameter	Observed value
Average weight	200.5 mg
Maximum weight	208.2 mg
Minimum deviation	192.4 mg
Percentage deviation limit	+7.5 % or -7.5 %
Status	Passes

Dissolution test –

Apparatus selection :

1. Apparatus 1 – The standard for immediate release and modified release formulation .
2. Apparatus 2 – The standard for capsule and tablet especially which floats.

Preparation of dissolution system –

Selection of the medium : Media consists 0.1 N HCl and phosphate buffer , it mimics physiological condition .

Degassing : Media should be degassed to prevent air bubbles from acting as a physical barrier on the surface of the dosage form , also affecting hydrodynamics.
Volumes : Standard volumes are 500 ml, 900 ml, 1000 ml .
Procedure –
Setup of temperature : Heat the medium using water bath at 37 °+0.5 °C to stimulate human body temperature .
Dosage placement : Apparatus 1 (Paddle) : Drop the dosage form at the bottom of the vessel before starting rotation .
Rotation speed : Set the RPM (usually at 50 RPM).
Sampling : Withdraw samples at specific time intervals (example- 5,15,30,45,60 minutes)
Analysis : Sample must be filtered immediately to stop further dissolution .
Use UV-Visible Spectroscopy or HPLC to determine concentration of
drug release .
Result : This test is conducted using USP apparatus II (Paddle) at 50 rpm. This formulation exhibit a controlled release pattern of 25.6 % in 2 hours and sustained release of 92% over 8 hours .

Table 8 : Dissolution rate

Time (hours)	**%Drug released**	**Purpose**
2	20-30 %	Initial burst
4	50-60 %	Intermediate sustained release
6	75-80 %	Late sustained release
8	>90%	Near complete release

Result :
Table 9 : Final Result

S No.	**Parameter**	**Result**
1.	Bulk density	0.33
2.	Tap density	0.46
3.	Angle of Repose	43 °
4.	Melting point	228°-233°
5.	Hardness test	6.7 kg/cm^2
6.	Weight variation	200.5 mg (Average)
7.	Dissolution test	This formulation exhibit a controlled release pattern of 25.6 % in 2 hours and sustained release of 92% over 8 hours .

Conclusion :

The present investigation successfully developed and evaluated a sustained release matrix tablet of Prednisolone (200 mg) employing HPMC as the rate controlling polymer. Pre-formulation studies confirmed physiochemical compatibility between the drug and selected excipients, establishing a sound basis for formulation development.
All formulated tablets complied with pharmacopoeial quality control specification as per the Indian Pharmacopoeia(IP). Weight variation remained within the limit and the drug content uniformity was confirmed across the batches, reflecting the precision of the manufacturing process.
In-vitro dissolution studies conducted using USP Apparatus II (Paddle method) demonstrated that the HPMC-based matrix effectively modulated drug release, achieving upto 92% release over 8 hours. The developed formulation presents a clinical meaningful approach to optimizing Prednisolone therapy in inflammation and other diseases .

References:

1.World Health Organization. Stuart MC, Kouimtzi M, Hill SR (eds.). WHO Model Formulary 2008. World Health Organization. 2009:221.

2. Andrawis M, Ellison LC, Riddle S, Mahan K, Collins CD, Brummond P, Carmichael J. Recommended quality measures for health-system pharmacy:
2019 update from the Pharmacy Accountability Measures Work Group. American Journal of Health-System Pharmacy. 2019 Jun 15;76(12):874-87.
3. Sayeed MA, Fiza S, Ayesha N, Sayeed MA. Association Rule Mining of Inactive Ingredients in Drugs. INTERNATIONAL JOURNAL. 2020;8(1):366-75.
4. Gaulton A, Hersey A, Nowotka M, Bento AP, Chambers J, Mendez D, Mutowo P, Atkinson F, Bellis LJ, Cibrián-Uhalte E, Davies M. The ChEMBL database in 2017. Nucleic acids research. 2017 Jan 4;45(D1):D945-54.
5.Kim KW, Roh JK, Wee HJ, Kim C. Cancer Drug Discovery. Berlin/Heidelberg, Germany: Springer; 2016.
6. World Health Organization. The selection and use of essential medicines, 2025: WHO Model List of Essential Medicines, 24th list.
7. Waljee AK, Rogers MA, Lin P, Singal AG, Stein JD, Marks RM, Ayanian JZ, Nallamothu BK. Short term use of oral corticosteroids and related harms among adults in the United States: population based cohort study. bmj. 2017 Apr 12;357.
8. Fralish Z, Chen A, Khan S, Zhou P, Reker D. The landscape of small-molecule prodrugs. Nature Reviews Drug Discovery. 2024 May;23(5):365-80.
9. Schwiebert LA, Beck LA, Stellato C, Bickel CA, Bochner BS, Schleimer RP. Glucocorticosteroid inhibition of cytokine production: relevance to antiallergic actions. Journal of allergy and clinical immunology. 1996 Jan 1;97(1):143-52.
10. Lee SH. Mechanisms of glucocorticoid action in chronic rhinosinusitis. Allergy, Asthma & Immunology Research. 2015 Nov 1;7(6):534-7.
11. Czock D, Keller F, Rasche FM, Häussler U. Pharmacokinetics and pharmacodynamics of systemically administered glucocorticoids. Clinical pharmacokinetics. 2005 Jan;44(1):61-98.
12. Fiel SB, Vincken W. Systemic corticosteroid therapy for acute asthma exacerbations. Journal of Asthma. 2006 Jan 1;43(5):321-31.
13. Spickett G. Urticaria and angioedema. Journal of the Royal College of Physicians of Edinburgh. 2014 Mar;44(1):50-4.
14. Thrower BW. Relapse management in multiple sclerosis. The neurologist. 2009 Jan 1;15(1):1-5.
15. Lambrou GI, Vlahopoulos S, Papathanasiou C, Papanikolaou M, Karpusas M, Zoumakis E, Tzortzatou-Stathopoulou F. Prednisolone exerts late mitogenic and biphasic effects on resistant acute lymphoblastic leukemia cells: Relation to early gene expression. Leukemia research. 2009 Dec 1;33(12):1684-95.
16. Miura M, Tamame T, Naganuma T, Chinen S, Matsuoka M, Ohki H. Steroid pulse therapy for Kawasaki disease unresponsive to additional immunoglobulin therapy. Paediatrics & Child Health. 2011 Oct 1;16(8):479-84.
17. Morshed N. Comparative evaluation of prednisolone 5MG tablets marketed in Bangladesh.
18. Gera K, Gupta N, Ahuja A, Shah A. Acute alveolar sarcoidosis presenting with hypoxaemic respiratory failure. BMJ Case Reports CP. 2014 May 1;2014:bcr2013202247.
19. Vethe NT, Midtvedt K, Asberg A, Amundsen R, Bergan S. Drug interactions and immunosuppression in organ transplant recipients. Tidsskrift for den Norske laegeforening: tidsskrift for praktisk medicin, ny raekke. 2011 Oct 1;131(20):2000-3.
20. Husebye ES, Allolio B, Arlt W, Badenhoop K, Bensing S, Betterle C, Falorni A, Gan EH, Hulting AL, Kasperlik-Zaluska A, Kämpe O. Consensus statement on the diagnosis, treatment and follow-up of patients with primary adrenal insufficiency. Journal of internal medicine. 2014 Feb;275(2):104-15.
21. Cocchiarella L, Andersson GB. AMA guides® to the evaluation of permanent impairment, 2001. InAMA Guides® to the Evaluation of Permanent Impairment, Fifth Edition, 2001 2001 Jan 1. American Medical Association.
23. Brunton LL, Knollmann BC, Hilal-Dandan R, editors. Goodman & Gilman's the pharmacological basis of therapeutics. New York: McGraw-Hill Education; 2018.
24. Jenkins ND. *A survey of collegiate voice students with asthma and allergies and their perceived impact on singer health and performance experiences–A pilot study* (Doctoral dissertation, James Madison University).
25. KhushiáSandeepáKachhwaha P. VarnnaáPrashob, AnitaáSingh, andáYuvrajáSingh. Complex Ophthalmic Dosage Forms: Advances in Biomedical Applications and Future Perspectives.:161.
26. Linn YH, Aziz S, Lian MS. Topical corticosteroid and antimicrobial combinations: balancing efficacy and resistance risks: YH Linn et al. Drugs & Therapy Perspectives. 2025 Jul;41(7):306-17.
27. Arslan N, Tepe D, Taştan E, Demirci M, Caydere M, Ustun H, Oguz H. Evaluation of the effectiveness of topical ciprofloxacin and prednisolone in the prevention of myringosclerosis. European Archives of Oto-Rhino-Laryngology. 2012 Nov;269(11):2335-41.
28. Wilhelmus KR, Gee L, Hauck WW, Kurinij N, Dawson CR, Jones DB, Barron BA, Kaufman HE, Sugar J, Hyndiuk RA, Laibson PR. Herpetic eye disease study: a controlled trial of topical corticosteroids for herpes simplex stromal keratitis. Ophthalmology. 1994 Dec 1;101(12):1883-96.
29. Gayam K, Ramulu PY, Rengaraj V, Srinivasan K. Safety and efficacy of 0.1% nepafenac versus 1% prednisolone acetate eye drops after laser peripheral

iridotomy: a prospective, randomized trial. Ophthalmology Glaucoma. 2020 May 1;3(3):174-80.
30. Carey N, Franklin P, Thomas T. Oxford Handbook of Prescribing for Nurses and Allied Health Professionals. Oxford University Press; 2025 Apr 30.
31. Gonzalez-Fierro A, Romo-Pérez A, Chávez-Blanco A, Dominguez-Gomez G, Duenas-Gonzalez A. Does therapeutic repurposing in cancer meet the expectations of having drugs at a lower price. Clinical Drug Investigation. 2023 Apr;43(4):227-39.
32. Fardet L, Nazareth I, Petersen I. Long-term systemic glucocorticoid therapy and weight gain: a population-based cohort study. Rheumatology. 2021 Mar 1;60(3):1502-11.
33. Da Silva JA, Jacobs JW, Kirwan JR, Boers M, Saag KG, Inês LB, de Koning EJ, Buttgereit F, Cutolo M, Capell H, Rau R. Safety of low dose glucocorticoid treatment in rheumatoid arthritis: published evidence and prospective trial data. Annals of the rheumatic diseases. 2006 Mar 1;65(3):285-93.
34. Maličević U, Agrawal DK. Anti-inflammatory Bowel Diseases Drugs and Cardiovascular Toxicity. InCardiovascular Toxicity: Incidence, Pathogenesis and Treatment Strategies 2025 Oct 1 (pp. 253-270). Cham: Springer Nature Switzerland.
35. Remine SG, Mcilrath DC. Bowel perforation in steroid-treated patients. Annals of surgery. 1980 Oct 1;192(4):581-6.
36. Cervin A, Andersson M. Intranasal steroids and septum perforation-an overlooked complication? A description of the course of events and a discussion of the causes. Rhinology. 1998 Sep 1;36(3):128-32.
37. De Bock M, Sienaert P. Corticosteroids and mania: a systematic review. The World Journal of Biological Psychiatry. 2024 Mar 15;25(3):161-74.
38. Chieh Yao T, Wang IJ, Lun Sun H, Shiou Ou L, Hui Yu H, Wang L, Hsing Hung C. Taiwan guidelines for the diagnosis and management of pediatric atopic dermatitis: Consensus statement of the Taiwan Academy of Pediatric Allergy, Asthma and Immunology.
39. Stahn C, Löwenberg M, Hommes DW, Buttgereit F. Molecular mechanisms of glucocorticoid action and selective glucocorticoid receptor agonists. Molecular and cellular endocrinology. 2007 Sep 15;275(1-2):71-8.
40. Schijvens AM, Ter Heine R, de Wildt SN, Schreuder MF. Pharmacology and pharmacogenetics of prednisone and prednisolone in patients with nephrotic syndrome. Pediatric Nephrology. 2019 Mar;34(3):389-403.
41. Wang X, Wang H, Yin G, Zhang YD. Network-based drug repurposing for the treatment of COVID-19 patients in different clinical stages. Heliyon. 2023 Mar 1;9(3).
42. Sands BE, Leung Y, Rubin DT, Gecse KB, Panés J, Goetsch M, Wang W, Woolcott JC, Smith CC, Wosik K, Schreiber S. Etrasimod Corticosteroid-Free Efficacy, Impact of Concomitant Corticosteroids on Efficacy and Safety, and Corticosteroid-Sparing Effect in Ulcerative Colitis: Analyses of the ELEVATE UC Clinical Program. Journal of Crohn's and Colitis. 2025 Mar;19(3):jjae150.
43. Elks J, editor. The dictionary of drugs: chemical data: chemical data, structures and bibliographies. Springer; 2014 Nov 14.
44. Schweizerischer Apotheker-Verein. Index Nominum 2000: International Drug Directory. Taylor & Francis; 2000.
45. Gaballa SA, Kompella UB, Elgarhy O, Alqahtani AM, Pierscionek B, Alany RG, Abdelkader H. Corticosteroids in ophthalmology: drug delivery innovations, pharmacology, clinical applications, and future perspectives. Drug Delivery and Translational Research. 2021 Jun;11(3):866-93.
46. Oral A. uses, side effects, interactions, pictures, warnings & dosing–WebMD [Internet]. 2024
47. Liu M. Side effects of agents that influence corticotrophins, corticosteroids, and prostaglandins. InSide effects of drugs annual 2023 Jan 1 (Vol. 45, pp. 383-393). Elsevier.
48. Woolf J, Wu M. Final report for the World Anti-Doping Agency June 2025.
49. Stringer W, Bryant R. Dose uniformity of topical corticosteroid preparations: difluprednate ophthalmic emulsion 0.05% versus branded and generic prednisolone acetate ophthalmic suspension 1%. Clinical Ophthalmology. 2010 Oct 5:1119-24.
50. Mazzarino M, Piantadosi C, Comunità F, de la Torre X, Botrè F. Urinary excretion profile of prednisone and prednisolone after different administration routes. Drug Testing and Analysis. 2019 Nov;11(11-12):1601-14.
51. D'arcy PF, Griffin JP, Jenkins JS, Kirk WF, Peacock AW. Sustained-release formulation of prednisolone administered orally to man. Journal of Pharmaceutical Sciences. 1971 Jul;60(7):1028-33.
52. Mohammadi-Samani S, Bahri-Najafi R, Yousefi G. Formulation and in vitro evaluation of prednisolone buccoadhesive tablets. Il Farmaco. 2005 Apr 1;60(4):339-44.