

# IMPACT OF GELLING AGENT ON PHYSICOCHEMICAL AND Q3 PROPERTIES OF CLOBETASOL PROPIONATE

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## BACKGROUND

- Gels are widely used pharmaceutical dosage forms for topical drug delivery.
- Variations in formulation composition or manufacturing processes can influence physicochemical and structural (Q3) properties, thereby affecting therapeutic effectiveness.
- Objective:** To investigate the effects of different concentrations, sources, and grades of gelling agents on the physicochemical and Q3 properties of 0.05% clobetasol propionate topical gels.

## MATERIALS AND METHODS

- Fifteen gel formulations containing 0.05% clobetasol propionate were prepared by varying the concentration, type, and grade of gelling agents, while keeping other excipients constant (**Table 1, Figure 1**).

Ingredients	Function	Carbopol 934 gels	HPMC-K4M (Pharmaceutical grade) gels	Gel A	Gel B	HPMC-K4M (Cosmetic grade) gels
Clobetasol propionate	API	0.05	0.05	0.05	0.05	0.05
Carbopol 934	Gelling agent	0.5 (Ref, +/-10% w/w)	---	0.25 (Ref, +/-10% w/w)	0.5 (Ref, +/-10% w/w)	---
HPMC-K4M	Gelling agent	---	0.5 (Ref, +/-10% w/w)	0.25 (Ref, +/-10% w/w)	0.5 (Ref, +/-10% w/w)	0.5 (Ref, +/-10% w/w)
Propylene glycol	Solvent	15	15	15	15	15
Ethanol	Co-solvent	40	40	40	40	40
Propylparaben	Preservative	0.60	0.60	0.60	0.60	0.60
Methylparaben	Preservative	0.30	0.30	0.30	0.30	0.30
Triethanolamine (99%)	Neutralizing agent	QS to pH 7	QS to pH 7	QS to pH 7	QS to pH 7	QS to pH 7
Deionized water	Vehicle	QS to 100 % w/w	QS to 100 % w/w	QS to 100 % w/w	QS to 100 % w/w	QS to 100 % w/w

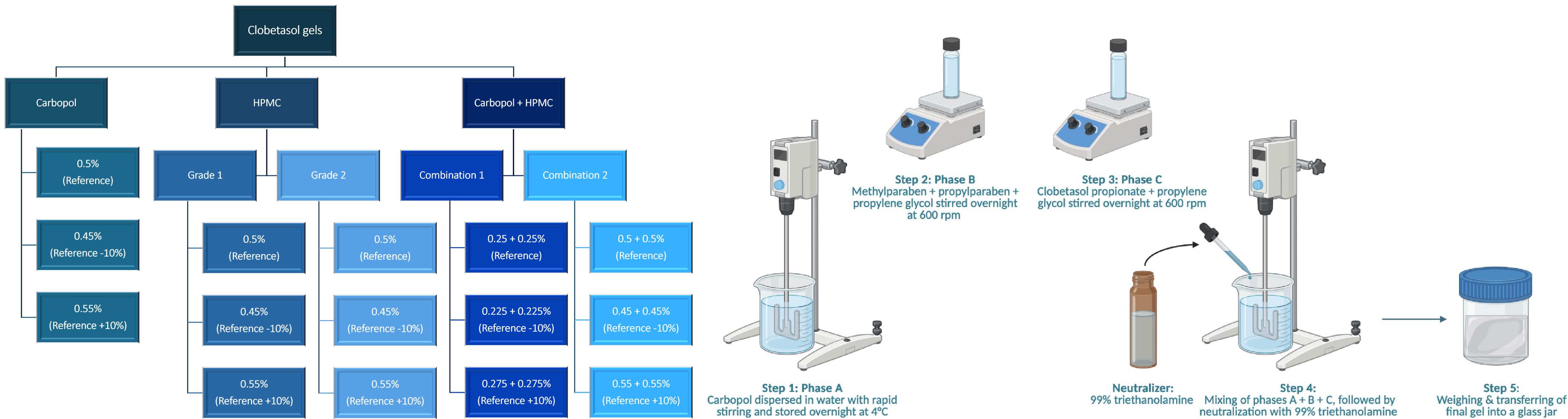
**Table 1. Formulas for gels containing 0.05% clobetasol propionate [1]**

- Each gelling system included a reference formulation with 0.25% or 0.5% w/w gelling agent(s), along with two variations containing  $\pm 10\%$  of the reference concentration.
- Gels were prepared following the process illustrated in **Figure 2**.
- All formulations were evaluated in triplicate for physicochemical and Q3 properties.

## RESULTS AND DISCUSSION

- All gels displayed comparable appearance, pH, and water activity (**Table 2**).
- Microscopy confirmed absence of particulate matter in all gels, indicating that the drug was fully dissolved (**Figure 3**).
- Drug content was within acceptable limits (90–110%) for most formulations, except cosmetic-grade HPMC-K4M gels.
- HPMC-K4M gels: slightly higher pH.
- Significant differences in viscosities observed across the gels containing different types of gelling agents/ systems.

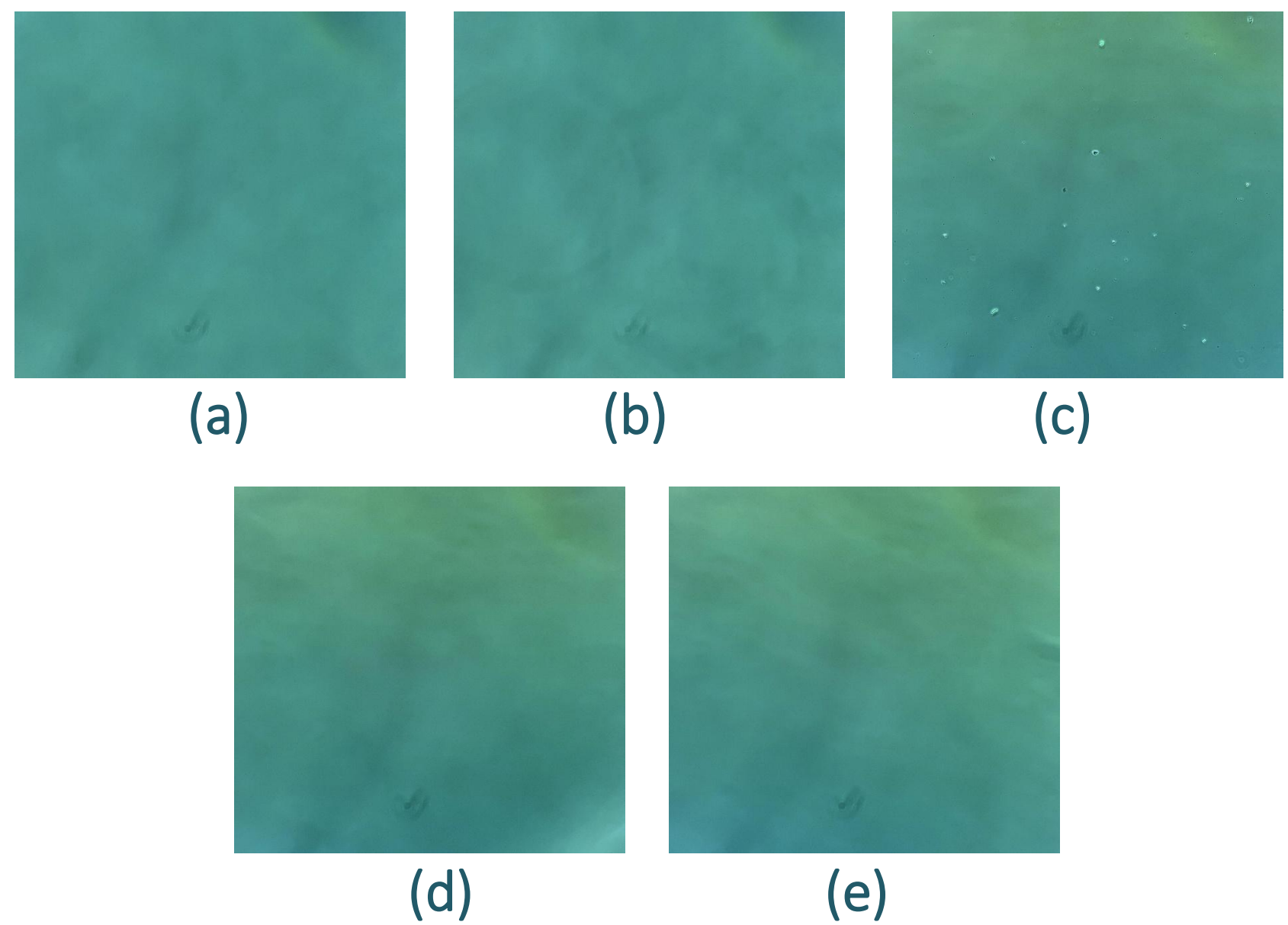
## GRAPHICAL ABSTRACT



**Figure 1. Flow chart outlining the formulation design strategy**

**Figure 2. Schematic representation of gel manufacturing process**

## RESULTS (CONTINUED)



**Figure 3. Representative micrographs for reference gels (a) Carbopol 934 gel, (b) HPMC-K4M (pharmaceutical grade) gel, (c) HPMC-K4M (cosmetic grade) gel, (d) Gel A, and (e) Gel B (200x magnification)**

## RESULTS (CONTINUED)

Gel Type	Visual appearance	Microscopy	Odor	pH	Water activity	Drug Content (%)
<b>1- 0.5% Carbopol 934 gels</b>						
Reference	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.84 $\pm$ 0.05	0.7867 $\pm$ 0.0002	94.84 $\pm$ 0.45
Reference +10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.80 $\pm$ 0.01	0.7904 $\pm$ 0.0016	99.95 $\pm$ 0.88
Reference -10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.82 $\pm$ 0.02	0.7917 $\pm$ 0.0002	90.18 $\pm$ 1.26
<b>2- 0.5% HPMC -K4M (Pharmaceutical grade) gels</b>						
Reference	Clear, colorless	Free from particulate matter	Chemical/ethanolic	7.30 $\pm$ 0.01	0.7855 $\pm$ 0.0004	92.66 $\pm$ 0.4
Reference+10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	7.66 $\pm$ 0.01	0.7858 $\pm$ 0.0013	90.26 $\pm$ 0.01
Reference -10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	7.24 $\pm$ 0.01	0.7893 $\pm$ 0.0033	89.01 $\pm$ 0.25
<b>3-Gel A (0.25% Carbopol 934 + 0.25% HPMC -K4M (Pharmaceutical grade))</b>						
Reference	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.88 $\pm$ 0.02	0.7896 $\pm$ 0.0002	90.03 $\pm$ 2.09
Reference+10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.91 $\pm$ 0.02	0.7892 $\pm$ 0.0061	95.21 $\pm$ 0.21
Reference -10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.82 $\pm$ 0.02	0.7951 $\pm$ 0.0018	90.25 $\pm$ 2.24
<b>4-Gel B (0.5% Carbopol 934 + 0.5% HPMC -K4M (Pharmaceutical grade))</b>						
Reference	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.81 $\pm$ 0.02	0.7967 $\pm$ 0.0002	106.24 $\pm$ 2.27
Reference +10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.81 $\pm$ 0.02	0.7876 $\pm$ 0.0005	106.55 $\pm$ 0.29
Reference -10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.83 $\pm$ 0.03	0.7857 $\pm$ 0.0006	90.25 $\pm$ 2.24
<b>5- 0.5% HPMC -K4M (Cosmetic grade) gels</b>						
Reference	Clear, colorless	Free from particulate matter	Chemical/ethanolic	7.20 $\pm$ 0.03	0.7863 $\pm$ 0.0013	78.33 $\pm$ 14.98
Reference+10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	6.94 $\pm$ 0.02	0.7876 $\pm$ 0.0013	89.44 $\pm$ 0.08
Reference -10%	Clear, colorless	Free from particulate matter	Chemical/ethanolic	7.22 $\pm$ 0.02	0.7886 $\pm$ 0.0008	86.07 $\pm$ 0.80

**Table 2. Physicochemical and structural (Q3) properties of resultant gels containing 0.05% clobetasol propionate (data are presented as Mean  $\pm$  SD, n=3)**

## RESULTS AND DISCUSSION (CONTINUED)

- Gels containing pharmaceutical or cosmetic grades of HPMC-K4M alone exhibited low viscosity  $\rightarrow$  pourable and unsuitable for use as sole gelling agents.
- Carbopol 934 gels  $\rightarrow$  higher viscosity.
- Carbopol 934 + pharmaceutical grade HPMC-K4M (1:1 ratio)  $\rightarrow$  gels with desirable viscosity and favorable physicochemical and Q3 characteristics.

## CONCLUSION AND FUTURE DIRECTION

- The type and concentration of gelling agents markedly influenced the physicochemical and Q3 properties of topical gels.
- Gels containing Carbopol 934 and pharmaceutical-grade HPMC-K4M (1:1 ratio) demonstrated optimal physicochemical and Q3 characteristics.
- Future work includes:
  - Performance testing:** In vitro release testing (IVRT), in vitro permeation testing (IVPT).
  - Stability testing:** Monitoring of physicochemical and Q3 properties.

## REFERENCES

- Verma AS, Singh SU, Kaur R, Jain UK. Formulation and evaluation of clobetasol propionate gel. Asian J Pharm Clin Res. 2013;6(5):15-8.

## ACKNOWLEDGEMENTS

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