IMPACT OF QUANTITATIVE DIFFERENCES IN CARBOMER ON DRUG RELEASE FROM DICLOFENAC SODIUM TOPICAL GELS

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BACKGROUND

- Differences in the formulation composition and/or the manufacturing process may influence the physicochemical and structural (Q3) properties, and thereby, the performance of topical products.
- Our aim was to assess the impact of quantitative differences in carbomer on a topical gel's Q3 properties and performance such as in vitro drug release (IVRT).

METHODS AND MATERIALS

- Gels containing 0.5% w/w diclofenac sodium were manufactured by varying the amount of gelling agent, carbomer homopolymer type C (Carbopol® 980) using the procedure depicted in **Figure 1**.
- The reference formulation contained 0.5% w/w carbomer **(Table 1)**, whereas the modified formulations contained 0.55% w/w (reference+10%), 0.45% w/w (reference-10%), 0.625% w/w (reference+25%) and 0.375% w/w (reference-25%) of carbomer.

Ingredients	Quantity (%w/w)
Diclofenac sodium	0.5
Carbopol® 980	0.5
Propylene Glycol	15
Methylparaben	0.1
Propylparaben	0.03
Sodium Hydroxide 18% w/v	Q. S to pH 7.3-7.5
Water	Q. S 100% w/w

Table 1. Formulation composition of diclofenac sodium gel, 0.5% w/w (reference formulation)

- The Q3 properties including visual appearance, microscopic images, pH, water activity and viscosity of the gels were evaluated.
- IVRT studies were performed using vertical diffusion cells **(Figure 2)**. The ratios of release rates (T/R ratios) were calculated and compared for the five gels using the recommendations within USP <1724>.[1]

REFERENCES

1. United States Pharmacopeia (2023). General Chapter <1724> Semisolid Drug Products—Performance Tests. USP-NF. Rockville, MD: United States Pharmacopeia.

ACKNOWLEDGEMENTS

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GRAPHICAL ABSTRACT

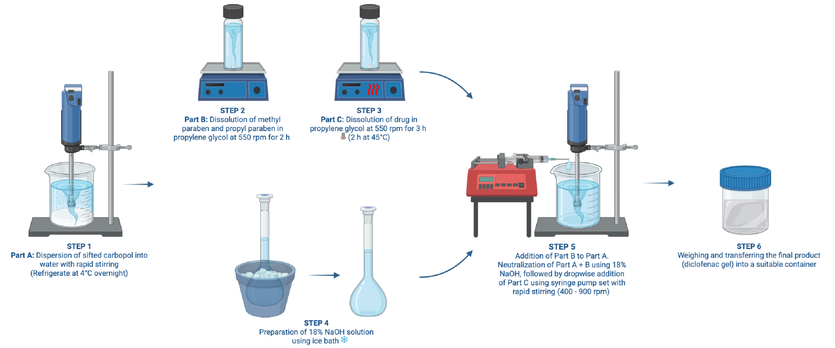


Figure 1. Schematic representation of the manufacturing process for diclofenac sodium gels

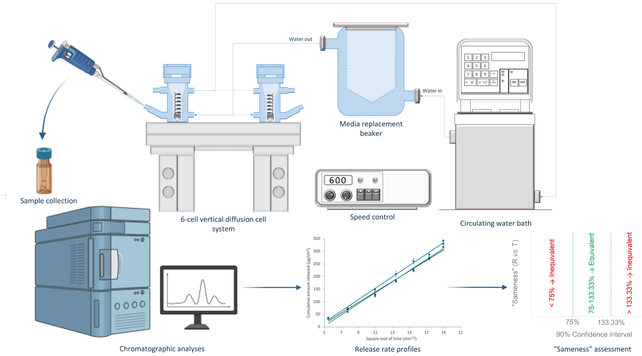


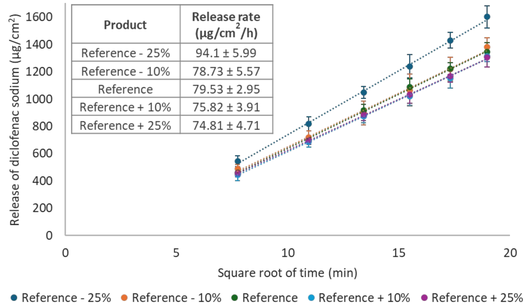
Figure 2. Schematic representation of the IVRT methodology

RESULTS

	Reference	Reference + 10%	Reference - 10%	Reference + 25%	Reference - 25%
pH	7.50 ± 0.01	7.31 ± 0.02	7.37 ± 0.03	7.55 ± 0.03	7.49 ± 0.01
Water activity readings					
25°C	0.9613 ± 0.0003	0.9607 ± 0.0012	0.9568 ± 0.0003	0.9628 ± 0.0010	0.9721 ± 0.0002
32°C	0.9552 ± 0.0010	0.9536 ± 0.0002	0.9553 ± 0.0023	0.9535 ± 0.0006	0.9618 ± 0.0018
Visual description					
Color	Colorless	Colorless	Colorless	Colorless	Colorless
Clear/ opaque	Clear	Clear	Clear	Clear	Clear
Texture	Smooth	Smooth	Smooth	Smooth	Smooth
Odor	Chemical odor	Chemical odor	Chemical odor	Chemical odor	Chemical odor
Particulate matter	None	None	None	None	None
Air bubbles	Very few on Day 1 None by Day 10	Very few on Day 1 None by Day 10	Very few on Day 1 None by Day 10	Very few on Day 1 None by Day 10	Very few on Day 1 None by Day 10
Microscopy					
Phase states	Single	Single	Single	Single	Single
Undissolved API	None	None	None	None	None
Drug content (%)	98.44 ± 2.49	97.7 ± 0.92	95.84 ± 0.90	98.81 ± 2.04	102.75 ± 1.36
Zero-shear viscosity (Pa.s)	2636.33 ± 413.49	3605 ± 509.82	1874 ± 100.04	4257.33 ± 620.52	901.33 ± 151.67

Table 2. Q3 properties of diclofenac sodium gels containing variable amount of Carbopol 980 (data are presented as Mean ± SD, n=3)

- Appearance, pH, and water activity → similar across all five gels **(Table 2)**.
- Microscopic images showed that drug was fully dissolved **(Table 2**; images not included**)**.
- Viscosity increased with the increase in carbomer concentration **(Table 2)**.
- The gel containing 0.375% w/w (reference-25%) carbomer appeared to have a higher release rate compared to other gels **(Figure 3)**, however, the 90% confident intervals (CI) were within the limits of 75-133.33% **(Table 3)**, indicating that there were no statistical differences in the diclofenac sodium release rates for the modified gels compared to the reference gel.



Product	Release rate (µg/cm²/h)
Reference - 25%	94.1 ± 5.99
Reference - 10%	78.73 ± 5.57
Reference	79.53 ± 2.95
Reference + 10%	75.82 ± 3.91
Reference + 25%	74.81 ± 4.71

Figure 3. IVRT profiles of diclofenac sodium gels (data are presented as Mean ± SD, n = 6)

Comparison	90% Confidence Interval	
	Lower Limit	Upper Limit
Reference vs Reference - 25%	111.69	126.47
Reference vs Reference - 10%	92.43	105.88
Reference vs Reference + 10%	91.09	100.73
Reference vs Reference + 25%	88.33	99.78

Table 3. Comparison of release rates across the 4 gels (T) vs. the reference gel (R)

CONCLUSION

- All five gels exhibited similar Q3 properties except viscosity; they also had similar drug release.
- Altering the quantitative amount of carbomer (i.e., to the extent of 25% difference compared to the reference gel), does not significantly affect the drug release across the diclofenac sodium gels evaluated in this study.